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EURASIAN MEDICAL EDUCATION PROGRAM OF THE AMERICAN COLLEGE OF PHYSICIANS

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Final Report

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Addenda

EXECUTIVE SUMMARY

The Eurasian Medical Education Program (EMEP) is a partnership between the Institute for Health Policy Analysis and the American College of Physicians (ACP). It provides continuing medical education (CME) for Russian physicians. It is designed to assist Russian physicians in managing diseases with high mortality and morbidity. The program has been functioning since 1998; there have been more than 35 programs which have involved 5500 Russian physicians. The program has been focused primarily on hypertension and cardiovascular disease, diabetes, and tuberculosis. The emphasis has been on disease recognition and management, continuity of care, prevention of complications, and management of acute and chronic complications. These diseases are responsible for almost 60 percent of all deaths in the Russian Federation.

The CME programs were developed in close collaboration with our Russian colleagues, who are responsible for CME in each of the five locations in which EMEP has functioned. The four locations are Ekaterinburg, Kazan, Tula, and Khabarovsk and the Jewish Autonomous Republic in the Russian Far East. The EMEP programs are fully integrated into the CME programs already in existence in each of these sites.

Visiting professors are recruited from the membership of the ACP and consist of persons who are both highly experienced in CME and focused specifically on an aspect of the EMEP program. These physicians volunteer their time and expertise. Some have visited the same location in Russia several times, thus achieving continuity of educational experience. These physicians have contributed more than 250 days of expertise and participation in Russia, an in-kind contribution conservatively estimated at a value of more than $250,000.

Three distinct audiences attend the programs: primary care doctors from the polyclinics, specialists from the hospitals, and academic faculty members. The program is designed using principles of CME developed by the ACP. There are lectures, small group discussions, case presentations, and visits to polyclinics to see patients. Programs for the academic faculty are in the model of "train the trainers" and slides and handouts, translated into Russian, are given to them for their subsequent use in their own lectures. It is estimated that about four times as many Russian physicians receive information than actually attend the EMEP lectures.

The basic EMEP program consists of a series of three programs: the first series of lectures deals primarily with early detection and management of disease. This phase emphasizes patient compliance with medications, lifestyle modification by patients, and continuity of care. The second series of lectures deals with complications of hypertension, diabetes, or tuberculosis, and emphasizes prevention, recognition, and management of these complications. The third phase includes data collection, analysis, and modification of the program based on results. In addition, there is discussion concerning the public education and awareness of the importance of disease prevention, compliance with medication, and lifestyle modification by patients. In all the programs, evidence-based information is provided.

In each of the locations in which EMEP functions data collection has been carried out and reports of the results of the six programs are a part of this report. In two locations hypertension "schools" have been developed in which patients are instructed in the importance of lifestyle

modification and compliance. In two locations data are being collected regarding the management of patients with diabetes with particular emphasis on prevention of complications. Tuberculosis data has been collected, with particular emphasis on compliance with medications and DOTS treatment.

In each of the locations there is EMEP collaboration with government officials, university and academic officials, and those responsible for clinical care of patients. This has required frequent meetings with representatives from the government, academic institution, and polyclinic or hospital. In each location, EMEP has a full-time medical program coordinator, two of whom have faculty appointments in their medical academies. These colleagues are of great value in the development of an infrastructure to facilitate EMEP activities. Each is respected by their Russian colleagues and has been an important contributor to EMEP's success.

There have been eight visits of delegations of Russian physicians to the United States, each for a specific purpose. These have ranged from study of CME systems to laboratory detection and drug treatment of tuberculosis. These visits have resulted in dramatic changes in the management of tuberculosis. The knowledge acquired by the Russian professors has been communicated to more than 1000 additional physicians and treatment models are changing from in-patient care of TB to outpatient, monitored, treatment of patients (DOTS). The EMEP tuberculosis program has included participation with the National Jewish Hospital in Denver, Johns Hopkins University in Baltimore, and the National TB Center in Newark. In each of these locations Russian TB doctors have visited formal programs regarding early detection, management, treatment of drug-resistant TB, and training for laboratory personnel. The latter visit lasted one month.

The experience that EMEP has garnered during the 35 programs has included an understanding and respect for the Russian medical system, and our ability to work within its structure. One example of this has been the appointment of Drs. Farmer and Burger as Professors in the Kazan State Medical Academy. As a result, working models for CME and for collaboration with Russian colleagues have been developed.

The primary commodity of EMEP is knowledge, and the basic concept of EMEP is the management of serious disease (including public education and awareness, early detection, and prevention of complications).

SUMMARY

5 Years in Russia: 1998-2003
Kazan, Ekaterinburg, Khabarovsk, Tula, Birobijan

Continuing Medical Education (CME)

- *Lectures* – 35 programs involving 5,500 Russian doctors
- *Train-the-Trainers* – slides, handouts and lectures by Russian professors, using Eurasian Medical Education Program (EMEP) information, to more than 1,500 Russian physicians in each location each year during their CME programs
- *Polyclinic Visits* – direct patient contact, data collection programs, 7 locations
- *Visiting Professors* – 22 members of the American College of Physicians

Program Emphasis

- Prevention, early detection, management, prevention of complications, continuity of care of diseases that can cause premature death
- Cardiovascular disease, diabetes, tuberculosis
- Women's health, public health, public education

Tuberculosis

- 8 visits of Russian physicians to the United States for training in DOTS and laboratory procedures – formal programs in Newark, Baltimore and Denver
- As a result of EMEP, DOTS officially established in Sverdlovsk by government decree
- Laboratory procedures based on culture and sensitivity developed
- Sverdlovsk Oblast – more than 1,500 Russian doctors trained in DOTS using EMEP materials
- Collaboration developed between prison and civilian tuberculosis treatment programs

Data Collection: Cardiovascular Disease and Diabetes

- *Cardiovascular*: 3 programs over 3 years, involving more than 750 patients
  - Significant increase in compliance with medication
  - Significant improvement in blood pressure control
  - Decrease in sick leave and disability
  - Great decrease in hospitalization
  - Improvement in lifestyle (exercise, diet)
  - Some decrease in smoking
- *Diabetes*: 2 programs over 3 years, involving 10,000 patients
  - Dramatic decrease in ketoacidosis
  - Significant decrease in hospitalization
  - Improvement in chronic diabetic foot conditions
  - Dramatic decrease in mortality
  - Improvement in patient compliance with medications, diet and lifestyle

CURRICULUM DEVELOPMENT

EMEP has taken very seriously our relationships and obligations to our Russian colleagues: all programs are developed with their full cooperation and agreement. After the original curriculum material were developed (attached to the Work Plan submitted last year), suggestions and modifications have taken place. Additional aspects of cardiovascular disease (atrial fibrillation, congestive heart failure, hyperlipidemia) have been subjects requested and presented. Complications of diabetes and multi-drug resistant tuberculosis were also discussed.

Additional subjects have been added at the request of our Russian colleagues: digestive disease, hepatitis, infectious diseases, rheumatology, osteoporosis, women's health issues, public health, preventive medicine, and social service subjects have been developed and presented. Thus EMEP has been able to expand its activities and respond to wishes and needs of our Russian colleagues.

Speakers are then chosen from ACP members who are experienced clinicians and teachers and have an interest in partnership. The visiting professors are almost all full professors and many have been presidents of national medical organizations (American Diabetes Association, New York Academy of Science, American College of Gastroenterology and the ACP).

Each speaker prepares slides and handout material, reviewed by the EMEP medical director, and translated into Russian. Handouts are given to each audience member and a set of slides is given to the Russian Medical Academy sponsor for subsequent use. Each program is then reviewed by our Russian colleagues and the exact timing of the lectures is determined by the EMEP medical director and our Russian coordinator.

Following each lecture there are questions from audience members; with frequent visits by EMEP, there is no longer hesitation about asking questions and making comments.

The original concept was for CME lectures, but the format has been altered to include visits to polyclinics on each visit. This has enabled the ACP visiting professors to interact with "front line" physicians, who often discuss cases seen that day. We have been able to visit hypertension and diabetes "schools" and see how patients are instructed in their care and lifestyle modification. These visits have greatly facilitated the data collection process.

PROGRAM DEVELOPMENT

The Eurasian Medical Education Program (EMEP), in partnership with physicians affiliated with the American College of Physicians (ACP) has developed continuing medical education (CME) programs in five locations in Russia during the past four years. There have been 35 programs in Russia, involving 5,500 Russian physicians. There have been 22 American visiting professors that have participated. CME is the initial entry point, and serves as a vehicle for much involvement of EMEP.

A. Location Selection
   1. Interest by local government and physicians (Ministry of Health)
   2. Relationship with government officials, academic physicians (Medical Academy) and clinicians, especially polyclinic doctors
   3. Ability to have forum for CME, preferably through an academic medical university or academy
   4. Ability to participate in ongoing CME programs for practicing physicians

B. Assessment of Problem (Epidemiology)
   1. Frequency of disease
   2. Current detection and awareness of public
   3. Management of medical problems, currently
   4. Availability of drugs (and cost)

C. Selection of Subjects to be Covered in CME Programs
   1. Collaboration with Russian physicians responsible for CME (which is mandatory for all Russian physicians who care for patients)
   2. Integration of EMEP into Russian CME programs – official part of CME with agreement by local Ministry and Medical Academy
   3. Subjects chosen represent diseases:
      - Which are frequent in Russia
      - Which cause significant illness, morbidity, disability, economic loss, and death
      - Which can be treated with medications and do not require "high-tech" intervention
      - Which can mainly be treated on an out-patient basis
      - Goals include: public awareness, prevention, early detection, management, prevention of complications
   4. EMEP programs expanded based on need and wishes of Russian colleagues

D. Selection of ACP visiting professor (s)
   1. Experience, education, clinician, and clinical researcher
   2. Each visiting professor donates his/her time and expertise – each lecture in the US would command an (average) honorarium of $1500. This represents a valuable in-kind contribution to EMEP and Russian physicians.

E. Curriculum Development
   1. Literature search, evidence-based information collected
   2. Up-grading in curriculum material from previous trips

3. Syllabus material prepared by ACP visiting professor and submitted to EMEP medical director
4. Development of slides by visiting professor and submission to EMEP Medical Director
5. Selection by Medical Director of slides to be translated into Russian (English language slides such as graphs and illustrations also used)
6. Translation into Russian – usually about 20 slides per program
7. Preparation of two sets of slides, one to leave with Russian colleagues

F. Initial Approach
1. Collaboration with local government, academic and clinical Physicians
2. Public awareness programs for disease, being discussed – prevalence, significance, lifestyle factors
3. Mechanisms for screening of patients for detection of hypertension, cardiovascular disease and diabetes
4. Cooperation with business interests (e.g. factories, workplaces) and service organizations (e.g. Rotary) to facilitate public awareness and education, as well as screening of people for cardiovascular and diabetes risk factors
5. Referral system to polyclinics for management and follow-up

G. Development of CME Programs for Physicians
1. Lectures during CME programs – audiences of 50-150 Russian physicians
2. Visits to polyclinics; work directly with physicians and patients, especially regarding dose management – audiences of 10-20 physicians
3. Lectures to hospital physicians who treat complications of diseases covered by CME programs
4. Small group sessions for those who lecture in CME programs ("train-the-trainer") – groups of 10-12 academic physicians
5. Slides, translated into Russian and a copy given to Russian lecturers

H. Assessment and Evaluation of CME programs and visits
1. Quantification of audience; recording of attendance and professional activities – about 75% of attendees have been polyclinic (primary care) physicians
2. Development (and validation by academic experts at Boston University) of an instrument to assess audience response to CME programs
3. Distribution and collection of evaluation instrument; quantification of results and use in development of future programs
4. Discussion with Ministry and Academy physician regarding future EMEP activities and development of additional programs

I. Development of Additional Programs
1. Family Medicine in Khabarovsk
- Academic program and polyclinic supported by Far East Medical University
- Direct CME programs in polyclinic
- Assistance to family physicians in detection and management of hypertension
- CME programs for other family medicine

2. Women's Health in Kazan
    - CME program (their request)
    - Organization of women's health program
    - Organization of social services and social work program
3. Gastroenterology CME programs lectures Ekaterinburg, Kazan, Khabarovsk, pediatric gastroenterology in Khabarovsk and Birobijan
4. Infectious disease CME in Ekaterinburg
5. Rheumatology CME in Kazan

J. Organization of Disease Management Programs for Hypertension and Diabetes
1. Polyclinics
2. Specialty clinics
3. Hospitals (mainly for complications)

K. Continuity of Care for Patients
1. Team approach, so patients return to same group of physicians
2. Emphasis on follow-up, compliance with medications, lifestyle modifications ("secondary prevention" of complications)
3. Development of "hypertension schools" for patient training and education (diet, exercise, smoking, alcohol, cholesterol, diabetes)

L. Data Collection (see attached)
1. Recording and updating patient data
2. Tracking progress against targets
3. Medication use / compliance
4. Complications

M. Quality Assessment of Data
1. Review of methodology of data collection
2. Review of oversight of data (supervisor)
3. Data review by EMEP medical director and US consultant (ACP)

N. Public Education – Formal and Informal
1. Media involvement
2. Health Fairs
3. Literature in layman language
4. Schools regarding smoking, exercise, diet

O. US Visiting Professors
1. ACP physician visits 3-5 times a year
2. Russian physician visits to US

MONITORING & EVALUATION

Assessment of the effectiveness of CME has been a problem for many years; it is generally accepted that some type of reinforcement is needed to ensure long-term effectiveness. Handout material that audience members can "take home" can be effective if "practical" information is included. Thus, outlined diagnostic and management algorithms have been extensively used – particularly in an evidence-based medicine format. (The ACP is the largest single CME organization in the United States, dating from 1915, and has had extensive experience in assessing effectiveness of CME. The ACP director of CME, the late Herbert Waxman, was especially helpful until his recent untimely death.)

Mechanisms to assess the effectiveness of the speaker's presentation of the subject, as analyzed by audience members, has also been an important evaluation mechanism. An evaluation investment was designed by the medical director and validated at Boston University; it has been used since the inception of EMEP.

The most important, but most difficult to assess, evaluation of CME effectiveness is how it translates to direct patient care. Since the primary subjects were management of diabetes, hypertension and tuberculosis, it was determined that data collection should be done to demonstrate effectiveness of EMEP activities. As noted, the initial lecture series consisted of three sets of lectures: recognition and diagnosis, basic management, management of complications. Thus all data collection was performed AFTER the three lectures in each subject. As a major goal was to improve effectiveness of management and decrease complications, a decrease in hospitalization was a significant measure. Therefore, data collection was focused on polyclinics rather than hospitals. There have been six data collection programs that have one-to-three year follow-ups and have been continuously carried out. Each of these is polyclinic based, data are collected by physicians actively involved in patient care. They are supervised by a senior physician, generally an academic professor, and closely monitored by the EMEP coordinator. Another person is responsible for record keeping and data storage. All data are reviewed each quarter and reports have been presented each 6 month period since inception of the data collection. As can be seen in the data collected for this report, there has been significant "behavior modification" of physicians caring for patients – and it demonstrates the value of CME.

While there were registries of patients with diabetes and tuberculosis, the programs of data collection have accomplished far more than registries require. There is substantial clinical and scientific validity to these programs. The hypertension data collection activities were not required, however, and have been developed and expanded by EMEP. These are truly unique programs.

Eurasian Medical Education Program

Results Framework - Work Plan

Strategic Objective

Management of conditions that are the leading causes of death and disability in the Russian Federation (cardiovascular disease, diabetes, tuberculosis) improved

Indicators:

1a. Number of cases of diabetic patients with diabetic foot in 2 selected sites
1b. Number of cases of diabetic patients with ketoacidosis requiring hospitalization in 2 selected sites
2. Percentage of hypertension patients with controlled blood pressure (below 140/90)
3. Number of patients completing continuous TB treatment, i.e. the DOTS protocol, in one oblast

Intermediate Result 1

Physician practice related to diagnosis and treatment of diabetes improved

Indicators:

1.1 Percent of diabetic patients complying with prescribed diet & medications in 2 selected sites
1.2 Number of diabetic patients hospitalized from 2 selected sites

Intermediate Result 2

Physician practice related to diagnosis and treatment of cardiovascular disease improved

Indicators:

2.1 Percentage of hypertension patients compliant with medication regime in 3 selected sites
2.2 Number of hospital admissions for hypertension patients with acute episode in 3 selected sites

Intermediate Result 3

Medical practice related to TB diagnosis and treatment improved

Indicators:

3.1 Number of doctors trained in TB standardized protocol (i.e. DOTS) in 3 sites
3.2 Number of patients initiating standardized DOTS treatment in 1 site

Sub - Intermediate Results

1a Evidence-based curriculum in diabetes management integrated into required Russian language CME in 2 oblasts
1b Evidence-based treatment of diabetes disease adopted in 2 sites
1c Patient education materials developed and disseminated

Sub - Intermediate Results

2a Evidence-based curriculum in cardiovascular management integrated into required Russian language CME in 3 oblasts
2b Evidence-based treatment of cardiovascular disease adopted by practicing physicians
2c Patient education materials developed and disseminated

Sub - Intermediate Results

3a Evidence-based curriculum in TB management integrated into required Russian language CME in 3 oblasts
3b Policy change requiring evidence-based treatment of TB adopted
3c Patient education materials developed and disseminated
3d Modern lab procedures for TB diagnosis & treatment documented in Russian manuals & disseminated

Eurasian Medical Education Program

Results Framework - Final Report

Strategic Objective

Management of conditions that are the leading causes of death and disability in the Russian Federation (cardiovascular disease, diabetes, tuberculosis) improved

Indicators:

1a. Kazan - 5%; Khabarovsk - 802 to 195
1b. Kazan - none; Khabarovsk - 16 to none
2. Blood pressure control up to 37-76% in 3 sites
3. DOTS completion up to 652 in 2002

Intermediate Result 1

Physician practice related to diagnosis and treatment of diabetes improved

Indicators:

1.1 Compliance up to 62% and up from 36 to 180 patients in Kazan and Khabarovsk

1.2 Hospitalized down to 37% from 94% and to 33% from 66% in Kazan Down from 230 to 100 in Khabarovsk

Sub - Intermediate Results

1a Evidence-based curriculum introduced
1b Evidence-based treatment of diabetes
1c Patient education materials developed and disseminated

Intermediate Result 2

Physician practice related to diagnosis and treatment of cardiovascular disease improved

Indicators:

2.1 Compliance from 0-10% to 35-93%

2.2 Hospital admissions - 11 patients in each of 2 sites and 2% in 3rd site

Sub - Intermediate Results

2a Evidence-based curriculum integrated
2b Evidence-based treatment of cardiovascular disease adopted 2c Patient education materials developed and disseminated

Intermediate Result 3

Medical practice related to TB diagnosis and treatment improved

Indicators:

3.1 Doctors trained in DOTS - 460

3.2 Initiated DOTS treatment - 1,289 in 2002

Sub - Intermediate Results

3a Evidence-based TB management
3b Policy change accomplished
3c Patient education materials developed and disseminated
3d Modern lab procedures for TB diagnosis & treatment developed & disseminated

MONITORING & EVALUATION

RESULTS FRAMEWORK

Hypertension:

1. Percentage with controlled blood pressure
   - Khabarovsk from none to 76%
   - Ekaterinburg from 9% to 51%
   - Kazan from none to 48%

2. Percentage of patients compliant with medications
   - Khabarovsk from none to 78%
   - Ekaterinburg from 10% to 67%
   - Kazan from 10% to 95%

3. Number of hospital admissions for acute episode
   - Khabarovsk 11 patients (9 months)
   - Ekaterinburg from 18 to 11 patients (2 years)
   - Kazan 2% (3 years)

4. Evidence-based curriculum integrated into CME programs and polyclinics

5. Evidence-based treatment adopted

6. Patient education materials developed and disseminated

MONITORING & EVALUATION

RESULTS FRAMEWORK

Tuberculosis - Ekaterinburg:

1. Number of patients completing continuous TB treatment – DOTS protocol
   2000 – 408
   2001 – 546
   2002 – 652
   2003 – 459

2. Number of doctors trained in DOTS – 460

3. Number of patients beginning DOTS treatment
   2000 – 987
   2001 – 1000
   2002 – 1289
   2003 – 1056

4. Evidence-based curriculum in TB integrated fully since 2000

5. Policy change requiring evidence-based treatment of TB – officially by Sverdlovsk Oblast government since 2001

6. Patient education materials developed and disseminated

7. Modern lab procedures for TB documented and disseminated since 2002

MONITORING & EVALUATION

RESULTS FRAMEWORK

Diabetes:

1. Percent of diabetic patients complying with prescribed diet and medications:
   Kazan: Adults – 33 to 62% control
   39 to 52% diet
   Khabarovsk: 36 patients to 180 patients

2. Number of diabetic patients hospitalized:
   Kazan: 94% to 37% children
   66% to 33% adults
   Khabarovsk: 230 patients to 100 patients

3. Number of patients with diabetic foot
   Kazan: 6% to 5% adults
   none – children
   Khabarovsk: 802 patients to 195

4. Number of patients with ketoacidosis
   Kazan: 1% to zero adults
   none – children
   Khabarovsk: 16 patients to none

5. Evidence-based curriculum integrated in both Kazan and Khabarovsk

6. Evidence-based treatment adopted

7. Patient education materials disseminated

EURASIAN MEDICAL EDUCATION PROGRAM

PERFORMANCE DATA TABLE

SO or IR	Results Statement	Indicator	Unit of Measure	Disaggregation	Baseline Year	Baseline Value	2001 Target	2001 Actual	2002 Target	2002 Actual	2003 Target	2003 Actual
SO	Management of conditions that are the leading causes of death and disability in the Russian Federation (cardio disease, diabetes, tuberculosis) improved.	(1a) # cases of diabetic patients with diabetic foot in 2 selected sites.	Sites 1&2: # cases in designated cohort Site 3: # Diabetic patients in cohort with diabetic foot divided by # registered diabetic patients in cohort		2000	Site 1: 802 Site 2: 6%		Site 1: 698 Site 2: 7%			Site 1: 615 Site 2: 6%	Site 1: 195 Site 2: 5%
		(1b) # cases of diabetic patients with ketoacidosis requiring hospitalization in 2 selected sites.	Sites 1&2: # cases in designated cohort whose cause of hospital admission is ketoacidosis			Site 1: 1 Site 2: 68		Site 1: 1 Site 2: 24			Site 1: 0 Site 2: 18	Site 1: 0 Site 2: 14
		(2) % cases of hypertension patients with controlled blood pressure (below 140/90).	# of hypertension patients in cohort with blood pressure below 140/90 divided by # hypertension patients in cohort		2002 2000 2000	Site 1: 0 Site 2: 9% Site 3: 20%		Site 2: 56% Site 3: 45%			Site 1: 60% Site 2: 60% Site 3: 50%	Site 1: 76% Site 2: 67% Site 3: 48%

SO or IR	Results Statement	Indicator	Unit of Measure	Disaggregation	Baseline Year	Baseline Value	2001 Target	2001 Actual	2002 Target	2002 Actual	2003 Target	2003 Actual
SO	Management of conditions that are the leading causes of death and disability in the Russian Federation (cardio disease, diabetes, tuberculosis). improved.	(3) # patients completing continuous TB treatment (i.e., DOTS protocol) in one oblast			2000	408		546		652	75%	459 (6 months)
IR 1	Physician practice related to diagnosis and treatment of diabetes improved	(1.1) % diabetic patients complying with prescribed diet & medications in 2 selected sites	# compliant diabetic patients divided by total # in cohort		2000	Site 1: 33% Site 2: 30%		Site 1: 46% Site 2: 44%			Site 1: 62% Site 2: 60%	
		(1.2) # diabetic patients hospitalized from 2 selected sites	Site 1: # diabetic patients admitted to hospital for complications Site 2: Numerator above divided by total # in cohort		2000	Site 1: 230 Site 2: 74%		Site 1: 125 Site 2: 27%			Site 1: 110 Site 2: 20%	Site 1: 100 Site 2: 8%

SO or IR	Results Statement	Indicator	Unit of Measure	Disaggregation	Baseline Year	Baseline Value	2001 Target	2001 Actual	2002 Target	2002 Actual	2003 Target	2003 Actual
IR 2	Physician practice related to diagnosis and treatment of cardiovascular disease improved	(2.1) % hypertension patients complying with medication regime in 3 selected sites	# hypertension patients compliant with medication regime divided by total # hypertension patients in cohort		1999 2002 1999	Site 1: 10% Site 2: 0 Site 3: 11%		Site 1: 63% Site 3: 93%			Site 1: 70% Site 2: 90% Site 3: 95%	Site 1: 67% Site 2: 78% Site 3: 95%
		(2.2) # of hospital admissions for hypertension patients with acute episode in 2 sites			1999 2002 1999	Site 1: 110 Site 3: 160		Site 1: 56 Site 2: 86 Site 3: 74			Site 1: 40 Site 2: 70 Site 3: 50	Site 1: 11 Site 2: 11 Site 3: 9
IR 3	Medical practice related to TB diagnosis and treatment improved	(3.1) # of doctors trained in TB standardized protocol (i.e.DOTS) in 1 site	# physicians		1999	Site 1: 0		Site 1: 305			Site 1: 400	Site 1: 460
		(3.2) # patients initiating standardized DOTS treatment in 1 site	# released prisoners with TB referred to civilian health care centers divided by # released prisoners with TB			Site 1: 25%		Site 1: 40%			Site 1: 60%	Site 1: 100%

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MONITORING & EVALUATION

KHABAROVSK

Hypertension:

Family Medicine Clinic – lectures to 1,923 family medicine doctors

- Patient education material from EMEP disseminated to 870 patients
- Dramatic improvement in blood pressure over the 9-month period
- Decrease in smoking
- Decrease in use of salt

Hypertension Report for the First Nine Months

	Beginning of Treatment	1st quarter	2nd quarter	3rd quarter
180/110	123	19	0	8
170/105	257	124	9	48
160/100	0	47	10	15
150/95	0	75	9	21
140/90	0	67	4	23
130/80	0	48	348	265
Total	380	380	380	380
Compliance		207	241	133
Only Drug Treatment		173	128	176
Pts Stopped Treatment on Own		0	11	71

during the 9 month period the following patients were hospitalized: 2 patients with coronary heart disease (CHD) and 1 patient with angina. 8 patients suffered hypertension crisis. All those patients enjoyed normal BP after some period of time those patients stopped the treatment without consultation with the doctor. There were no registered cases of acute cerebral blood flow.

Drugs prescribed to the patients for the 3 rd quarter:

Enalapril	20 mg/24hrs	- 72 patients
Ramipril	5 mg/24hrs	- 70 patients
Enalapril Indap Retard	20 mg/24hrs plus 1.5 mg/24 hrs	- 63 patients
Ramipril Indap Retard	5 mg/24hrs plus 1.5 mg/24 hrs	- 63 patients
Metaprolol Indap Retard	100mg/24 hrs plus 1.5 mg/24 hrs	- 64 patients

1923 family medicine doctors, residents, students... listened to EMEP lectures during 5 years.

The evidence-based curriculum integrated into the Family Medicine Program:

1. Identification of hypertension

2. Diagnostics principles
    a) the right way to measure BP
    b) whole clock round BP monitoring
    c) laboratory examinations
    d) additional laboratory examinations

3. Hypertension classification

4. Identification of the risk groups (criteria, risk stratification) disease stages/phases

5. General principles of hypertension patients management
    a) Life style modification
    b) Drug therapy
    c) Evidence-based treatment by using efficient anti-hypertension drugs and combination of different anti-hypertension.
    d) Principles of dynamic observation
    e) Hypertension treatment among specific groups of patients

6. Urgent conditions/states among hypertension patients

7. Indications for hospitalization

Patient education material was prepared in Family Medicine Clinic based on EMEP recommendations. It was disseminated to 870 patients (including 380 patient control group).

Hypertension Report for the Last Quarter of 2002

Total # of hypertension patients 380

	Total	Men	Women
		144	236
Average age		54	62
BP at the beginning:			
180/110	123	51	72
160/100	257	93	164
	380	***144***	***236***
BP during 3 month period treatment:			
180/110	19	9	10
170/105	47	19	28
160/100	124	41	83
150/95	75	26	49
140/90	67	32	35
130/80	48	17	31
	380	***144***	***236***

Hospitalized patients: 1 (angina); 8 patients were hospitalized during the year 2002
Number of patients on sick leaves: 3; 19 for 2002
Out of 93 smokers 7 gave up smoking

All patients were recommended exercises:
18 patients – activities in gym
38 patients walk daily 3 km
15 patients swim
207 patients drastically reduced or stopped using salt.

Hypertension Report for the First Quarter of 2003

Total # of hypertension patients 380

	Men	Women
Total	144	236
Average age	54	62

BP during 3 month period treatment:

180/110	0	0	0
170/105	10	5	5
160/100	9	5	4
150/95	9	4	5
140/90	4	2	2
130/80	348	128	220
	380	***144***	***236***

Hospitalized patients: 1 coronary heart disease (CHD).
Number of patients on sick leaves: 4; the average sick leave duration is 4 days each.
Out of 93 smokers 7 gave up smoking during previous 3 month period plus 2 more patients stopped smoking this quarter. ***Altogether 9 stopped smoking.***

All patients were recommended exercises:

18 patients – activities in gym
38 patients walk daily 3 km
15 patients swim
207 patients drastically reduced or stopped using salt

After 3 months of treatment, 48 patients had the BP 130/80 and even lower after ***6 months of treatment 300 patients had the BP 130/80 and even lower on top of those 48.*** 32 patients had high BP despite of the 6 month treatment.

16% inefficiency of treatment is due to:

- 8 patients did not take medicine regularly
- 6 patients did not lose weight due to poor eating habits (excessive calories and high salt (NaCl) consumption)

Drugs prescribed to the patients:

Enalapril	20 mg/24hrs	- 92 patients
Ramipril	5 mg/24hrs	- 98 patients
Enalapril Indap Retard	20 mg/24hrs plus 1.5 mg/24 hrs	- 63 patients
Ramipril Indap Retard	5 mg/24hrs plus 1.5 mg/24 hrs	- 63 patients
Metaprolol Indap Retard	100mg/24 hrs plus 1.5 mg/24 hrs	- 64 patients

MONITORING & EVALUATION

EKATERINBURG

Hypertension:

150 patients followed for 2 years following EMEP lectures and training

- Compliance with therapy increased from 10% to 67%
- Decrease in smoking
- Increase in exercise
- Decrease in hypercholesterolemia
- Dramatic decrease in sick leave, hospitalization and duration of hospitalization
- Hypertension school developed for patient education and training. These have now been established in all districts of Ekaterinburg
- Every man coming to a polyclinic is now screened for hypertension

HYPERTENSION

Percentage of AH patients with controlled blood pressure (below 140/90)
150 patients followed up for 2 years:

	Before School (2001)	1st Year after School (2002)	2nd Year after School (2003)
Compliance with therapy	10%	55%	67,3%
Control of BP (140/90 or less)	9%	37%	51%
Average BP changes during the time	165/95	155/90	145/90
% of pts., visited > 80% of the lessons	-	63%	85%
% smoking pts.	34%	20%	18%
% of pts., started phys. exercising	-	47,3%	67,3%
% of overweight pts.	36,7%	28%	24,3%
% of pts. with weight lost > 5%	-	7,3%	12,4%
Hypercholesterolemia (% of pts.)	69,3%	52,6%	36,7%
Number of Sick Leaves	1986	985	574
Number of Sick Days	16456	6512	4341
Average Duration of Sick Leaves (days)	8,3	6,6	4,3
Length of Stay in Hospital (days)	468	98	76
Average Stay in Hospital (days)	26,5	18	6,7

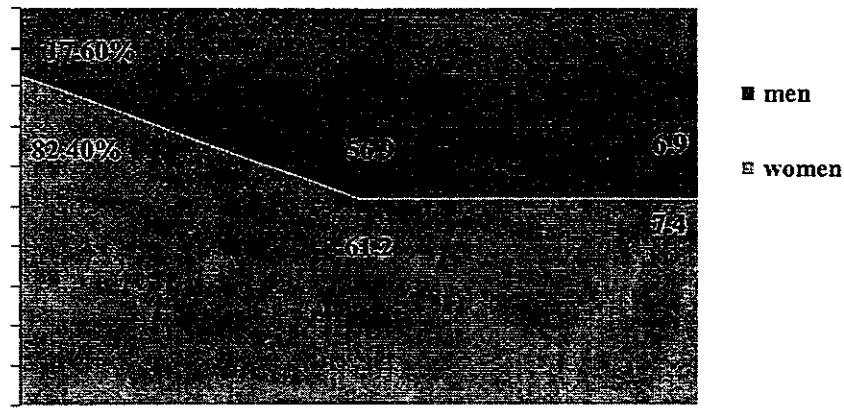
Evidence based curriculum integrated due to the lectures and experience exchanges with Dr. Greenberg.

Evidence-based treatment for hypertension adopted. Combined therapy has been in 90,3% of patients and came to 95,5% of patients. The change of combination (adding or changing of the ACE-inhibitor, statin, etc.) has been done in 40,5% of patients.

Patients' education material: the diary for the patients with arterial hypertension published and disseminated in Ekaterinburg.

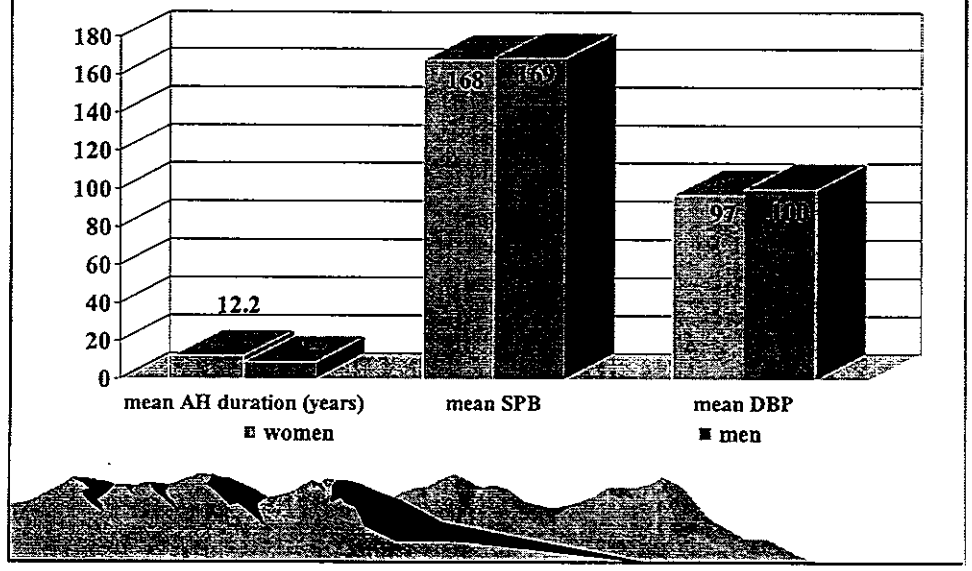
AHS results

Investigated group characteristics (n=150)

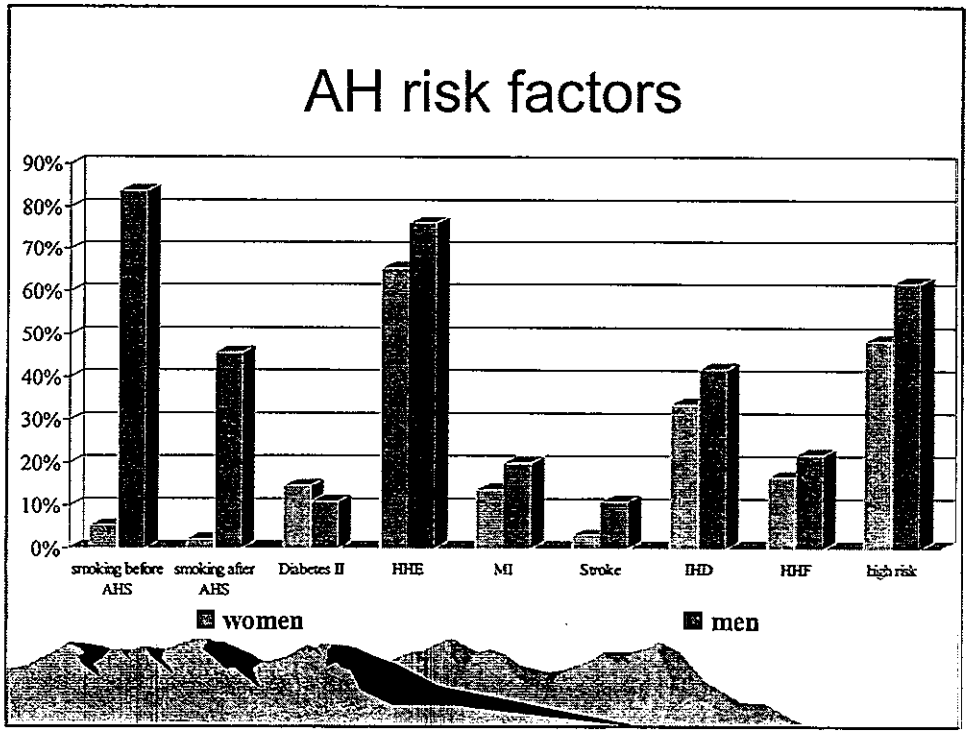


Following up for 1 year

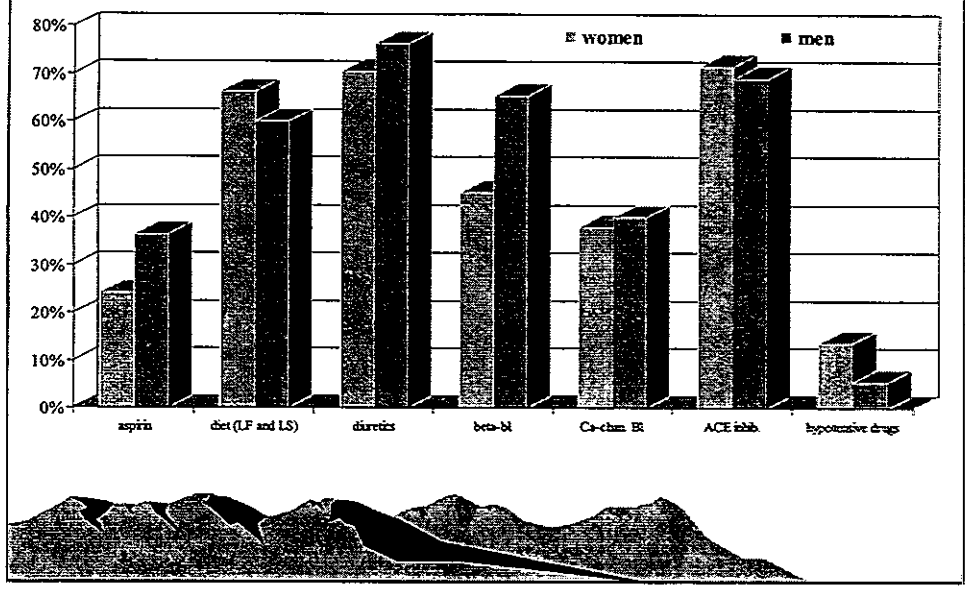
Primary characteristics of the AH in men and women



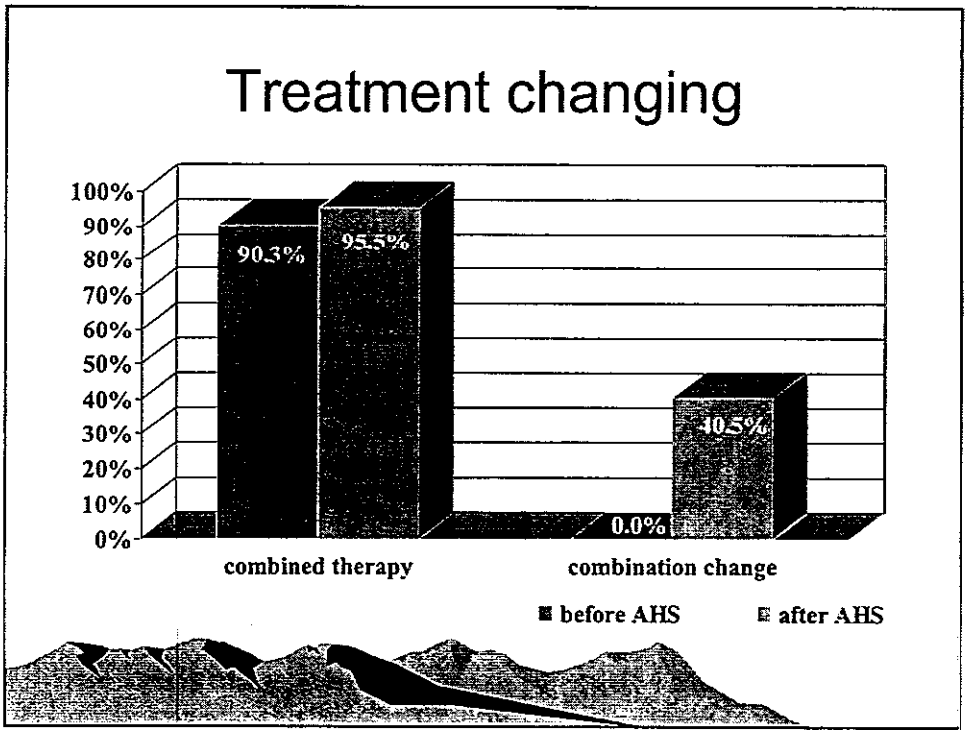
AH risk factors



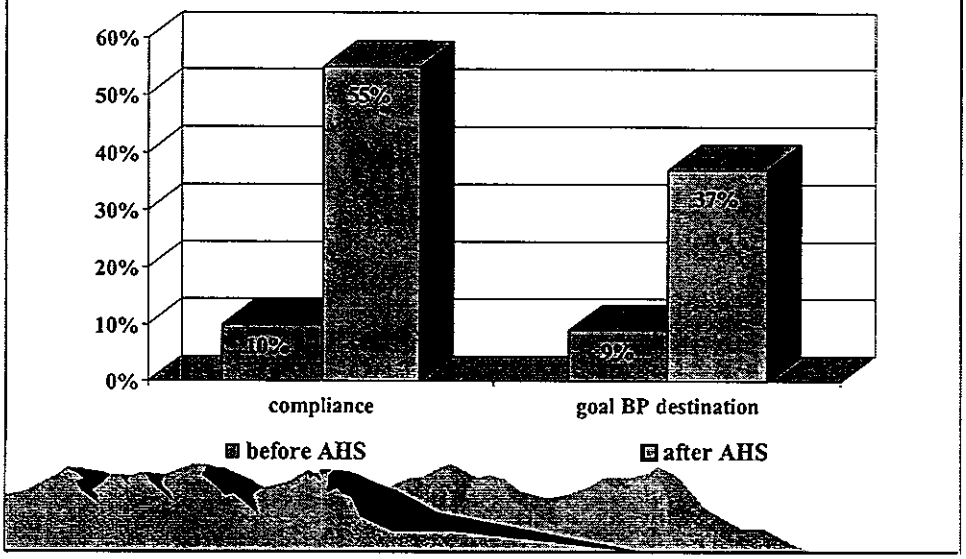
AH treatment in men and women



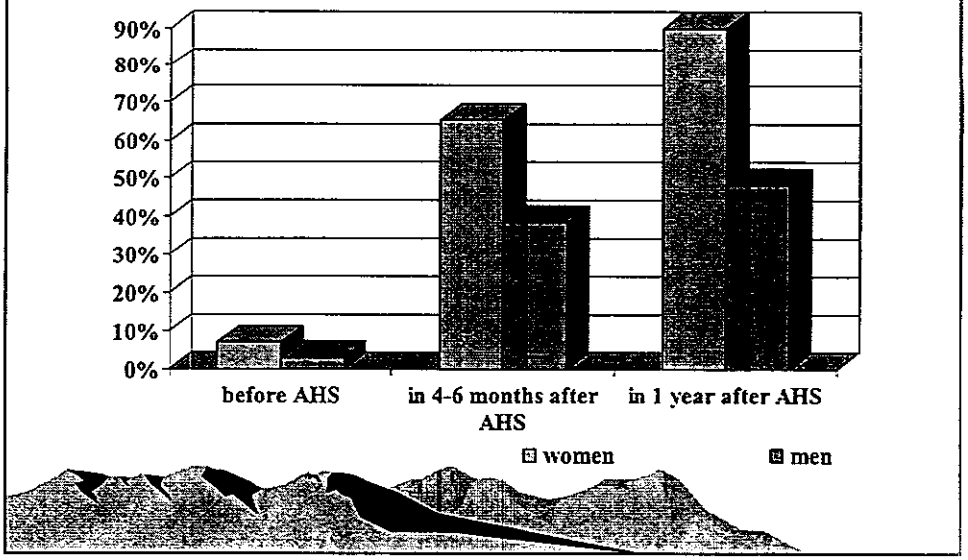
Treatment changing



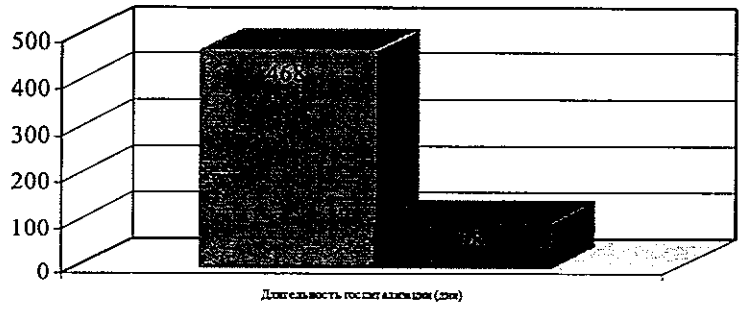
Compliance and BP dynamics



Number of patients, perfectly following physician's recommendations (%)



Hospitalization duration (days)



SF-36 in dynamics

SF-36	Before AHS	After AHS
PF	36,4 ± 3,9	42,7 ± 3,7*
RP	13,3 ± 3,8	22,2 ± 5,1
BP	44,3 ± 4,2	59,4 ± 4,7*
GH	38,3 ± 2,5	46,4 ± 2,7*
VT	37,0 ± 3,2	49,8 ± 3,4*
SF	55,0 ± 4,2	61,9 ± 4,6
RE	30,4 ± 5,5	40,0 ± 5,8
MH	49,2 ± 3,0	60,5 ± 2,5*

* p < 0,05

MONITORING & EVALUATION

KAZAN

Hypertension:

Three-year follow up of 352 patients with arterial hypertension (AH), with or without diabetes mellitus (DM)

- Cohorts based in two polyclinics and managed by therapists (GPs), supervised by Professor Galyavich, Chief Cardiologist, Tartarstan (report included)
- Evidence-based EMEP lectures to physicians in both polyclinics
- 90% of patients have been in compliance with medications and follow up visits
- 30-50% have reached target blood pressure (BP)
- Complications (myocardial infarction and stroke) less than 2% over the three years

Summary Report

Results of Long-Term Management of Hypertensive Patients in the City of Kazan (in the Framework of the Eurasian Medical Education Program)

The demographic and Epidemiology data on the incidence and prevalence of hypertension and its complications is presented in the power point attachment (extracted from the Ministry of Health report and included in the presentation of Professor Galyavich at the April conference).

The basic patient characteristics, percentage of overweight, smoking patients, patients with acute and chronic complications of AH in history with blood pressure and laboratory data over the 3 years of management and research (in 6 stages of data collection – polyclinic 18 and 3 stages of data collection – policlinic 11) are presented in tables and graphs (see attached files).

The positive changes for the 3 year period of observation and management (01.07.2000r. – 01.06.2003r.):

- The percentage of patients who have reached target BP level increased gradually over the 3 years of management and control.

	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6
Patients AH	0	20,1	26,7	32,5	38,9	34,6
Patients AH+DM	0	30,5	37,3	40,5	40,4	45,1

- The number of patients who developed hypertension complications over the study period was low: 1,5% of AH+DM patients and 1,7% of AH+DM patients have developed complications (MI and stroke)
- Compliance with medications was about 95% at all the visits over the 3 years.
- Compliance with follow-up visits was continuously increasing with the progression of the management study: it was 50% on the 2d visit, 65% - on the 3 visit, 73% - on the 4 visit, and 93% - on the 5 - 7 visits (percentage of patients compliant with the follow-up visits).
- Compliance with the regimen was the poorest. It was about 35% with physical activity (the increase over the 3 years was 7% → 35%), 60% with the diet (the increase over the 3 years was 35% → 69%). Non of the patients quit smoking, but about 60% of them restricted the number of cigarettes per day.
- All the positives changes in the BP control and compliance represent the result of continuous medical education of the physicians in the framework of EMEP on the basis of the latest achievements of EBM.
- Since 2000 2 cohorts of hypertensive patients in 2 polyclinics of the city of Kazan have been enrolled and followed up with the computerized registration of BP changes, clinical, laboratory and treatment specifications.

- During the years of the EMEP management study (2000-2003) the following activities were implemented on the basis of the evidence-based medicine approach:

    - EBM-teaching of physicians: EMEP run conferences, workshops and seminars, EMEP-initiated teaching courses at the Kazan State Medical Academy with provision of EBM-based teaching materials, results of systematic reviews and latest clinical trials as well as visuals and hand-outs.
    - Complex free-of–charge examination of hypertensive patients at the polyclinics 18 and 11 by cardiologists and physicians of other sub-specialties with laboratory testing.
    - Furthering observation and follow-up of patients with the resultant improvement in quality of life in hypertensive patients.
    - The system of patient schools has been established and improved during the years, ensuring self-control of BP with the major involvement of nurses in the patient-teaching process – EBM-approach implemented.
    - New EBM approaches to patient and community education have been implemented with the help of mass media and patient and community hand-out materials – dissemination of material on risk factors, diet and life-style requirements, compliance with life-style and diet, compliance with medications and follow-up visits.

As a result of all the above described activities in the Republican (the Republic of Tatarstan) program on hypertension management has been developed.

Arterial Hypertension as a Major Problem for Public Health

The objective of our study was to show how the active management of chronically ill patients can influence the course of the disease, the level of blood pressure (BP), biochemical characteristics and compliance.

We have been examining and treating 2 groups of patients since March 2000. The 1st group consists of 218 patients with arterial hypertension of different stages of severity from 33 to 76 years of age. The second group consists of 134 patients who have AH and diabetes mellitus (DM), from 47 to 74 years of age. In 67,9% of these patients AH developed earlier than DM.
Basic characteristics of the patients are presented in the table 1.

Table 1 Baseline characteristics of the groups of patients with isolated AH and with AH and DM

	AH	AH+DM
All patients	218	134
Men	25,2%	18,7%
Women	74,8%	81,3%
BMI>25 kg/m^2	80,7%	95,9%
Total cholesterol >5,2mmol/l	60,5%	77,6%
LVH	57,3%	40,3%
MI	10,5%	9,7%
Stroke	5%	5,2%
Smoking	9,63%	4,48%

BMI- body mass index MI-myocardial infarction
LVH-left ventricular hypertrophy

Table 2 Changes of blood pressure in the patients with AH on 7 consecutive visits

AH	1visit	2visit	3visit	4visit	5visit	6visit	7visit
SBP	169,5± 20,5	163,5± 23,5	158,1± 26,1	155,2± 14,1	154± 23,6	158± 24,1	154,4± 21,7
DBP	100,5± 14,2	98,5± 14,8	95,6± 24,1	94,6± 16,8	93,4± 13,9	94,5± 13,8	93,5± 14,1

SBP-systolic blood pressure DBP-diastolic blood pressure

Table 3 Changes of blood pressure in the patients with AH+DM on 7 consecutive visits

AH+DM	1v	2v	3v	4v	5v	6v	7v
SBP	163,9± 22,8	158,6± 24,3	153,6± 21,9	150,4± 22,2	155,1± 22,2	153,8± 25,7	143,3± 17,7
DBP	94,8± 14,8	91,5± 14,6	90,4± 14,9	88,5± 14,2	89,1± 15,1	88,4± 16,2	83,9± 12,6

Table 4 Changes of blood pressure in men with AH on 7 consecutive visits

AH	1v	2v	3v	4v	5v	6v	7v
SBP	169,8± 17,6	159,8± 20,7	155,9± 24,8	149,9± 24	148,7± 21,4	155,5± 27,4	154,5± 24,4
DBP	102,6± 15,3	97,4± 16,1	95,1± 14,3	91,1± 15,2	91,4± 13,6	94,1± 15,8	95,5± 18,5

Table 5 Changes of blood pressure in women with AH on 7 consecutive visits

AH	1	2v	3v	4v	5v	6v	7v
SBP	170,2± 21,1	162,5± 24,1	160,3± 26,4	158,9± 24	161,4± 24	160,1± 22,3	156,8± 19,7
DBP	100,9± 13,8	98,2± 14,3	96,4± 14	96,9± 17	96± 14,1	95± 13,3	95,8± 12

Table 6 Changes of blood pressure in men with AH+DM on 7 consecutive visits

AH+DM	1	2v	3v	4v	5v	6v	7v
SBP	166,1± 25,3	168,9± 26,2	159,8± 24,3	158,6± 20,1	163,1± 23,6	166,7± 33,1	145,5± 14,6
DBP	98,8± 12,7	99,1± 14,8	94,8± 11,2	95,8± 11	93,1± 12	90,4± 18,4	85,5± 15

Table 7 Changes of blood pressure in women with AH+DM on 7 consecutive visits

AH+DM	1	2v	3v	4v	5v	6v	7v
SBP	163,4± 22,3	156± 23,3	152,4± 21,1	148,4± 22,8	153,7± 23,6	150,9± 23	142,6± 20
DBP	93,8± 15,2	89,6± 13,3	89,7± 15,5	86,8± 14,5	88,2± 15,8	88± 15,8	82,9± 13,6

Table 8 Changes in total plasma cholesterol level, fasting blood glucose and glycosilated hemoglobin in patients on the first and the last visit

	Cholesterol		FBS		HbA1c	
	begin-ning	end	beginning	end	begin-ning	end
AH Patients	6,39± 1,5	6,31± 1,6				
AH men	6,2± 1,7	6,1± 1,5				
AH women	6,46± 1,5	6,36± 1,7				
AH+DM patients	6,87± 2,1	6,1± 1,7	7,1± 1,9	7± 1,8	9± 2,24	8,9± 1,8
AH+DM men	6± 1,7	5,1± 1,9	7,1± 1,9	7,07± 2,3	8,2± 1,8	8,4± 1,5
AH+DM women	7± 2,1	6,37± 1,6	7,2± 1,9	6,9± 1,7	9,2± 2,3	9,1± 1,9

Outcomes and Compliance

37,6% of AH patients have reached target BP: 50% of men and 34% of women

48,4% of AH+DM patients have reached target BP: 29,2% of men and 53% of women

93% of patients in both groups have shown good compliance to the treatment and follow-up visits

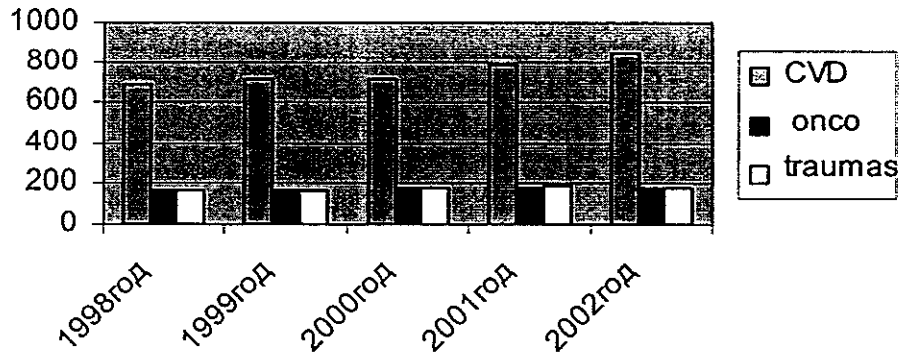
Prevention of Cardiovascular Complications in Patients with Hypertension
Results of New Research

Chief cardiologist of the Ministry of Health of the Republic of Tatarstan and of the Department of Health of the city of Kazan

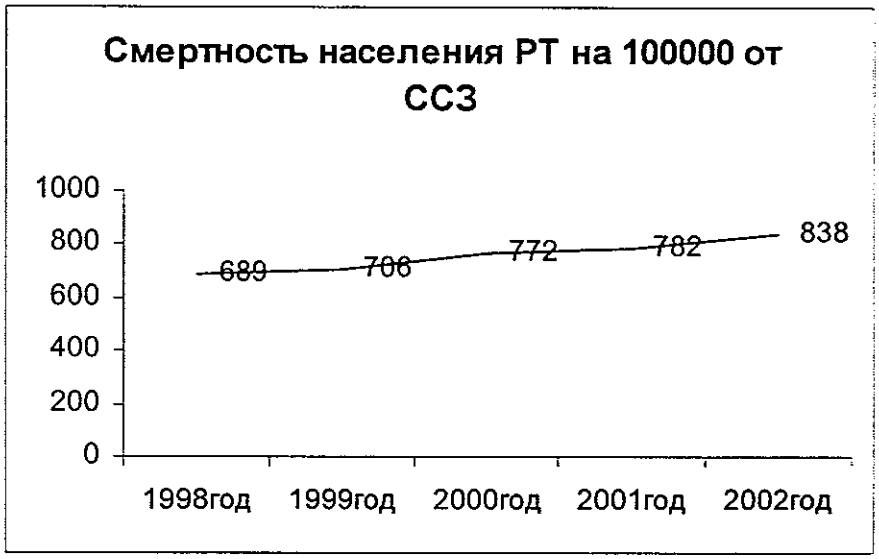
доктор медицинских наук,

Professor A.S. Galyavich, MD, PhD, D.Sci (KSMU)

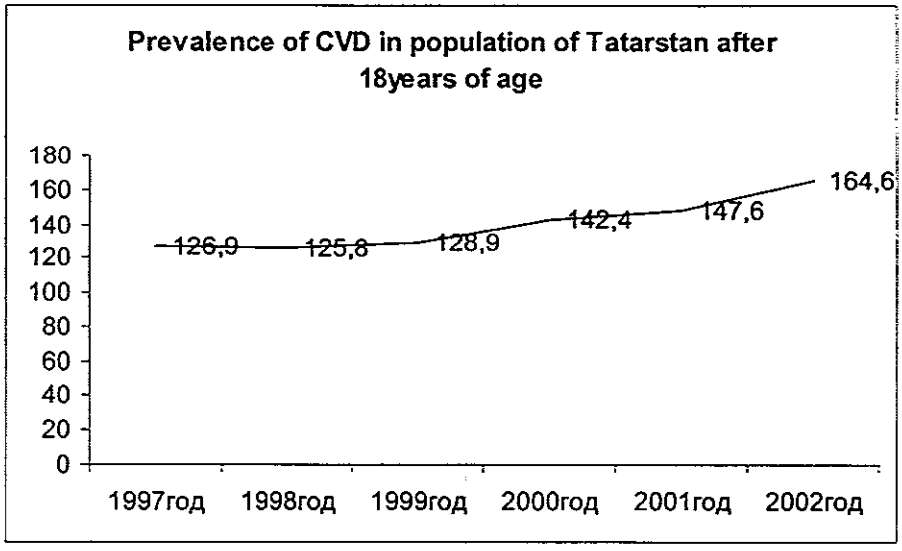
Mortality rate because of major causes in population of Tatarstan



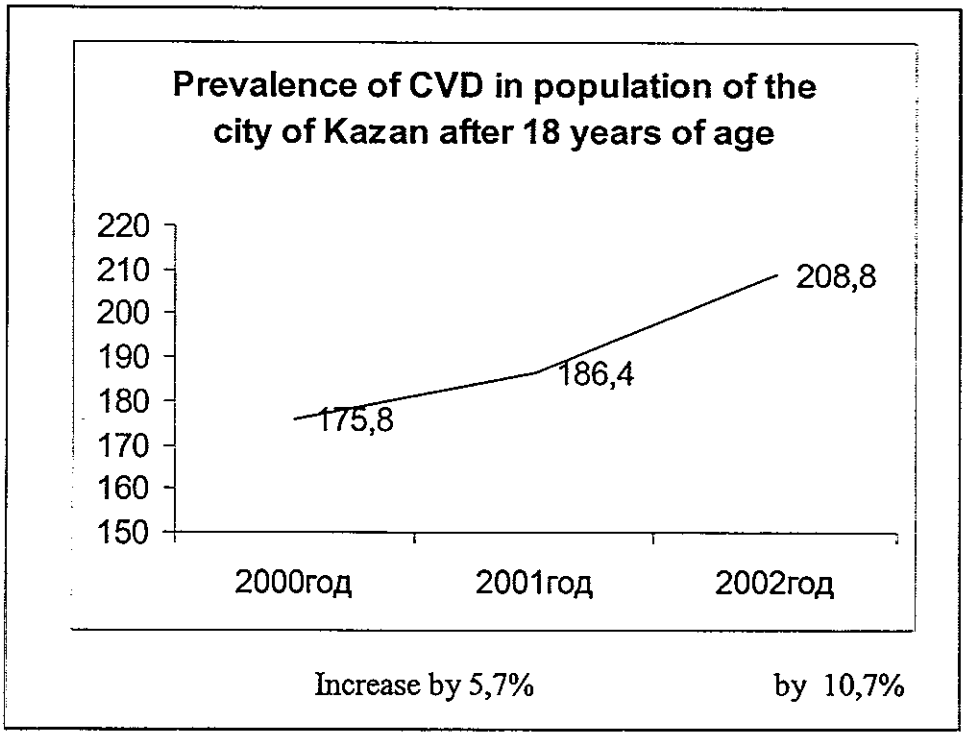
Mortality rate per 100 000 population in Republic of Tatarstan because of CVD



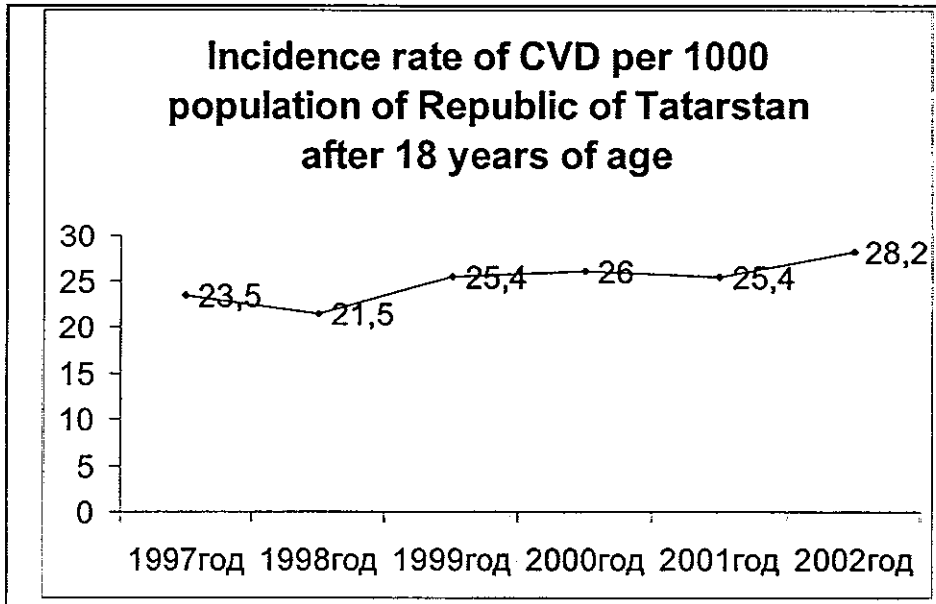
Increase by 6,7%



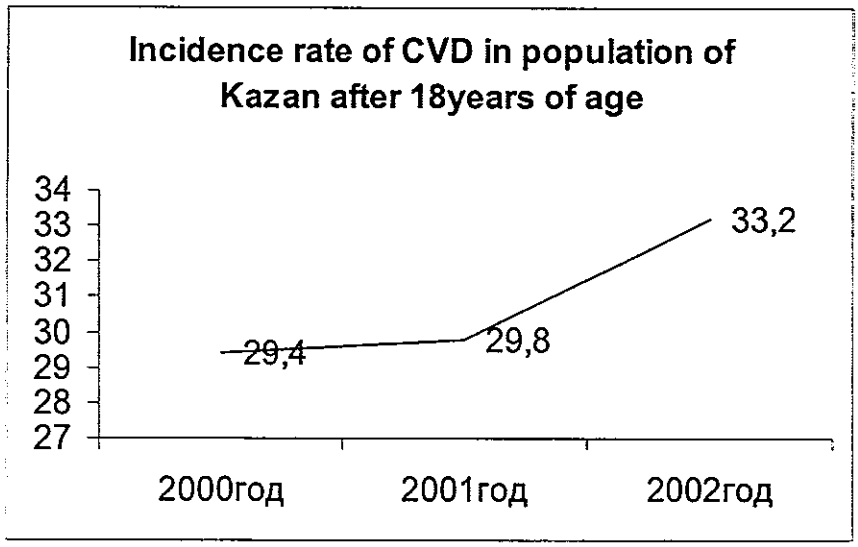
Рост на 3,5% на 10%



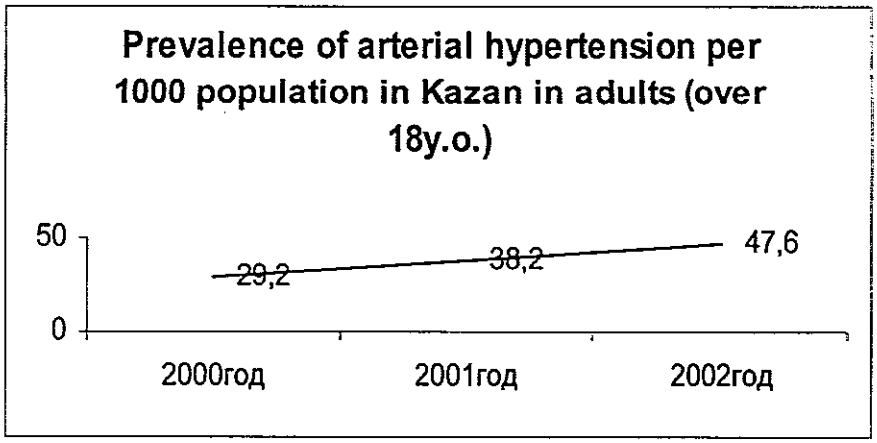
Increase by 5,7% by 10,7%



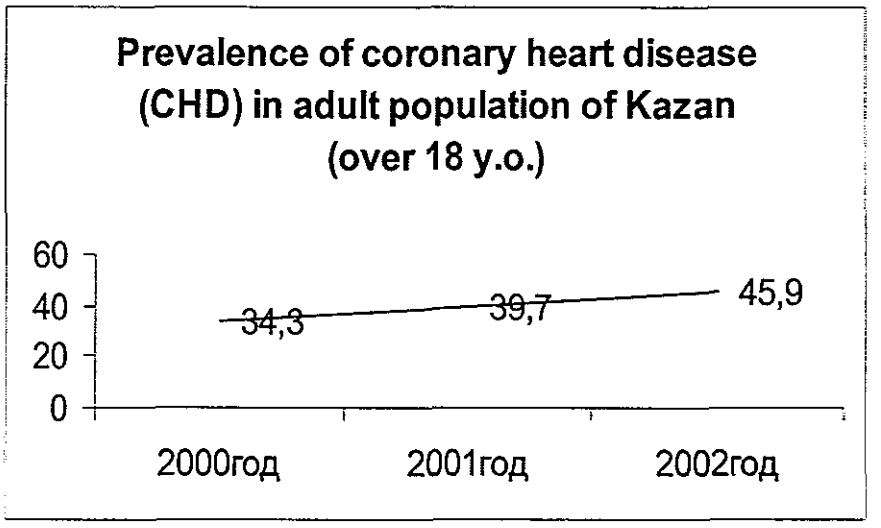
Increase by 9,9%



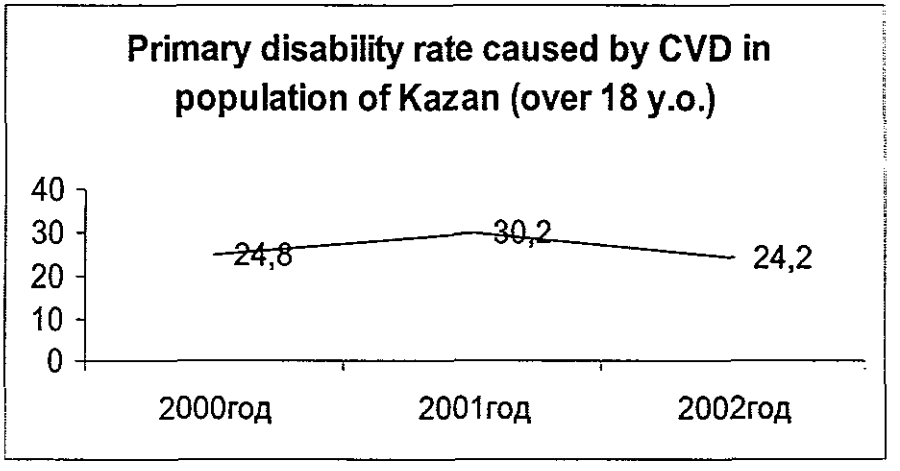
Increase by 13% by 10,2%



Increase by 23,6% by 19,7%



Increase by 13,6% by 13,5%



Increase by17,9% Decrease by 24,8%

EPOCH - Epidemiologic Study (CVD)

Major CVDs in European part of Russia:

1. Hypertension – 39,7%
2. Stable angina - 12,1%
3. MI - 2,3%
4. Valvular defects - 1,1%
5. History of stroke 2,5%
6. Diabetes mellitus - 2,9%
7. CHF – 2,3 % of population.

EPOCH (Arterial Hypertension AH – 39,7%)

AH I-degree - 49,1%

AH II-degree - 29,5%.

AH III-degree - 7,2%

Effectively treated patients (BP in one measurement <140/90 mm Hg) - 7,2%.

EPOCH in Tatarstan (AH – 32,4%)

City of Kazan	Country side
Prevalence of AH –29% (women – 59%)	Prevalence – 32% (women – 68%)
1 degree - 71 %	1 degree – 83%
2 degree – 22%	2 degree – 16%
3 degree – 7%	3 degree – 1%
Do not measure BP – 49%	Do not measure BP – 61%

EPOCH (drugs)

The number of preparations analyzed - 10022

% of cases

ACE inhibitors - 22,6%

Beta-blockers - 9,3%

Nitrates – 9,9%

Diuretics - 7,8%

Calcium channel blockers - 5,4%

Rawolfia preparations - 10,1%

Other drugs, metabolites and sedatives, not affecting prognosis and outcomes - 24,3%.

Disease needs to be prevented at the very beginning,

it is too late to prepare a drug when disease is already here.

Publyi Ovidyi Nazon,

43y b.c. - 18 a.c.

MONITORING & EVALUATION

EKATERINBURG

Tuberculosis:

- DOTS introduced in 2000, following training in United States
- Laboratory personnel trained in the United States – March 2002
- Policy change required evidence-based treatment
- Evidence-based curriculum introduced by EMEP
- Prison system patients – 100% DOTS
- Children now have 100% DOTS compliance and completion
- For adults, completion has increased from 58% to 72% since 2000
- Ural TB control program developed with EMEP collaboration

TUBERCULOSIS

- # of patients completing continuous TB treatment (DOTS protocol)

  2000 — 408

  2001 — 546

  2002 — 652

  2003 — 459

In GUIN system 100% pts. have DOTS (GUIN is the Russian system of punishment realization – the penitentiary system.)

- # of doctors trained in DOTS during 3 years is **460**

- # of patients beginning DOTS treatment:

  2000 — 987

  2001 — 1000

  2002 — 1289

  2003 — 1056

- Evidence-based curriculum in TB integrated in CME antibacterial therapy using the first line drugs. **For children** the use of protocols is 100% and 100% effectiveness (so, all the patients are cured, that is certified by the serological and bacteriological investigations); **For adults** — first line drugs; second line drugs only 20% of the patients, who need this therapy. The mortality rate is 0,02%. The effectiveness in adults is 90-95% of clinical cure for the primary diagnosed patients.

- Policy change requiring evidence based treatment of TB — since the year of 2000 the police of the TB treatment in Ekaterinburg and Sverdlovsk region began to change. Previously all the officials consider that the treatment of TB has to be individual (individually composed drugs, length of treatment, etc.). During the EMEP the head TB people of Sverdlovsk region and Ekaterinburg have trained in DOTS and evidence-based treatment of TB and realized the need of changes. Now in Ekaterinburg, Sverdlovsk region and the penitentiary system there are DOTS protocols. DOTS is provided by the doctors and the nurses of the phtysiopulmonology service.

  Due to the EMEP mostly all the doctors and nurses were trained in DOTs and evidence based curriculum for the TB. Today all the penitentiary patients are coming from the GUIN system to the civilian care, but only 25% of them can complete the therapy. The numbers are 400-500 pts. per year (from 2000 of discharged).

- Patient education materials developed and disseminated: the guide for the patients with TB

  Modern lab procedures for TB diagnosis and treatment documented and disseminated: The reference regional bacteriological laboratory has been created due to the EMEP.

- The effect of MDR (multi-drug resistant TB): 8-14% of MDR in the region. The second line drugs unfortunately are not available for every patient, but approximately 1-2% of the MDR patients receive the correct treatment.

In general, the Russian colleagues are very grateful to the EMEP as it was the first to bring DOTS, epidemiological studies and an evidence-based curriculum to Sverdlovsk. EMEP also helped a great deal with the reference laboratory.

THE URAL TB CONTROL PROGRAM

Y.P. Chugaev, D.N. Golubev

Introduction

Development of this program is initiated by the Ural State Medical Academy and Sverdlovsk oblast TB dispensary in Ekaterinburg (Director — O. Nechaeva) in collaboration with the Institute for Health Policy Analysis, Washington, DC (Director — E.J. Burger, Public Health Director — H.I. Sloane).

Designation

Anti-TB measures effectiveness increasing by using modern internationally adopted methods of diagnosis, treatment and prophylaxis. Also this program is intended to evaluate the possibility of implementing a new cost-effective approach for diagnosis, treatment and prophylaxis of tuberculosis in the Urals.

State of the problem

Sverdlovsk oblast with 4,6 million people population is situated in the center of Russia on the Europe-Asia boundary between 57° and 63° latitudes North. It has sharp continental climatic conditions. The territory is an industrial region with a developed set of motorways and railroads. Most of the population lives in cities and workmen's settlements. Health service institutions of municipal, regional and federal submission provide medical help in the region. Ekaterinburg is the capital of the Ural Federal Area (UFA) with 13 million people population.

There are 2825 hospital beds and 56 anti-TB centers in Ekaterinburg and Sverdlovsk region. About 5000 medical workers, 418 physicians among them, work in this phthisiatric service. Besides, there are 55 phthisiatricians working in penitentiary system of Sverdlovsk oblast. Bacteriology investigations for MBT are held in 17 laboratories.

Specimens from about 85% of patients in the civilian population are tested in a few laboratories: Central TB dispensary of the city of Ekaterinburg, oblast TB dispensary, the Ural Regional TB Research Institute, the oblast TB hospital "Crystal", Nizhny Tagil, Kamensk-Uralsky, and TB sanatoria in he city of Pervouralsk. The remaining workload north of the oblast is served by small laboratories in Krasnouralsk, Krasnoturinsk, Serov, Asbest, Irbit, and Berezovsky. Also there are 6 "seeding stations" (Kirivograd, Neviansk, Artemovsky, Polevskoy, Alopaevsk) collecting specimens for initial inoculation of the specimens into L-J medium, forwarded to the oblast dispensary. The penitentiary system does not have TB laboratories, and the diagnosis is based primarily on x-ray examination and direct smear (Z-N stained) examination of the sputum.

There is the Chair of Phthisiology in the Ural State Medical Academy (USMA). The Chair guides UFA anti-TB services personnel training; carries out general compulsory education in Phthisiology of all USMA students according to the 78-hour program; annually training of 150 phthisiatricians according to 144-500 hour programs and teaching TB diagnosis and prophylaxis problems for about 1000 general practitioners and pediatricians.

Furthermore, the diagnosis, treatment and scientific research of TB are held at the Ural Regional TB Research Institute with a 350-bed hospital and bacteriologic laboratory.

However, the epidemiological indices on TB are still strained: in the year 2000, 3182 new cases were diagnosed among the civilian population (69.1 per 100,000) and 1687 cases were reported among the prisoners, or a total of 4, 869 cases (105.8 per 100,000). The growing incidence among the civilian population is significantly related to the settlement of released TB prisoners within the oblast, and infection occurring from contacts with these individuals. The penitentiary system (under the Ministry of Justice) holds about 42,000 prisoners, and there are about 4,000 of them who have tuberculosis, with approximate entry and exit of 1,000 annually.

In the year 2001 the regional TB morbidity was 100/100 000 (88,2/100 000 in Russia) and the TB mortality rate was 25 per 100 000 (19,9 per 100 000 in Russia). In all 70 000 TB patients no less than 10% of 50 000 convicts are with active forms of TB, especially in the penitentiary system.

Thus, the number of TB patients in Sverdlovsk oblast is large. The system of anti-TB measures includes both polyclinics (out-patients') and hospital services, educational and scientific research institutes.

During several years the Ural State Medical Academy along with American College of Physicians (ACP) and the Institute for Health Policy Analyses (IHPA) are cooperating their efforts in the struggle against TB. We suppose, that the major and most important effect of cooperation will be obtained by mutual exchange of information about TB control experience.

On one hand the USA specialists may teach engaged in personnel training and TB control arrangement faculty here in the Urals or at National TB control centers and Universities in the USA (as it has been done in Denver). On the other hand Russian phthisiatricians may adopt their progressive methods and share the information about the organizational and clinical work experience in the condition of TB epidemic in large region of Russia.

Main Purpose

Improvement of the epidemiological situation concerning tuberculosis in Sverdlovsk oblast by means of the advanced TB control measures introduction.

Tasks (Stages, Problems)

- Based on world achievements elaboration and introduction of practical measures complex aimed against TB epidemic in Sverdlovsk oblast.
- TB patients revealing system improvement concerning the common medical net, detection of patients with drug resistance, implementing a new cost-effective approach for full and timely diagnosis of tuberculosis.
- Providing conditions for DOT and DOT-PLUS strategies using in tuberculosis treatment.
- Improvement of TB control in Sverdlovsk oblast penitentiary institutions.
- Joint research of problems concerning spreading of drug resistant forms of MBT.

Arrangements

1. Organization of the medical personnel **REGIONAL EDUCATIONAL CENTER** for advanced methods of revealing, diagnosis, treatment and prophylaxis of tuberculosis training.
2. Development and implementing of TB control educational programs for phthisiatricians, general practitioners, pediatricians, medical personnel and population.
3. Adaptation and implementing of DOT and DOT-PLUS strategies clinical aspects in regional TB control service and penitentiary institutes.
4. Modernization and re-organization of current TB laboratory services.
5. Epidemical state monitoring improvement by computer technologies using.

Financial Support

The Program is maintained by means of Federal, Regional and municipal budgets along with international sources (Bill Heitz fund, EMEP, USAID, etc.).

Participants and stages

№	Stage	Participants, personnel	Sverdlovsk oblast institutions	USA institutions
1.	Organization of the **UFA Regional Educational Center** for qualification improvement and advanced methods of revealing, diagnosis, treatment and prophylaxis of tuberculosis training	Rector of the USMA Prof. A.P. Yastrebov Prof. Y.P. Chugaev Prof. D.N. Golubev	USMA	–
2.	Educational programs supply for: 2-1 Faculty 2-2 Phthisiatricians 2-3 Phthisiatricians-bacteriologists 2-4 Phthisiatricians-epidemiologists 2-5 Phthisiatricians, non-pulmonary TB specialists 2-6 Phthisiatricians of the penitentiary system 2-7 Medium medical personnel (nurses, laboratory workers, etc.) 2-8 General practitioners 2-9 Population	Prof. Y.P. Chugaev Prof. D.N. Golubev Prof. L.M. Greenberg Prof. S.N. Skornyakov Capt. A.A. Kozahmetova	USMA Central TB dispensary of the city of Ekaterinburg Oblast TB dispensary	ACP IHPA
3.	Educational and popular literature publishing		USMA	IHPA

4	DOT and DOT-PLUS strategies of chemotherapy and chemoprophylaxis technologies studying including patients with associations of TB and AIDS, TB and HIV, and patients with multiple drug resistant MBT forms: 4-1 Training at National TB control centers and Universities in the USA 4-2 Training at educational structures of the UFA	Physicians, chairpersons of TB institutions, phthisiatricians including the UFA penitentiary system doctors	USMA City and oblast TB dispensaries	ACP IHPA
5.	Modern and advanced TB laboratory technologies training at the specialized laboratories in USA: 5-1 Faculty 5-2 Microbiologists 5-3 Laboratory personnel (assistants)	Microbiologists, chairpersons of the regional bacteriological service	USMA City and oblast TB dispensaries	IHPA
6.	Training of TB epidemiological situation monitoring with computer (digital) programs using	Chairpersons of phthisiology service, epidemiologists, faculty, medical statistics specialists	USMA	IHPA
7.	Joint research of problems concerning: 7-1 Adaptation and effectiveness of DOT and DOT-PLUS strategies 7-2 Treatment of patients with drug resistant forms of MBT, especially in from penitentiary system 7-3 Spreading of drug resistant forms of MBT in the UFA	Prof. Y.P. Chugaev Prof. D.N. Golubev Prof. S.N. Skornyakov	USMA Ural Regional TB Research Institute	IHPA National Jewish Medical and Research Center, Denver

MONITORING & EVALUATION

KHABAROVSK

Diabetes:

Lectures to more than 500 physicians

- EMEP written material is included in postgraduate training
- EMEP evidence-based material distributed to 2,350 diabetes doctors, residents, students
- EMEP patient education material disseminated to 3,300 diabetes patients
- Dramatic decrease in number of cases of ketoacidosis (no mortality this year)
- Dramatic decrease in hospitalized patients
- Dramatic decrease in diabetic foot problems

Khabarovsk Diabetes Registry

	1999	2000	2001	2002
Total # of registered diabetics	6,940	6,836	7,211	7700
Complications				
Ketoacidosis	68	45	24	14
Retinopathy	2,354	2,821	2,694	2677
Neuropathy	3,012	2,982	2,844	2835
Diabetic Foot	802	758	698	195
Cause – Specific Mortality (# of patients)				
Ketoacidosis	16	10	8	0
Myocardial Infarctions	138	158	196	177
Stroke	57	79	97	78
Chronic Renal Failure	13	8	10	12
Gangrene	24	15	7	7
Chronic Heart Failure	54	43	48	54
Demographics				
Type I	538	407	393	445
Males	45%	44.6%	45.2%	45%
Females	55%	55.4%	54.8%	55%
Type II	6,401	6,429	6,818	7315
Males	24.3%	23%	24.9%	24%
Females	75.7%	77%	75.1%	76%
# of Patients attended Diabetic School	578	507	481	450
Have Glucometer	36	159	230	180
Hospital Treatment	230	158	125	100

MONITORING & EVALUATION

KAZAN

Diabetes:

Registry developed with assistance and support from EMEP including 18,395 adults and 196 children. Cohorts of patients now followed quarterly, including 216 adults and 166 children.

- Evidence-based EMEP curriculum with teaching materials and lectures, seminars, and workshops for diabetes doctors (estimated contact with 90% of diabetes doctors)
- Dramatic increase in diabetes control, use of glucose monitoring devices and near 100% attendance at diabetes schools
- Dramatic decrease in both ketoacidosis and hypoglycemic coma; none in the past year
- Model for diabetes management and control developed, with assistance from EMEP

Summary Report
Results of Long-Term Management of Diabetic Patients in the City of Kazan (in the Framework of the Eurasian Medical Education Program)

18395 adult patients with DM are registered in the city of Kazan by 01.01.2003, including 1177 patients with type 1 DM and 17218 – with type 2 DM. The incidence of DM type 1 is 0,7 per 10 000 adult population, the prevalence is – 13,7 per 10 000 adult population. The incidence of DM type 2 is 17,6 per 10 000 adult population, the prevalence is –199,7 per 10 000 adult population. There is a definite increase in the incidence and prevalence of DM type 2 in the city of Kazan. Incidence and prevalence of type 1 DM are stable for the past 3-5 years.

196 patients with Diabetes mellitus type 1 under 18 years of age are registered in the city of Kazan by 01.01.2003 and 3 patients with type 2 Diabetes. The incidence of Diabetes mellitus is 1,27 per 10 000 children (under 18years of age): in 2001 – the incidence was 0,85, in 2000 – the incidence was 0,9 per 10 000 children. The prevalence of DM is 6,9 per 10 000 children: in 2001г. – 8,5, in 2000г. – 7,2.

The age distribution, duration of the disease, percentage of overweight patients, patients compliant with prescribed diet and medications, acute and chronic complications of DM over the 3 years of management and research (in 6 stages of data collection) with demographic and laboratory data are presented in tables and graphs (see attached files).

The positive changes for the 3 year period of observation and management (01.07.2000г. – 01.06.2003г.):

- The number of children and adults with active self-control has increased: 81% → 100% (total numbers); regular self-control in adults also increased 33% → 62%.
- The number of patients with self-control with the help of individual glucometers has increased: 54% → 96% in children and 12% → 45% in adults.
- The number of adults with DM compliant with diet has increased: 39% → 52%.
- The coverage of children and adults with DM by laboratory monitoring (HbA1c, microalbuminuria, albumin/creatinine level etc) has increased due to the increase in patients' (parents') motivation and compliance.
- All the patients have been switched from animal insulins on to the human insulins, the number of patients injecting their insulins with the halp of pen0-fills has increased.
- The decrease in the numbers of acute DM complications (ketoacidic and hypoglycemic comas, from 1% to 0%) and chronic complications (microvascular complications) – diabetic nephropathy: initial increase in children proving better diagnosis with the subsequent decrease demonstrating improvement in the management and compliance.
- The prevalence of late chronic complications of DM in adults has increased due to the improvement of diagnostics and involvement of physicians of other sub-specialties in the diagnostic process – the result of continuous nedical education of the physicians in the framework of EMEP on the basis of the latest achievements of EBM.
- Since 2000 the computerized registry of DM patients has been created and is functioning.

- During the years of the EMEP management study (2000-2003) the following activities were implemented on the basis of the evidence-based medicine approach:

    - EBM-teaching of physicians: EMEP run conferences, workshops and seminars, EMEP-initiated teaching courses at the Kazan State Medical Academy with provision of EBM-based teaching materials, results of systematic reviews and latest clinical trials as well as visuals and hand-outs.
    - Complex free-of–charge examination of DM patients at the Endocrinology Center by endocrinologists and physicians of other sub-specialties with thorough laboratory testing.
    - Furthering observation and follow-up of patients and coordination of activities of out- and in- patient services with the resultant improvement in quality of life in diabetic patients.
    - The succession of continuity of care has been ensured between children and adult care services: individualized approach to the move into the adult system on the basis of peculiarities of physical and psychological development of a child.
    - The system of patient schools has been established and improved during the years, ensuring self-control of DM with the major involvement of nurses and laboratory technicians in the patient-teaching process – EBM-approach implemented.
    - The system of computerized registry of DM patients has been evolved and is being constantly maintained. This enables quarterly analysis of the results of the patient management and follow-up.
    - New EBM approaches to patient and community education have been implemented with the help of mass media and patient and community hand-out materials – dissemination of material on risk factors, diet and life-style requirements, compliance with life-style and diet, compliance with medications and follow-up visits.

As a result of all the above described activities in 2001 the municipal program on perfection of diabetes mellitus management in the city of Kazan has been approved. Plans for the future: furthering equipment of the endocrinology center with modern diagnostic machinery, organization of specialized offices ("Diabetic foot", etc), further improvement of the patient-education system and continuous education of physicians – endocrinologists and other specialties in diabetology problems.

166 People Under 18 Registered in Kazan Endocrinology Dispenser
164 with Diabets I Type and 2 with Diabetes II Type

DataBase: Kids (166)

Changes from last point (04.30.2002)

Total on 01.01.2003	159
Has been moved to adults database (age > 19)	3
Has moved to another city	0
New patients in Kazan Endocrinology Dispancer (age < 19)	10
Total on 06.01.2003	166

Insulin-Dependent Diabetes (156) **Period: 01.01.2003 - 06.01.2003**

Sex	**Male**: 80	**Female**: 86		
Age (years):	**<4**: 7	**5-9**: 22	**10-14**: 75	**15-18**: 62
Duration of disease		**<4**: 91	**5-9**: 50	**10-16**: 25
Body mass index:		**<18.5**: 106	**18.5-24.9**: 54	**25-30** : 6 **>30**:0
Diet:	**Yes**: 91	**No**: 13	**Not regular**: 62	
Self-control:	**Regular**:80	**Episodic**:86	**None**: 0	
Glucometer	**Yes**: 156	**No**: 10		
Diabetic school:		**Yes**: 166	**No**: 0	
Inheritance:		**Yes**: 8	**No**: 158	

Obtained hospital treatment: 61
Average time spent in hospital: 15,3 days

Average insulin dose per day : 36.9
Insulin therapy, based on human insulin: 166
Receive insulin in cartridges: 166
Receive insulin in vials: 0

Amount of injections per day:	**3**: 2	**4**: 1	**5**: 163	**6**: 0
Complications amount per patient	**0: 94**	**1: 37**	**2: 17**	
	3: 12	**4: 4**	**5: 2**	

Laboratory Analysis					
HbA1c (%)					
<6.5: 2	6.6-7.5: 6	7.5-9.5: 28	>9.5: 66	No data*: 64	
HbA1 (%) (Current research is not necessary for all patients)					
<8: 0	8.1-9.5: 0	>9.5: 0	**No data*: 166**		
Total cholesterol (mmol/l)					
<3,9: 39	3,9-5.2: 42	5.3-6,5: 10	>6.5: 3	**No data*: 72**	
Creatinine (mkmol/l)					
<60: 19	60-130: 55	>130: 0	**No data*:18**		
No need in such observation: 74					
Proteinuria					
Yes: 4		**No: 44**		**No data*: 24**	
No need in such observation: 94					
Microalbuminuria (Microbumin test Bayer)					
"-":51	"+":13	"++":2	"+++": 0	"++++":0	No data*: 35
No need in such observation: 65					
Albumin/Creatinin (mg/mmol)					
<2.5 : 22		**2.5-25: 3**	**>25: 0**	**No data*: 0**	
No need in such observation: 141					

Complications		
	New	Total
Diabetic coma	0	0
Hypoglycemic coma	0	0
Hold up in physical development	2	6
Hairopathy	2	47
Diabetic cataract	0	9
Diabetic retinopathy	1	49
Diabetic nephropathy	0	8
Diabetic sensory neuropathy	1	14
Autonomous neuropathy	0	0
Diabetic foot	0	0
Arterial hypertension	0	0

Lethality: 0

* Laboratory examination wasn't made for the reasons, not dependent on doctor's recomendation

Register of t[illegible]atients Under 18 with Insulin-Dependent Diabetes and Insulin-Indepen[illegible] Diabetes
(all kids of the[illegible]azan)

		I stage 143 people 07.01.2000-12.31.2000		II stage 153 people 01.01.2001-06.30.2001		III stage 164 people 07.01.2001-12.31.2001		IV stage 154 people 12.31.2001-04.30.2002		V stage 159 people 04.30.2002-12.31.2002		VI stage 166 people 01.01.2003-06.01.2003	
		amount	%	amount	%	amount	%	amount	%	amount	%	amount	%
1. Body mass index kg/m2	<18.5	95	66%	89	58%	87	53%	89	58%	99	62%	106	63%
	18.5-24.9	46	32%	62	41%	75	46%	63	41%	54	34%	54	33%
	25.0-29.9	2	1%	2	1%	2	1%	2	1%	6	4%	6	4%
	30.0-39.9	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
	>40.0	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
	No data*	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
2. Diet													
	Yes	59	41%	68	44%	90	55%	98	64%	83	52%	91	55%
	No	15	11%	15	10%	14	9%	6	4%	17	11%	13	8%
	Not regular	69	48%	70	46%	60	36%	50	32%	59	37%	62	37%
3.Selfcontrol													
	Regular	31	22%	35	23%	60	37%	62	40%	76	48%	80	48%
	None	27	19%	21	14%	28	17%	2	1%	0	0%	0	0%
	Episodic	81	56%	97	63%	76	46%	90	59%	83	52%	86	52%
	Vital	4	3%	0	0%	0	0%	0	0%	0	0%	0	0%
4. Studied in the Diabetic school	Yes	143	100%	153	100%	164	100%	154	100%	159	100%	166	100%
	No	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
5.Glucometer													
	Yes	77	54%	82	54%	91	56%	109	71%	152	96%	156	94%
	No	66	46%	71	46%	73	44%	45	29%	7	4%	10	6%
6. Average insulin dose per day		38.04 pts		37.4 pts		39.28 pts		36.74pts		36.62pts		36.9 pts	
7. Obtained hospital treatmont		134	94%	84	55%	58	36%	38	26%	75	47%	61	37%

57

Laboratory Analysis

8. HbA1c													
%	< 6.5	16	11%	0	0%	2	1%	2	1%	3	2%	2	1%
	6.6 - 7.5	40	28%	0	0%	0	0%	1	1%	5	3%	6	4%
	7.5-9.5	57	40%	0	0%	64	40%	28	18%	28	18%	28	17%
	>9.5	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	77	48%	66	40%
	*No data**	30	21%	153	100%	98	59%	123	80%	46	29%	64	39%
9. HbA1													
%	< 8.0	0	0%	2	1%	2	1%	0	0%	0	0%	0	0%
	8.1 - 9.5	0	0%	1	1%	0	0%	0	0%	0	0%	0	0%
	> 9.5	0	0%	28	18%	10	6%	1	1%	0	0%	0	0%
	No data*	143	100%	122	80%	152	93%	153	99%	159	100%	166	100%
10. Total cholesterol													
mmol/l	<3.9					15	9%	9	6%	42	26%	39	24%
	3.9 - 5.2	120	84%	53	35%	28	17%	28	18%	40	25%	42	25%
	5.3 - 6.5	20	14%	12	8%	16	10%	13	8%	12	9%	10	6%
	> 6.5	3	2%	4	2%	3	2%	1	1%	7	4%	3	2%
	No data*	0	0%	84	55%	102	62%	103	67%	58	36%	72	43%
11. Creatinine													
mkmol/l	<60	100	0%	48	31%	29	17%	26	17%	24	15%	19	11%
	61-130	43	0%	18	12%	21	13%	12	8%	58	36%	55	33%
	>130	0	0%	0	0%	1	1%	0	0%	0	0%	0	0
	No need in such observation	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	65	41%	74	45%
	No data*	0	0%	87	57%	113	69%	116	75%	12	8%	18	11%
12. Proteinuria													
	Yes	18	13%	25	16%	23	14%	6	4%	5	3%	4	2%
	No	125	87%	127	83%	135	82%	44	28%	47	30%	44	27%
	No need in such observation	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	86	54%	94	57%
	No data*	0	0%	1	1%	6	4%	104	68%	21	13%	24	14%
13. Microalbuminuria													
Microbumin test Bayer	-			29	19%	17	10%	20	13%	46	29%	51	31%
	+			10	7%	7	4%	9	6%	14	9%	13	8%
	++			5	3%	2	1%	1	1%	3	2%	2	1%
	+++			0	0%	1	1%	1	1%	0	0%	0	0%
	++++			0	0%	0	0%	1	1%	0	0%	0	0%
	No need in such observation	*n/a*	*n/a*	*n/a*	*n/a*	n/a	n/a	n/a	n/a	56	35%	65	39%
	No data*	143	100%	109	71%	137	84%	122	78%	40	25%	35	21%
14. Albumin/Creatinin (mg/mmol)													
	<2.5									30	19%	22	13%
	2.5-25									6	4%	3	2%
	>25									0	0%	0	0%
	No need in such observation											141	85%
	No data*									123	77%	0	0%

* Laboratory examination wasn't made for the reasons, not dependent on doctor's recomendation

Register of the Patients Under 18 with Diabetes
(all kids and teenagers of the city of Kazan)

13 Complications data

1.Ketoacidotic coma	1	1%	1	1%	0	0%	1	1%	0	0%	0	0%
2.Hypoglycemic coma	0	0%	1	1%	0	0%	1	1%	0	0%	0	0%
3.Diabetic retinopathy	67	47%	71	46%	71	45%	56	36%	48	30%	49	31%
4.Diabetic cataract	8	6%	11	7%	11	7%	9	6%	9	6%	9	6%
5.Diabetic nephropathy	12	8%	21	14%	31	19%	11	7%	8	5%	8	5%
6.Diabetic sensory neuropathy	18	13%	22	14%	23	14%	12	8%	13	8%	14	9%
7.Diabetic autonomous neuropathy	1	1%	1	1%	1	1%	1	1%	0	0%	0	0%
8.Diabetic foot syndrome	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
9.Hold up in physical and sexual development	4	3%	5	3%	5	3%	5	3%	4	3%	4	3%
10.Hairopathy	0	0%	12	8%	30	19%	40	26%	45	28%	47	30%
Myocardial infarction	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
Stenocardia	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
Artorial hypertension	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
Cerebral circularity disturbance	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
Lethality	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%

Register of the Patients Under 18 with Insulin-Dependent Diabetes and Insulin-Independent Diabetes

Changes in database:	I point	II point	III point	IV point	V point
Came from previous point:	0	143	156	167	154
Was added to create representative selection	143	0	0	0	0
New patients in Kazan endocrinology Dispancer (age<19)	0	14	12	11	19
Moved from kids database (age>19)	0	0	0	23	13
Moved out	0	1	1	1	1
Died	0	0	0	0	0
Total at point	143	156	167	154	159

DataBase: Adults (216) New patient:0

Insulin-Dependent Diabetes (172) **Period: 01.01.2003 - 06.01.2003**

Sex	**Male**: 76	**Female**: 96			
Age (years):	18-29: 84	30-39: 24	40-49: 32	50-59:24	60-69:6
					>70:2
Duration of	<5: 30	6-10: 58	11-20: 55	21-30: 19	
disease	31-40: 10	>40:0			
Body mass index:		<18.5: 10	18.5-24.9: 131	25-30: 25	>30:5
Diet:	Yes: 90	No: 12	Not regular: 70		
Self-control:	Regular:43	Episodic:64	None: 65		
Glucometer	Yes: 77	No: 96			
Diabetic school:		Yes: 172	No: 0		
Inheritance:		Yes: 5	No: 167		

Obtained hospital treatment: 57

Average time spent in hospital: 17 days

Average insulin dose per day : 49,54

Insulin therapy, based on human insulin: 172

Receive insulin in cartridges: 160

Receive insulin in vials: 12

Mixed (vials+cartridges): 0

Amount of injections per day: **3**: 3		**4**: 27	**5**: 135	**6**: 7
Complications amount per patient 0: 7	1: 22	2: 23	3: 35	4: 37
	5: 32	6: 11	7: 1	8: 1

Laboratory analysis

HbA1c (%)

<6.5: 1	**6.6-7.5**: 3	**7.5-9.5**: 6	**>9.5**: 8	No data*: 154

HbA1 (%) (Current research is not necessary for all patients)

<8: 0	**8.1-9.5**: 0	**>9.5**: 0	**No data***: 172

Total cholesterol (mmol/l)

<3,9: 9	**3,9-5.2**: 30	**5.3-6,5**: 20	**>6.5**: 5	**No data***: 108

Creatinine (mkmol/l)

<60: 5	**60-130**: 42	**>130**: 4	**No data***:57

No need in such observation: 64

Proteinuria

Yes: 17	**No**: 26	**No data***: 56

No need in such observation: 73

Microalbuminuria (Microbumin test Bayer)

"-":0	"+":6	"++":0	"+++": 0	"++++":0
No need in such observation: 40			No data*: 124	

61

Complications		
	New	Total
Diabetic coma	0	0
Hypoglycemic coma	0	0
Hold up in physical development	0	0
Hairopathy	4	27
Diabetic cataract	4	33
Diabetic retinopathy	0	145
Diabetic nephropathy	0	81
Diabetic sensory neuropathy	5	129
Autonomous neuropathy	5	16
Macroangiopaty of lower limbs	7	19
Diabetic foot	0	9
Stenocardia	2	7
Myocardial infarction	0	0
Cerebral circularity disturbance	0	1
Arterial hypertension	14	58

Lethality 1

* Laboratory examination wasn't made for the reasons, not dependent on doctor's recomendation

Register of Patients with Insulin-Dependent Diabetes (adults, representative selection)

		I stage 122 people 07.01.2000-12.31.2000		II stage 154 people 01.01.2001-06.30.2001		III stage 149 people 07.01.2001-12.31.2001		IV stage 165 people 01.01.2002-30.04.2002		V stage 173 people 05.01.02-12.31.02		VI stage 172 people 01.01.2003-	
		amount	%	amount	%	amount	%	amount	%	amount	%	amount	%
1. Body mass index kg/m2	<18.5	0	0%	0	0%	4	3%	7	4%	9	5%	10	6%
	18.5-24.9	99	82%	120	78%	106	71%	123	75%	130	75%	131	76%
	25.0-29.9	20	16%	29	19%	35	23%	30	18%	28	16%	25	15%
	30.0-39.9	3	2%	4	2%	4	3%	5	3%	6	3%	6	3%
	>40.0	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
	No data*	0	0%	1	1%	0	0%	0	0%	0	0%	0	0%
2. Diet													
	Yes	36	30%	48	31%	64	43%	81	49%	89	51%	90	52%
	No	5	4%	11	7%	13	9%	12	7%	16	9%	12	7%
	Not regular	81	66%	95	62%	72	48%	72	44%	67	39%	70	41%
3.Selfcontrol													
	Regular	40	33%	57	37%	57	38%	27	16%	35	20%	43	25%
	None	39	32%	43	28%	53	36%	49	30%	67	39%	65	38%
	Episodical	42	34%	54	35%	39	26%	89	54%	71	41%	64	37%
	Vital	1	1%	0	0%	0	0%	0	0%	0	0%	0	0%
4. Studied in the Diabetic school	Yes	99	81%	154	100%	149	100%	165	100%	173	100%	172	100%
	No	23	19%	0	0%	0	0%	0	0%	0	0%	0	0%
5.Glucometer													
	Yes	15	12%	28	18%	41	28%	66	40%	77	45%	77	45%
	No	107	88%	126	82%	108	72%	99	60%	96	55%	95	55%
6. Average insulin dose per day		45.4 pts		46.1 pts		45.9 pts		48.3 pts		49.9 pts		49.54 pts	
7. Obtained hospital treatment		80	66%	43	28%	47	31%	30	18%	54	33%	57	33%

Laboratory Analysis

8. HbA1c %	< 6.5	0	0%	0	0%	0	0%	0	0%	1	1%	1	1%
	6.6 - 7.5	1	1%	0	0%	0	0%	1	1%	3	2%	3	2%
	7.5-9.5									10	6%	6	3%
	> 9.5	1	1%	0	0%	4	3%	2	1%	7	4%	8	5%
	No data*	120	98%	154	100%	145	97%	162	98%	152	87%	154	89%
9. HbA1 %	< 8.0	0	0%	2	1%	1	1%	1	1%	0	0%	0	0%
	8.1 - 9.5	0	0%	1	1%	0	0%	0	0%	0	0%	0	0%
	> 9.5	0	0%	1	1%	1	1%	0	0%	0	0%	0	0%
	No data*	122	100%	150	97%	147	98%	164	99%	173	100%	172	100%
10. Total cholesterol mmol/l	<3.9					10	7%	8	5%	10	6%	9	5%
	3.9 - 5.2	78	64%	23	15%	20	13%	21	13%	45	26%	30	17%
	5.3 - 6.5	32	26%	7	5%	11	7%	13	8%	15	9%	20	12%
	> 6.5	11	9%	5	3%	8	5%	3	2%	9	5%	5	3%
	No data*	1	1%	119	77%	100	68%	120	73%	94	54%	108	63%
11. Creatinine mkmol/l	0-60	33	27%	5	3%	8	5%	5	3%	7	4%	5	3%
	61-130	69	57%	20	13%	32	21%	32	19%	46	27%	42	25%
	>130	5	4%	2	1%	3	2%	1	1%	4	2%	4	2%
	No need in such observation	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	64	37%	64	37%
	No data*	15	12%	127	83%	106	72%	127	77%	52	30%	57	33%
12. Proteinuria	Yes	24	20%	24	16%	35	23%	18	11%	14	8%	17	10%
	No	98	80%	54	35%	88	60%	31	19%	26	15%	26	15%
	No need in such observation	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	73	42%	73	42%
	No data*	0	0%	76	49%	26	17%	116	70%	60	35%	56	33%

* Laboratory examination wasn't made for the reasons, not dependent on doctor's recomendation

Register of Patients with Insulin-Dependent Diabetes
(adults, representative selection)

13 Complications data

1.Ketoacidotic coma	1	1%	0	0%	0	0%	1	1%	1	1%	0	0%
2.Hypoglycemic coma	3	2%	0	0%	0	0%	0	0%	0	0%	0	0%
3.Diabetic retinopathy	96	79%	135	88%	132	89%	145	88%	145	84%	145	84%
4.Diabetic cataract	16	13%	22	14%	28	19%	29	18%	29	17%	33	19%
5.Diabetic nephropathy	46	38%	76	49%	74	50%	77	47%	81	47%	81	47%
6.Diabetic sensory neuropathy	70	57%	102	66%	111	74%	124	75%	124	72%	129	75%
7.Diabetic autonomous neuropathy	1	1%	4	3%	5	3%	10	6%	11	6%	16	9%
8.Macroangiopathy of lower limbs	7	6%	9	6%	9	6%	12	7%	12	7%	19	11%
9.Diabetic foot syndrome	2	2%	9	6%	9	6%	10	6%	9	5%	9	5%
10.Hold up in physical and sexual development	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
11.Hairopathy	6	5%	8	5%	10	7%	22	13%	23	13%	27	16%
Myocardial infarction	0	0%	0	0%	1	1%	1	1%	1	1%	0	0%
Stenocardia	4	3%	6	4%	5	3%	5	3%	5	3%	7	4%
Arterial hypertension	10	8%	22	14%	27	18%	30	18%	44	25%	58	34%
Cerebral circularity disturbance	0	0%	0	0%	1	0%	1	1%	1	1%	1	1%
Lethality	0	0%	0	0%	5	3%	3	2%	4	2%	1	1%

Register of patients with insulin-dependent Diabetes(adults, representative selection) Changings in database:					
	I point	II point	III point	IV point	V point
Came from previous point:	0	122	154	149	165
Was added to create representative selection	122	32	0	0	0
Moved from kids database (age>19)	0	0		23	13
Moved out	0	0	0	4	1
Died	0	0	5	3	4
Total at point	**122**	**154**	**149**	**165**	**173**

Insulin-Independent Diabetes (44) **Period: 01.01.2003 - 06.01.2003**

Sex	**Male**: 15	**Female**: 29			
Age (years):	18-29: 0	30-39: 1	40-49: 6	50-59:15	60-69:17
					>70:5
Duration of disease	<5: 2	6-10: 11	11-20: 20	21-30: 10	
	31-40: 1	>40:0			
Body mass index:		<18.5: 0	18.5-24.9: 9	25-30: 16	>30:19
Diet:	Yes: 22	No: 5	Not regular: 17		
Self-control:	Regular:9	Episodic:6	None: 29		
Glucometer	Yes: 8	No: 36			
Diabetic school:		Yes: 44	No: 0		
Inheritance:		Yes: 3	No: 41		
Obtained hospital treatment: 15 Average time spent in hospital: 17,3 days					
Complications amount per patient	0: 1	1: 1 5: 6	2: 7 6: 8	3: 3 7: 7	4: 10 8: 1

Laboratory analysis				
HbA1c (%)				
<6.5: 0	**6.6-7.5**: 2	**7.5-9.5**: 2	**>9.5: 0**	No data*: 40
HbA1 (%) (Current research is not necessary for all patients)				
<8: 0	**8.1-9.5**: 0	**>9.5**: 0	**No data***: 44	
Total cholesterol (mmol/l)				
<3,9: 0	**3,9-5.2**: 10	**5.3-6,5**: 9	**>6.5**: 5	**No data***: 20
Creatinine (mkmol/l)				
<60: 1	**60-130**: 15	**>130**: 2	**No data***: 4	
No need in such observation: 20				
Proteinuria				
Yes: 1		**No**: 7		**No data***: 16
No need in such observation: 20				
Microalbuminuria (Microbumin test Bayer)				
"-":0	**"+"**: 4	**"++":0**	**"+++": 0**	**"++++":0**
No need in such observation: 15			No data*: 25	

Complications		
	New	Total
Diabetic coma	0	0
Hypoglycemic coma	0	0
Hold up in physical development	0	0
Hairopathy	0	3
Diabetic cataract	0	17
Diabetic retinopathy	0	41
Diabetic nephropathy	0	20
Diabetic sensory neuropathy	0	41
Autonomous neuropathy	0	4
Macroangiopaty of lower limbs	3	17
Diabetic foot	0	3
Stenocardia	0	19
Myocardial infarction	0	0
Cerebral circularity disturbance	0	7
Arterial hypertension	0	32

Lethality 1 Chronic cardiac insufficiency

* Laboratory examination wasn't made for the reasons, not dependent on doctor's recomendation

Therapy:

Insulin therapy, based on human insulin: 43 Average insulin dose: 37,4

Insulin monotherapy: 31

Insulin + glibenclamide/gliclazide: 9

Insulin + glibenclamide/gliclazide + metformin: 3

Cart. : 35 Vials: 8 Mixed: 0

Injections/day: 1:0 2: 6 3: 2 4: 11 5: 24

glibenclamide + metformin: 1

Register of the Patients with Diabetes II Type
(adults, representative selection)

		I stage 35 people 07.01.2000-12.31.2000		II stage 46 people 01.01.2001-06.30.2001		III stage 45 people 07.01.2001-12.31.2001		IV stage 45 people 01.01.2002-30.04.200		IV stage 45 people 05.01.02-12.31.02		V stage 44 people 01.01.03-06.01.03	
		amount	%	amount	%	amount	%						
1. Body mass index kg/m2	<18.5	0	0%	0	0%	1	2%	0	0%	0	0%	0	0%
	18.5-24.9	9	26%	9	20%	10	22%	13	28%	8	28%	9	20%
	25.0-29.9	15	43%	19	41%	17	38%	16	36%	17	38%	16	36%
	30.0-39.9	11	31%	18	39%	17	38%	16	36%	20	44%	19	44%
	>40.0	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
	No data*	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
2. Diet													
	Yes	12	34%	20	44%	24	53%	20	45%	22	49%	22	50%
	No	1	3%	2	4%	1	2%	1	2%	5	11%	5	11%
	Not regular	22	63%	24	52%	20	45%	24	53%	18	40%	17	39%
3.Selfcontrol													
	Regular	6	17%	11	24%	9	20%	5	11%	7	15%	9	20%
	None	18	52%	21	46%	25	56%	27	60%	30	67%	29	66%
	Episodical	11	31%	14	30%	11	24%	13	29%	8	18%	6	14%
	Vital	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
4. Studied in the Diabetic school	Yes	23	66%	46	100%	45	100%	45	100%	45	100%	44	100%
	No	12	34%	0	0%	0	0%	0	0%	0	0%	0	0%
5.Glucometer													
	Yes	1	1%	5	11%	6	13%	8	18%	8	18%	8	18%
	No	34	99%	41	89%	39	87%	37	82%	37	82%	36	82%
7. Obtained hospital treatment		26	74%	14	30%	13	29%	12	27%	11	25%	15	34%

Laboratory Analysis													
8. HbA1c													
%	<6.5	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
	6.6 - 7.5	0	0%	0	0%	1	2%	0	0%	2	4%	2	5%
	7.5-9.5	0	0%	0	0%	1	2%	5	11%	2	4%	2	5%
	>9.5	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	0	0%	0	0%
	No data*	35	100%	46	100%	43	96%	40	89%	41	92%	40	90%
9. HbA1													
%	J 8.0	0	0%	2	4%	0	0%	0	0%	0	0%	0	0%
	8.1 - 9.5	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
	> 9.5	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
	No data*	35	100%	44	96%	45	100%	45	100%	45	100%	44	100%
10. Total cholesterol	<3.9					2	4%	1	2%	1	2%	0	0%
mmol/l	3.9 - 5.2	12	34%	4	9%	4	9%	7	16%	7	16%	10	23%
	5.3 - 6.5	17	49%	2	4%	5	11%	5	11%	5	11%	9	20%
	> 6.5	6	17%	1	2%	8	17%	2	4%	4	9%	5	11%
	No data*	0	0%	39	85%	26	59%	30	67%	28	62%	20	46%
11. Creatinine													
mkmol/l	<60	4	11%	0	0%	1	2%	2	4%	2	4%	1	2%
	61-130	19	55%	4	9%	11	24%	6	13%	9	20%	15	34%
	>130	0	0%	0	0%	1	2%	2	4%	2	4%	2	5%
	No need in such observation	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	20	45%	20	45%
	No data*	12	34%	42	91%	32	72%	35	79%	12	27%	6	14%
12. Proteinuria													
	Yes	9	26%	4	9%	14	30%	6	14%	2	4%	1	2%
	No	26	74%	20	43%	21	46%	11	24%	7	16%	7	16%
	No need in such observation	n/a	n/a	n/a	n/a	n/a	n/a	n/a	n/a	20	44%	20	46%
	No data*	0	0%	22	48%	10	24%	28	62%	16	36%	16	36%

* Laboratory examination wasn't made for the reasons, not dependent on doctor's recomendation

Register of the patients with Diabetes II type
(adults, representative selection)

13 Complications data

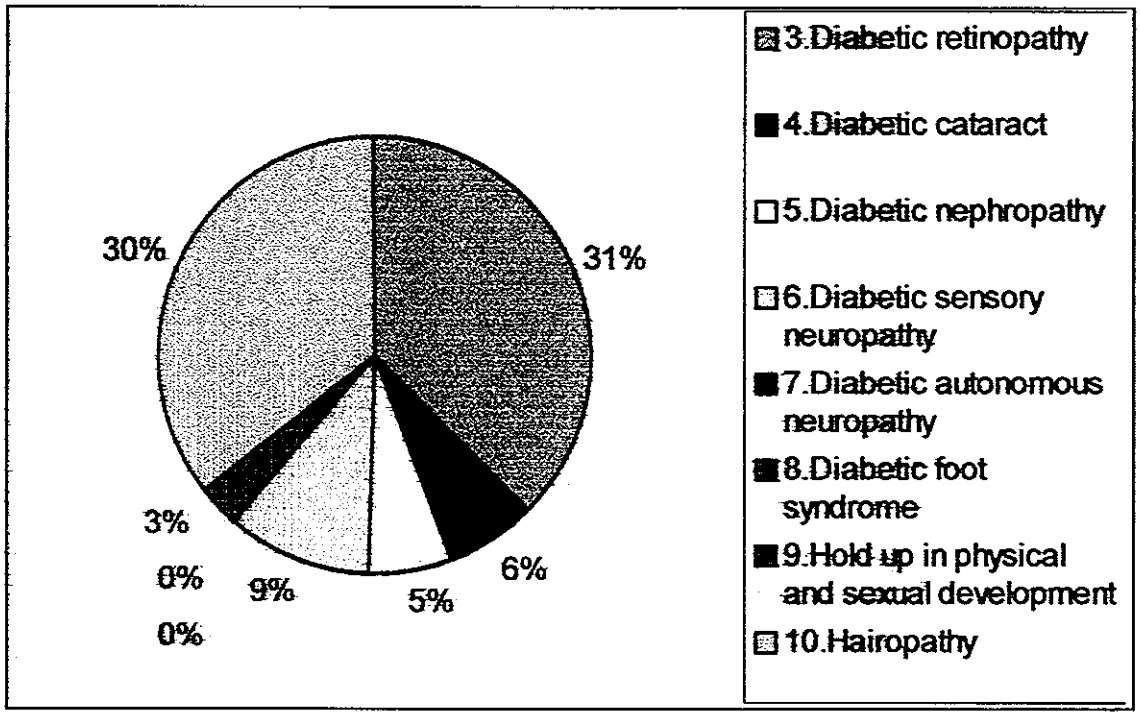
1.Ketoacidotic coma	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
2.Hypoglycemic coma	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
3.Diabetic retinopathy	28	80%	40	87%	39	87%	40	89%	41	91%	41	93%
4.Diabetic cataract	8	23%	14	30%	17	38%	19	42%	19	42%	17	39%
5.Diabetic nephropathy	10	29%	15	33%	18	40%	20	44%	21	47%	20	45%
6.Diabetic sensory neuropathy	29	83%	36	78%	36	80%	41	91%	41	91%	41	93%
7.Diabetic autonomous neuropathy	1	3%	1	2%	1	2%	4	9%	4	9%	4	9%
8.Macroangiopathy of lower limbs	11	31%	12	26%	12	26%	14	31%	14	31%	17	39%
9.Diabetic foot syndrome	2	6%	2	4%	2	4%	3	7%	3	7%	3	7%
10.Hold up in physical and sexual development	0	0%	0	0%	0	0%	0	0%	0	0%	0	0%
11.Hairopathy	0	0%	0	0%	1	2%	2	4%	3	7%	3	7%
Myocardial infarction	7	20%	7	15%	7	16%	7	16%	7	16%	0	0%
Stenocardia	7	20%	12	26%	13	29%	19	42%	19	42%	19	43%
Arterial hypertension	8	23%	14	30%	17	38%	30	67%	32	71%	32	73%
Cerebral circularity disturbance	3	9%	3	7%	0	0%	7	16%	7	16%	7	16%
Lethality	0	0%	0	0%	0	0%	0	0%	0	0%	1	2%

Register of the Patients with Diabetes II Type (Adults, Representative Selection)

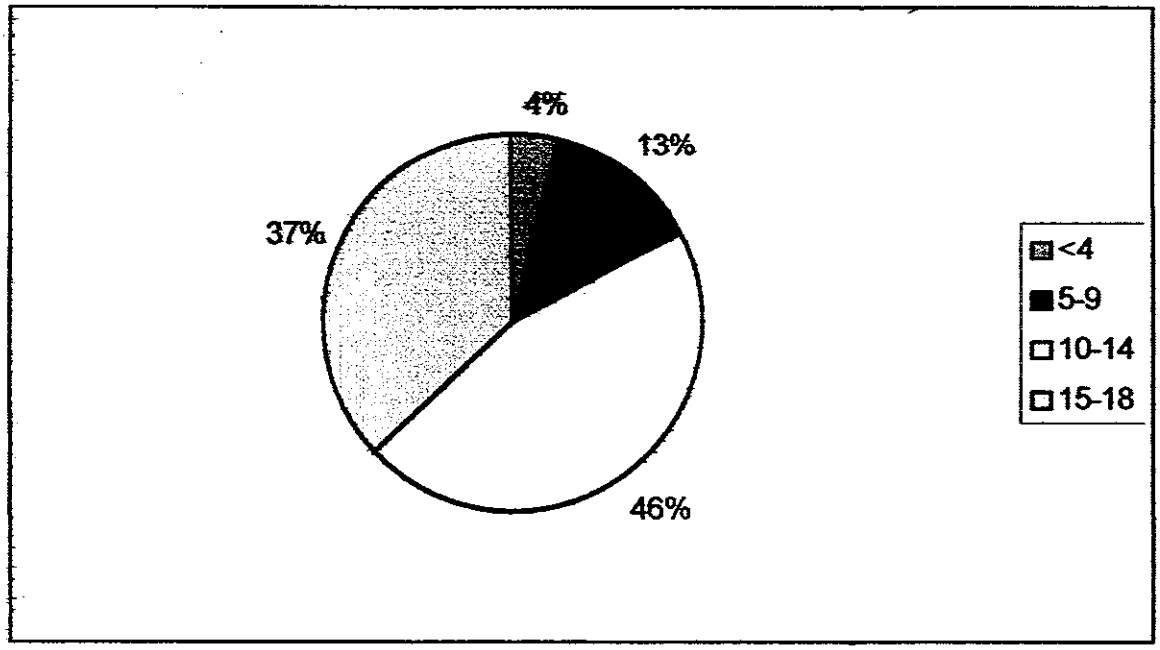
Changes in database:

	I point	II point	III point	IV point	V point	VI point
Came from previous point:	0	35	46	45	45	45
Was added to create representative selection	35	11	0	0	0	0
Moved from kids database (age>19)	0	0		0	0	0
Moved out	0	0	1	0	0	0
Died	0	0	0	0	0	1
Total at point	35	46	45	45	45	44

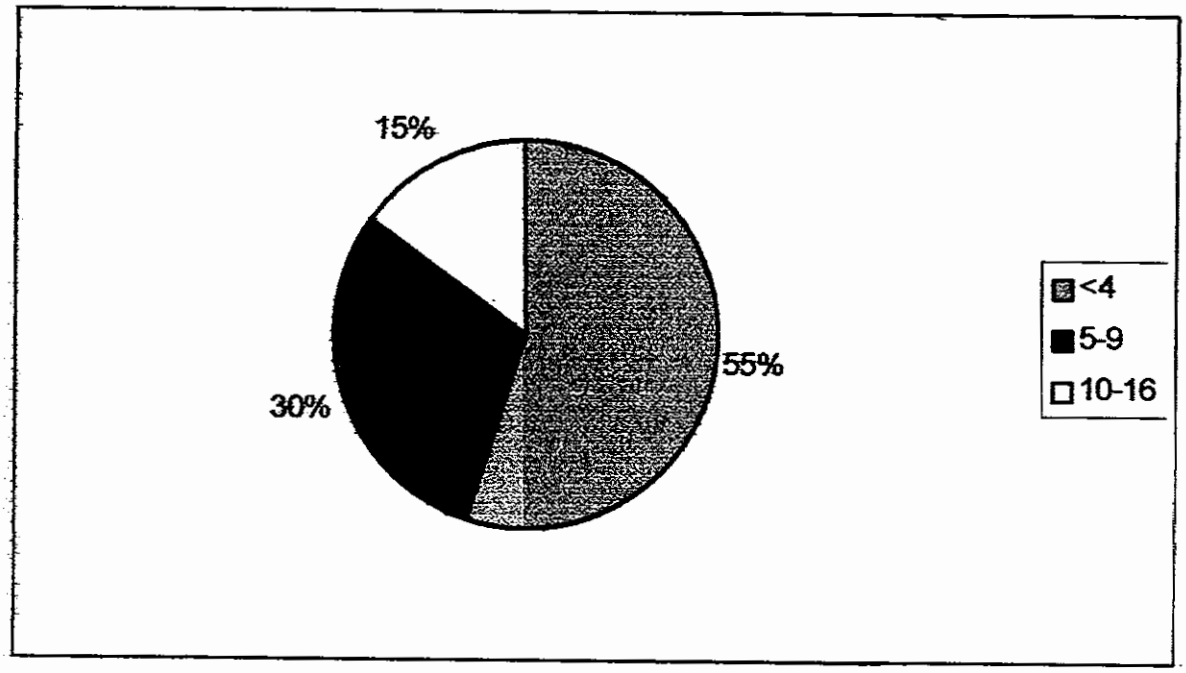
Complications in patients under 18 years of age with Diabetes mellitus of type 1 by the 1st of June 2003 (01.06.2003)



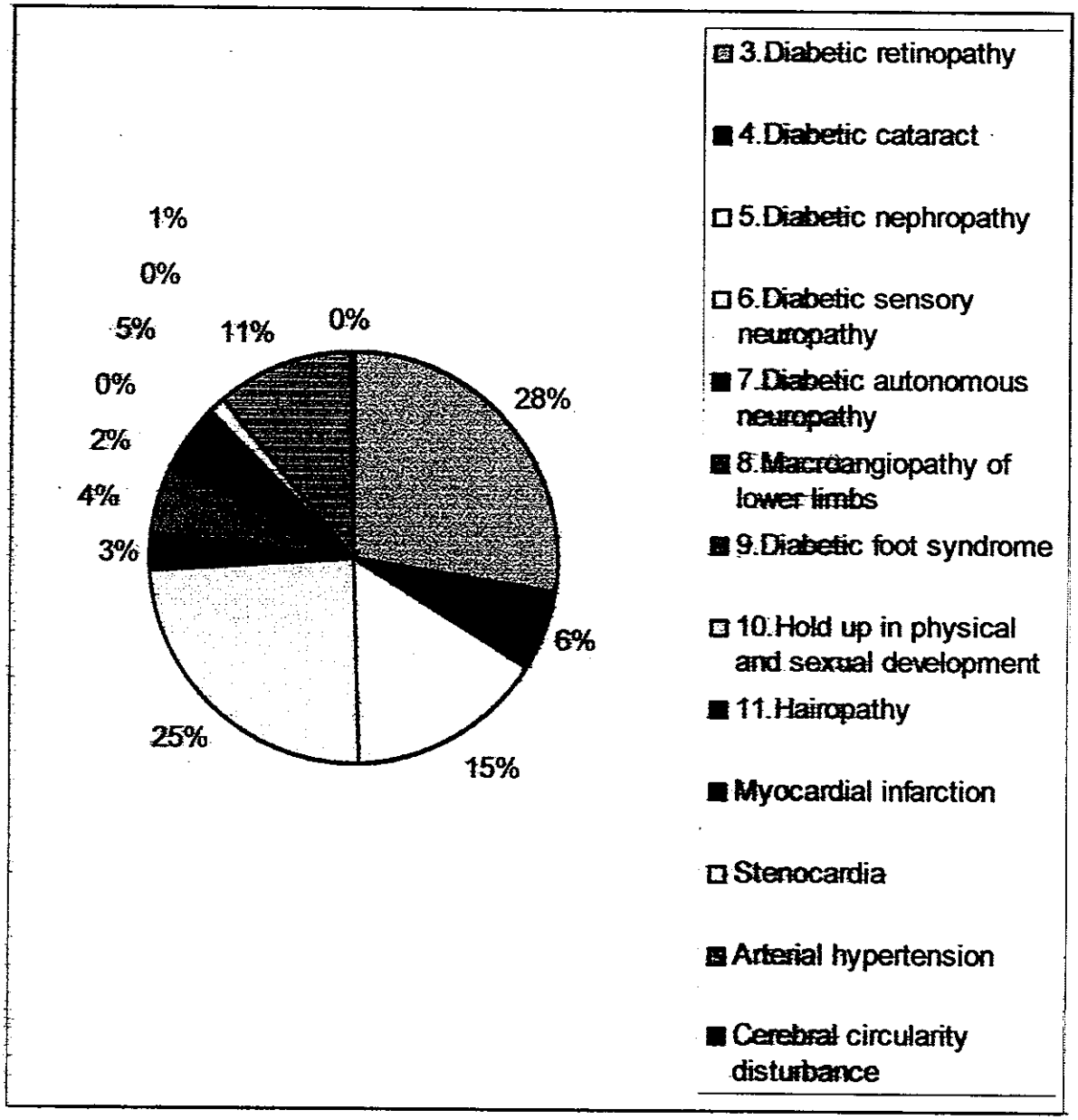
Distribution by age of patients under 18 years of age with Diabetes mellitus of type 1 by the 1st of June 2003 (01.06.2003, Kazan)



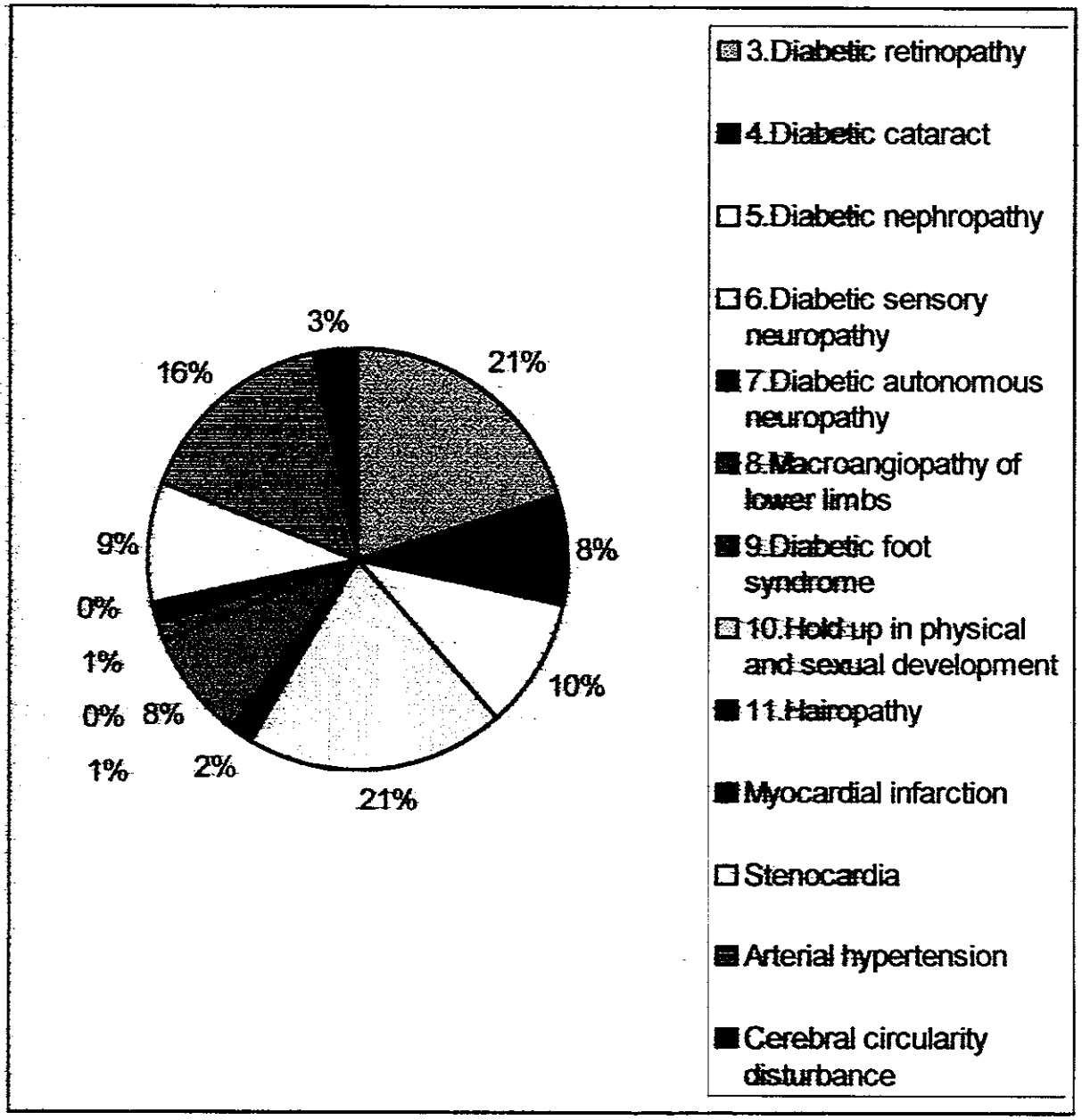
Duration of the disease in patients under 18 years of age with Diabetes mellitus of type 1 by the 1st of June 2003 (01.06.2003, Kazan)



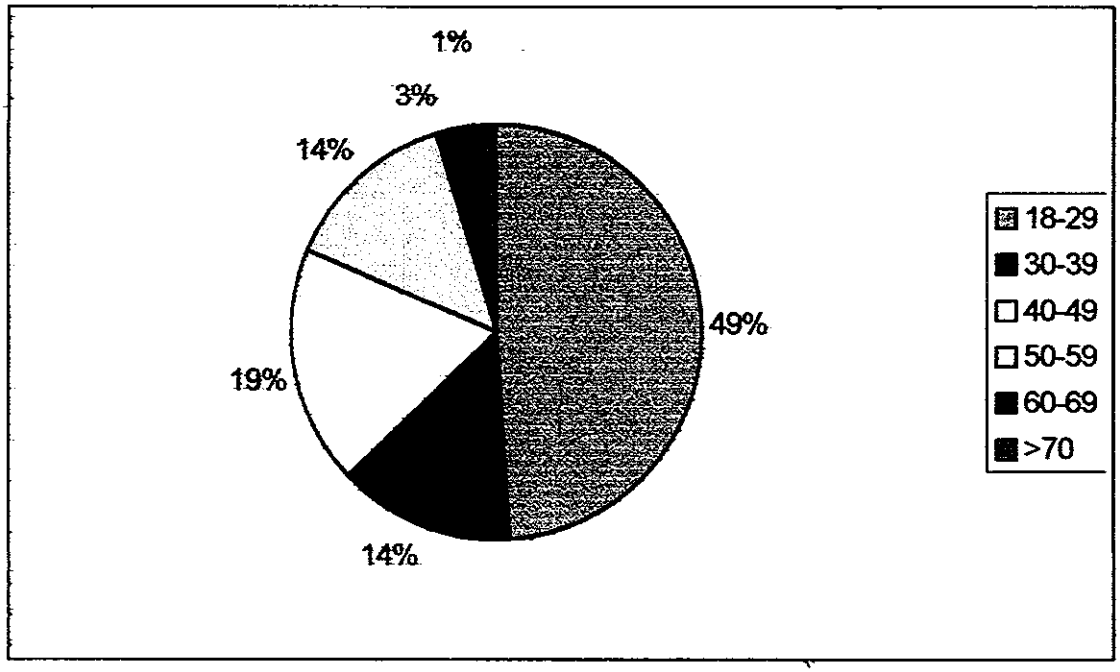
Complications in patients over 18 years of age with Diabetes mellitus of type 1 by the 1st of June 2003 (01.06.2003)



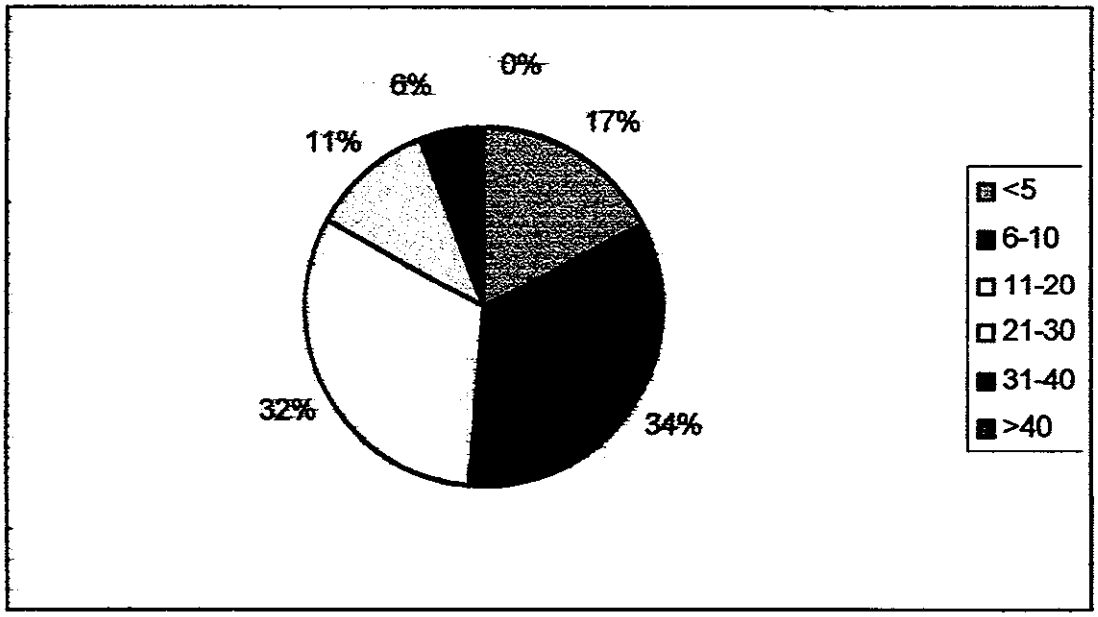
Complications in patients over 18 years of age with Diabetes mellitus of type 2 by the 1st of June 2003 (01.06.2003)



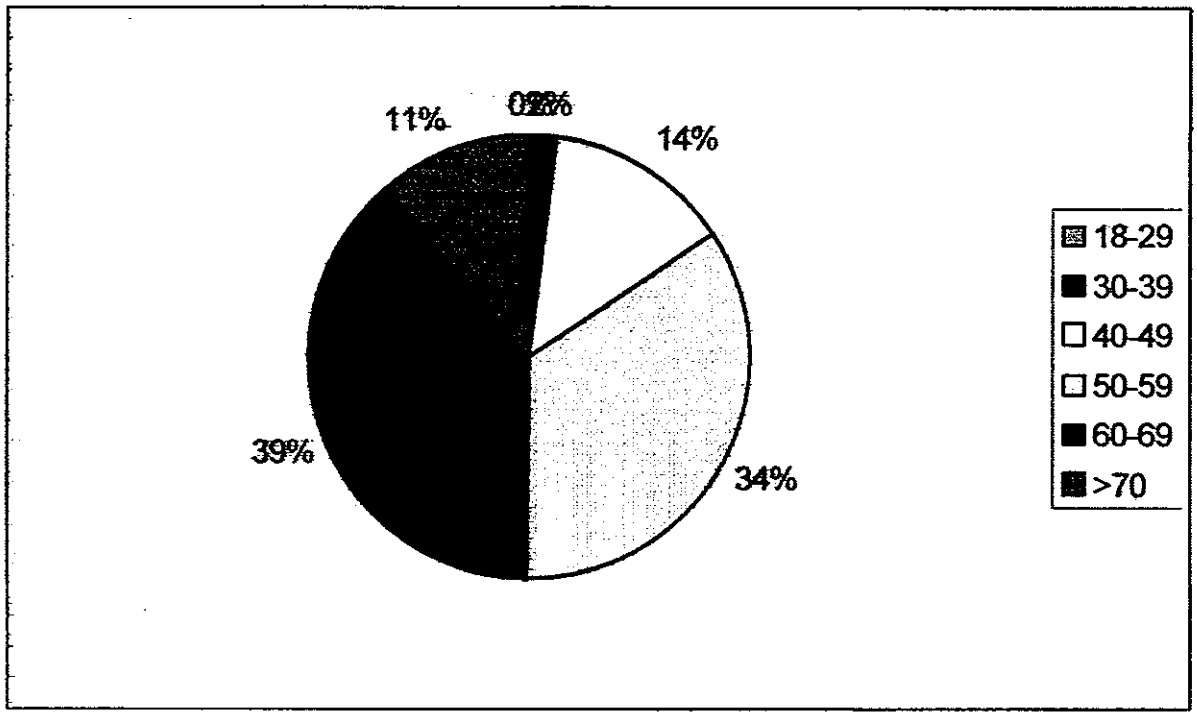
Distribution by age of patients over 18 years of age with Diabetes mellitus of type 1 by the 1st of June 2003 (01.06.2003, Kazan)



Duration of the disease in patients over 18 years of age with Diabetes mellitus of type 1 by the 1st of June 2003 (01.06.2003, Kazan)



Distribution by age of patients over 18 years of age with Diabetes mellitus of type 2 by the 1st of June 2003 (01.06.2003, Kazan)



Duration of the disease in patients over 18 years of age with Diabetes mellitus of type 2 by the 1st of June 2003 (01.06.2003, Kazan)

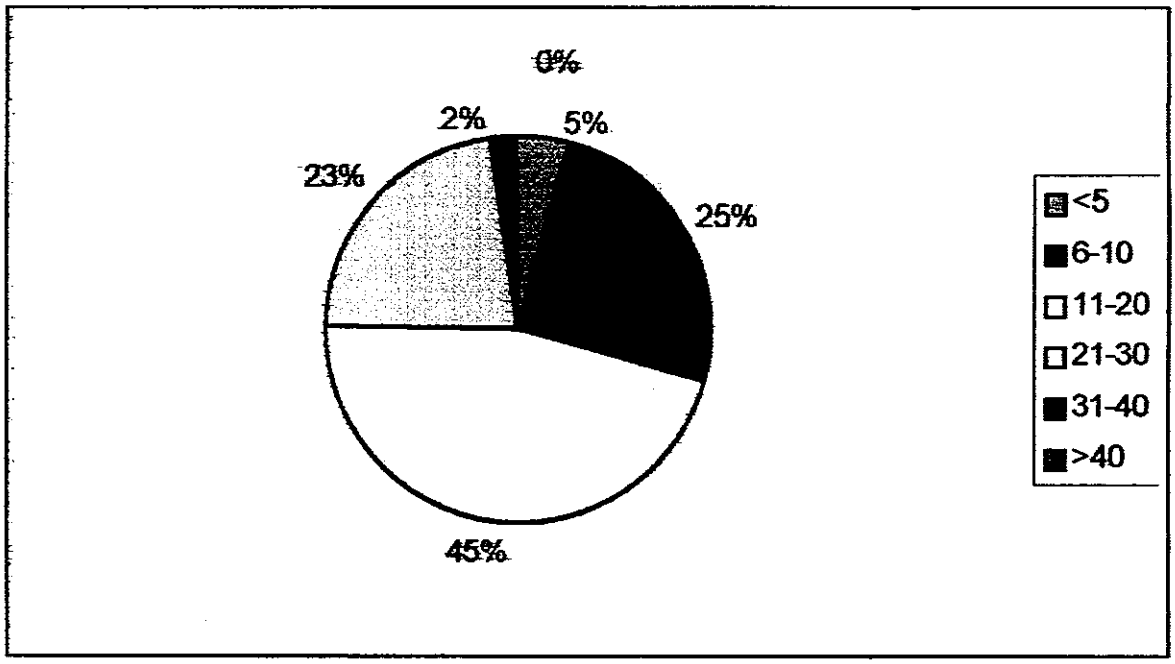


Table. The results of evaluation by the audience of the course of lectures by the EMEP visiting professors given at: (absolute/percentage, n=)

NN	Statement	Fully agree	Agree	Neutral	Disagree	Fully disagree
1.	The lecturer was well prepared					
2.	The lecturer communicated his subject well					
3.	The lecturer stimulated interest in the topic					
4.	The lecturer clearly interpreted abstract ideas and theories					
5.	The lecturer demonstrated a favorable attitude toward the audience					
6.	The lecturer encouraged the audience to think for themselves					
7.	The lecturer presented material in an organized manner					
8.	The lecturer appears to be an enthusiastic teacher					
9.	The lecturer used clear illustrations to clarify the material					
10.	The lecturer tried to cover too much material					
11.	The lecturer stimulated me to want to learn more					
12.	The lecture was geared to an appropriate level					
13.	The lecturer made good use of audiovisuals					
14.	The general quality of the lecture was excellent					

Table 1. The results of evaluation by the audience of the course of lectures by the EMEP visiting professors given at the Republican conference "Women's health – interdisciplinary approach" (9-10/10/2002) (absolute/percentage, n=81)

NN	Statement	Fully agree	Agree	Neutral	Disagree	Fully disagree
1.	The lecturer was well prepared	48/59	32/40	1/1	0	0
2.	The lecturer communicated his subject well	54/67	26/32	1/1	0	0
3.	The lecturer stimulated interest in the topic	43/53	36/45	1/1	1/1	0
4.	The lecturer clearly interpreted abstract ideas and theories	20/25	51/63	10/12	0	0
5.	The lecturer demonstrated a favorable attitude toward the audience	48/59	30/37	3/4	0	0
6.	The lecturer encouraged the audience to think for themselves	23/28	42/52	15/19	1/1	0
7.	The lecturer presented material in an organized manner	46/57	31/38	4/5	0	0
8.	The lecturer appears to be an enthusiastic teacher	32/40	43/53	5/6	1/1	0
9.	The lecturer used clear illustrations to clarify the material	36/45	39/48	6/7	0	0
10.	The lecturer tried to cover too much material	4/5	10/12	31/38	33/41	3/4
11.	The lecturer stimulated me to want to learn more	13/16	51/63	16/20	1/1	0
12.	The lecture was geared to an appropriate level	19/23	56/70	6/7	0	0
13.	The lecturer made good use of audiovisuals	37/46	38/47	5/6	1/1	0
14.	The general quality of the lecture was excellent	36/45	41/50	4/5	0	0

Table. The results of evaluation by the audience of the course of lectures by the EMEP visiting professors given at the Republican conference «**Prevention of Chronic diseases as the major public health problem (cardiology, rheumatology, pharmacology и managerial aspects)» 21-22 April 2003.**
(absolute/percentage, n=46)

NN	Statement	Fully agree	Agree	Neutral	Disagree	Fully disagree
1.	The lecturer was well prepared	28/61	18/39	½	0	0
2.	The lecturer communicated his subject well	29/63	16/35	1/2	0	0
3.	The lecturer stimulated interest in the topic	24/52	21/46	1/2	0	0
4.	The lecturer clearly interpreted abstract ideas and theories	16/35	25/54	5/10,8	0	0
5.	The lecturer demonstrated a favorable attitude toward the audience	28/61	18/39	0/0	0	0
6.	The lecturer encouraged the audience to think for themselves	7/15	32/70	7/15	0/0	0
7.	The lecturer presented material in an organized manner	26/46	17/37	3/6,5	0	0
8.	The lecturer appears to be an enthusiastic teacher	19/41	22/48	5/10,8	1/2	0
9.	The lecturer used clear illustrations to clarify the material	22/48	20/43	4/8,7	0	0
10.	The lecturer tried to cover too much material	4/8,7	6/13	26/56	8/17	2/4
11.	The lecturer stimulated me to want to learn more	5/10,8	32/70	9/19	0/0	0
12.	The lecture was geared to an appropriate level	10/21,7	29/63	6/13	½	0
13.	The lecturer made good use of audiovisuals	23/50	21/46	2/4	0/0	0
14.	The general quality of the lecture was excellent	25/54	17/37	4/8,7	0	0

On the 21st April 220 participants registered
On the 22d April 121 participants registered

ACKNOWLEDGEMENTS & COMMENTS

Participation in the Eurasian Medical Education Program (EMEP) has been a rewarding experience for all concerned; there is a palpable impression that Russian patients are benefiting from the medical information and knowledge transmitted to their physicians. The spirit of volunteerism and the desire to impart one's own professional experience to others are strong motivating factors. Much credit to the American College of Physicians (ACP), the largest medical professional organization in the United States with more than 100,000 physician members, is due.

The concept of partnership with the ACP and the Institute for Health Policy Analysis (IHPA) – a 501 (c)(3) organization – was developed by its director, Dr. Edward Burger, and me (former ACP regent) in 1997. Dr. Burger made the first trip and made arrangements for collaboration with academic institutions in Kazan, Ekaterinburg, and Khabarovsk, and recruited coordinators to serve as the in-country organizers of the continuing medical education (CME) programs. This partnership has continued to the present.

Dr. Alexei Sirotin – and now Dr. Maria Syrochkina – have served in Ekaterinburg, Dr. Lilia Ziganshina in Kazan, and Anatoli Fomine, MBA, in Khabarovsk. Each has been superb and has enabled EMEP to maintain close working relationships with academic, governmental and clinical leadership in each location. The respect by their colleagues has been a major factor in EMEP success.

Our EMEP colleagues in Washington have likewise been essential. Ms. Roberta Wirth, MAS, an experienced international program and organizational participant, has been outstanding in financial administration, program organization and administrative management experience. Dr. Harvey Sloane, former commissioner of health for the District of Columbia, has been primarily responsible for EMEP tuberculosis activities; he has visited TB wards in prisons in all three locations, one of few American physicians to have done so. Ms. Elizabeth Evanoff has been an able administrative assistant, coordinating each trip, visas, accommodations and financial details; she also has served as support for Ms. Wirth.

Our ACP colleagues have been both supportive and advisory. Dr. Joseph E. Johnson III, formerly dean of the University of Michigan, has been EMEP liaison with the ACP as well as served as visiting professor of infectious diseases. Dr. Walter McDonald and Dr. John Tooker, CEO of the ACP, have been highly supportive. Ms. Eve Swiacki, administrator of the International Subcommittee of the ACP, to which EMEP reports, has greatly facilitated this interaction. Dr. Sara Walker, president of the ACP in 2002-2003, served as visiting professor for EMEP during her presidency and was instrumental in advising regarding women's health issues. Dr. John Noble was an early participant in EMEP and was of assistance in establishing EMEP relations in TB.

Visiting professors who made multiple visits were the core of the CME programs. Dr. Henry Greenberg, FACP, Columbia University, served as cardiovascular consultant for EMEP and was instrumental in developing programs in Ekaterinburg and Kazan. Dr. Bruce Lloyd, FACP, Georgetown University, served as cardiovascular professor/advisor in Khabarovsk and Tula (latter 1999-2001). Dr. Gerald Bernstein, FACP, and Dr. Frank Vinicor, FACP, each a former president of the American Diabetes Association, developed the core information for the diabetes program. Dr. Michael Iseman, FACP, University of Colorado, was essential in the tuberculosis (TB) programs and teams of Russian physicians visited him in Denver on three occasions.

EMEP could not have functioned without the wholehearted support by our Russian colleagues. In each location, EMEP has been fully integrated into the formal CME programs of the academic institution responsible for the mandatory CME programs in the Russian Federation.

The rectors of the academic centers in each location gave their full support – Professor Yasterbov in Ekaterinburg (the Urals State Medical Academy), Professor Mikhailov in Kazan (Kazan State Medical Academy) and Professor Kogut in Khabarovsk (Far Eastern Medical University).

In the Republic of Tartarstan, there was additional support from Deputy Prime Minister Burnashov, Minister of Health Kamil Sh. Zyatdinov, and Deputy Minister Galiullin.

As medical (program) director, I worked directly with those responsible for CME programs; planning for each program was done collaboratively. In Ekaterinburg, Dr. Yuri Chugaev was vice-rector of CME as well as director of tuberculosis educational programs. In Kazan, Vice-Rectors Tsibulkin and Nizamov were instrumental in program development, implementation and evaluation. In the Far East, Professor Kogut had a specific interest in family medicine, from which programs and data collection emanated. Dr. Charles Christianson, University of North Dakota, has served as EMEP advisor in family medicine. For purposes of data collection, Dr. Zyangirova in Kazan developed a diabetes program with EMEP assistance that can serve as a model. Professor Galyavich served as supervisor to the cardiovascular data collection in Kazan; Dr. Arkhipov served a similar role in Ekaterinburg. In all of these activities, the professional relationships developed by EMEP and ACP with Russian colleagues enabled the success of the programs themselves, their organization and data collection.

The original concept of EMEP was to address diseases that are serious, often fatal, require enormous resources, and are best served by chronic disease management, primary and secondary prevention, lifestyle modification, and "low tech" management. The emphasis has been on outpatient care, and involvement by primary care physicians and others in the health care system. The diseases addressed by EMEP cause approximately 60% of all deaths (at all ages, from all causes) in the Russian Federation and are largely responsible for the decrease in population and male longevity over the past several years.

The vehicle of CME is only the beginning of EMEP activity in Russia: involvement in polyclinics and data collection followed. Expression of programs, including women's health, public health, prevention programs and public education have been results of EMEP-initiated contact and relationships developed.

Richard G. Farmer, MD, MACP
Medical Director, EMEP
July 2003

Eurasian Medical Education Program

Performance Indicator Reference Sheet

Strategic Objective: Management of conditions that are the leading causes of death and disability in Russia is improved.

Intermediate Result:

SO Indicator 1a: # cases of diabetic patients with diabetic foot in two selected sites, % of diabetic patients with diabetic foot in third site.

DESCRIPTION

Precise Definition: The incidence of diabetic foot that occurs in the cohort of diabetic patients followed by the project. Diabetic foot is a complication of diabetes manifested by an infection in the feet that could lead to gangene and possible amputation. It is a leading cause of disability and death among patients with uncontrolled diabetes. Successful physician management of diabetes should result in minimal cases of diabetic foot.

Unit of Measure: Diabetic patients with diabetic foot in two selected sites. In the third site the number of patients with diabetic foot is divided by the total number of diabetic patients in the cohort. There is a predetermined cohort of patients registered for treatment at the Diabetes Center. The unit will be those diabetic patients who have symptoms of diabetic foot.

Disaggregated by:

Justification/Management Utility: Diabetes impairs nerve function and blood flow to the feet, increasing the risk of infection. Diabetic foot is a serious complication that occurs when cuts and sores on the feet are not treated promptly.

PLAN FOR DATA ACQUISITION BY USAID

Data Collection Method: Data on each patient registered at the Diabetes Center is collected on a form designed through a collaboration between EMEP and local Russian Academic professors.

Method of Acquisition by USAID: EMEP reports data to USAID as required.

Data Source(s): The Diabetes Center maintains the data for its patients.

Timing/Frequency of Data Acquisition: Data is collected on each patient during mandatory quarterly visits to the Center.

Estimated Cost of Data Acquisition: Data on control of blood sugar and complications of diabetes are routinely recorded in the patient's medical record. Subsequently, the data is transferred to a data collection form that lists the entire cohort of patients followed in this project.

Responsible Individual(s) at USAID: Data is reported to Elena Gurvich, USAID/Moscow

PLAN FOR DATA ANALYSIS, REVIEW, & REPORTING

Data Analysis: Data is analyzed by at least three physicians: 1) the EMEP partner, a Russian academic professor, 2) an EMEP US Board Certified physician specializing in diabetes and 3) a US Board Certified specialist in internal medicine.

Presentation of Data:

Review of Data: Data is reviewed quarterly upon submission by Diabetes Center to EMEP.

Reporting of Data: The Diabetes Center reports quarterly to EMEP

DATA QUALITY ISSUES

Date of Initial Data Quality Assessment:

Known Data Limitations and Significance (if any): The data relates to the cohort of patients followed by the study and is *representative of the results of the CME training of physicians.* It does not measure all patients that are benefiting from the physician training.

Actions Taken or Planned to Address Data Limitations: It is not feasible to follow all patients benefiting from the study. A cohort study is a valid protocol.

Date of Future Data Quality Assessments: Data is reviewed semi-annually by EMEP physician.

Procedures for Future Data Quality Assessments: The chief of the Diabetes Center and a person responsible for data collection in the clinic are trained by EMEP and Russian academics in the data collection methodology for the project. Thereafter, the chief of the Diabetes Center supervises the person who has been trained in data collection and conducts the first level of review of the data.

OTHER NOTES

(e.g., on baselines and targets; key to performance data table; location of data storage; etc.)

Note on Baselines/Targets: Baseline data was collected before the EMEP program was implemented.

Key to data table: Site 1: Ekaterinburg, Site 2: Kharbarovsk, Site 3: Kazan

THIS SHEET LAST UPDATED ON: 12/17/02

Eurasian Medical Education Program

Performance Indicator Reference Sheet

Strategic Objective: Management of conditions that are the leading causes of death and disability in Russia is improved.

Intermediate Result:

SO Indicator 1b: # cases of diabetic patients with ketoacidosis requiring hospitalization in two selected sites.

DESCRIPTION

Precise Definition: The incidence of ketoacidosis that occurs in the cohort of diabetic patients followed by the project. Ketoacidosis is a complication of diabetes, which can lead to a loss of consciousness.

Unit of Measure: Diabetic patients with ketoacidosis requiring hospitalization in selected sites. There is a predetermined cohort of patients registered for treatment at the Diabetes Center. The unit will be those diabetic patients who have symptoms of uncontrolled blood sugar levels resulting in inpatient treatment.

Disaggregated by:

Justification/Management Utility: Diabetes occurs when the pancreas stops producing insulin or does not produce enough insulin to absorb glucose in the blood. When diabetes is not controlled, glucose builds up in the blood and the body gets its energy from fat. This leads to a dangerous condition known as ketoacidosis, which can cause a diabetic coma. Ketoacidosis is the leading cause of death and disability among patients with uncontrolled diabetes. Successful management of diabetic cases should lead to minimal incidences of ketoacidosis requiring hospitalization.

PLAN FOR DATA ACQUISITION BY USAID

Data Collection Method: Data on each patient registered at the Diabetes Center is collected on a form designed through a collaboration between EMEP and local Russian Academic professors.

Method of Acquisition by USAID: EMEP reports data to USAID as required.

Data Source(s): The Diabetes Center maintains the data for its patients.

Timing/Frequency of Data Acquisition: Data is collected on each patient during mandatory quarterly visits to the Center.

Estimated Cost of Data Acquisition: Data on control of blood sugar and complications of diabetes are routinely recorded in the patient's medical record. Subsequently, the data is transferred to a data collection form that lists the entire cohort of patients followed in this project.

Responsible Individual(s) at USAID: Data is reported to Elena Gurvich, USAID/Moscow

PLAN FOR DATA ANALYSIS, REVIEW, & REPORTING

Data Analysis: Data is analyzed by at least three physicians: 1) the EMEP partner, a Russian academic professor, 2) an EMEP US Board Certified physician specializing in diabetes and 3) a US Board Certified specialist in internal medicine.

Presentation of Data:

Review of Data: Data is reviewed quarterly upon submission by Diabetes Center to EMEP.

Reporting of Data: The Diabetes Center reports quarterly to EMEP

DATA QUALITY ISSUES

Date of Initial Data Quality Assessment: Data is reviewed quarterly. EMEP physician meets with data collector to review data quality semiannually.

Known Data Limitations and Significance (if any): *The data relates to the cohort of patients followed by the study and is* representative of the results of the CME training of physicians. It does not measure all patients that are benefiting from the physician training.

Actions Taken or Planned to Address Data Limitations: It is not feasible to follow all patients benefiting from the study. A cohort study is a valid scientific protocol.

Date of Future Data Quality Assessments: Data is reviewed quarterly.

Procedures for Future Data Quality Assessments: The chief of the Diabetes Center and a person responsible for data collection in the clinic are trained by EMEP and Russian academics in the data collection methodology for the project. Thereafter, the chief of the Diabetes Center supervises the person who has been trained in data collection and conducts the first level of review of the data.

OTHER NOTES

(e.g., on baselines and targets; key to performance data table; location of data storage; etc.)

Note on Baselines/Targets: Baseline data was collected before the EMEP program was implemented.

Key to data table: Site 1: Ekaterinburg, Site 2: Kharbarovsk

Data Storage:

THIS SHEET LAST UPDATED ON: 12/17/02

Eurasian Medical Education Program

Performance Indicator Reference Sheet

Strategic Objective: Management of conditions that are the leading causes of death and disability in Russia is improved.

Intermediate Result:

SO Indicator 2: % hypertension patients with controlled blood pressure (below 140/90).

DESCRIPTION

Precise Definition: Blood pressure over 140/90 is considered elevated. Patients with blood pressure below 140/90 are controlling their blood pressure.

Unit of Measure: The percentage of hypertension patients in three selected sites who have controlled blood pressure. The *number of patients with cardiac disease who have controlled blood pressure is divided by the total number of cardiac* patients in the cohort. There is a predetermined cohort of patients registered for treatment at the selected polyclinics.

Disaggregated by:

Justification/Management Utility. High blood pressure is symptom of coronary artery disease, a leading cause of disability and death in the Russian Federation. Successful physician management of elevated blood pressure should result in minimal cases of complications from hypertension. Increasing the percentage of hypertension patients with controlled blood pressure is the objective of improved physician management.

PLAN FOR DATA ACQUISITION BY USAID

Data Collection Method: Data on each hypertension patient is collected on a form designed through a collaboration between EMEP and local Russian Academic professors.

Method of Acquisition by USAID: EMEP reports data to USAID as required.

Data Source(s): The polyclinics maintain the data for their patients.

Timing/Frequency of Data Acquisition: Data is collected on each patient during physician visits.

Estimated Cost of Data Acquisition: Blood pressure is routinely recorded in the patient's medical record. Subsequently, the data is transferred to a data collection form that lists the entire cohort of patients followed in this project.

Responsible Individual(s) at USAID: Data is reported to Elena Gurvich, USAID/Moscow

PLAN FOR DATA ANALYSIS, REVIEW, & REPORTING

Data Analysis: Data is analyzed by at least three physicians: 1) the EMEP partner, a Russian academic professor, 2) an EMEP US Board Certified physician specializing in cardiology and 3) a US Board Certified specialist in internal medicine.

Presentation of Data:

Review of Data: Data is reviewed quarterly upon submission to EMEP.

Reporting of Data: The partner institutions report quarterly to EMEP

DATA QUALITY ISSUES

Date of Initial Data Quality Assessment:

Known Data Limitations and Significance (if any): The data relates to the cohort of patients followed by the study and is representative of the results of the CME training of physicians. It does not measure all patients that are benefiting from the physician's new continuing education curriculum.

Actions Taken or Planned to Address Data Limitations: It is not feasible to follow all patients benefiting from the study. A cohort study is a valid protocol.

Date of Future Data Quality Assessments: Data is reviewed by EMEP physician semi-annually.

Procedures for Future Data Quality Assessments: The chief of the polyclinic and a person responsible for data collection in the clinic are trained by EMEP and Russian academics in the data collection methodology for the project. Thereafter, the chief of the polyclinic supervises the person who has been trained in data collection and conducts the first level of review of the data.

OTHER NOTES

(e.g., on baselines and targets; key to performance data table; location of data storage; etc.)

Note on Baselines/Targets: Baseline data was collected before the EMEP program was implemented.

Key to data table: Site 1: Ekaterinburg, Site 2: Khabarovsk, Site 3: Kazan

Storage of Data: Primary data from the medical records is stored at the polyclinic. Aggregated data is stored at the academic center and reported to EMEP.

THIS SHEET LAST UPDATED ON: 12/17/02

Eurasian Medical Education Program

Performance Indicator Reference Sheet

Strategic Objective: Management of conditions that are the leading causes of death and disability in Russia is improved.

Intermediate Result:

SO Indicator 3: # of patients completing continuous TB treatment, *i.e. the DOTS protocol, in one oblast.*

DESCRIPTION

Precise Definition: # of patients who completed continuous TB treatment (DOTS)

Unit of Measure: Those who fully completed treatment, without interruption

Disaggregated by: Patients in city, oblast, prisons

Justification/Management Utility: Indicator of both CME and disease management

PLAN FOR DATA ACQUISITION BY USAID

Data Collection Method: Central data collection system, based on EMEP (DOTS) principles of treatment

Method of Acquisition by USAID: EMEP and Russian TB specialists

Data Source(s): City, oblast and prison data, coordinated by EMEP

Timing/Frequency of Data Acquisition: Annually, as part of official registry

Estimated Cost of Data Acquisition: Included in EMEP

Responsible Individual(s) at USAID: Data is reported to Elena Gurvich, USAID/Moscow

PLAN FOR DATA ANALYSIS, REVIEW, & REPORTING

Data Analysis: Comparison of previous experience before EMEP/DOTS protocols

Presentation of Data: Based on collaboration among city, oblast, and prison TB specialists

Review of Data: By Russian academic and clinical physicians, EMEP and US TB specialists

Reporting of Data: Reported as result of EMEP activities

DATA QUALITY ISSUES

Date of Initial Data Quality Assessment: Baseline, followed by prekazes and policy change

Known Data Limitations and Significance (if any): Potential due to release of prisoners into civilian TB system

Actions Taken or Planned to Address Data Limitations: Programs specifically to address collaboration

Date of Future Data Quality Assessments: Assessment annually (or sooner, if possible)

Procedures for Future Data Quality Assessments: Based on results of treatment

OTHER NOTES

(e.g., on baselines and targets; key to performance data table; location of data storage; etc.)

Note on Baselines/Targets: Results of the continuous TB treatment (DOTS) protocols directly attributable to EMEP activities. CME and TOT programs in Russia, and 8 visits to the US to learn and observe directly DOTS programs in 3 locations (Newark, Baltimore, Denver).

Key to data table: Site 1: Ekaterinburg, Site 2: Kharbarovsk, Site 3: Kazan

Storage of Data: Local TB centers and EMEP

THIS SHEET LAST UPDATED ON: 12/17/02

Eurasian Medical Education Program

Performance Indicator Reference Sheet

Strategic Objective: Management of conditions that are the leading causes of death and disability in Russia is improved.

Intermediate Result 1: Physician practice related to diagnosis and treatment of diabetes improved.

IR Indicator 1.1: % diabetic patients complying with prescribed medications and diet in three selected sites.

DESCRIPTION

Precise Definition: In the cohort of diabetic patients followed by the project, the percentage of total cohort patients whose records show that they are complying with the regime of prescribed medications and diet.

Unit of Measure: Diabetic patients in selected sites who are complying is the numerator. The denominator is the total number of patients in the cohort in each site. There is a predetermined cohort of patients registered for treatment at the Diabetes Center.

Disaggregated by:

Justification/Management Utility: Lack of compliance with medications is a leading cause of uncontrolled blood sugar levels. Physicians who have completed the EMEP training should note in the medical record whether the patient is following the prescribed regime of medications. This notation is a proxy for the appropriate medical protocol for diabetes management, which includes routinely asking patients about compliance with their medication regime, testing patients to determine if they are complying, providing on-going counseling to patients about the importance of compliance for control of diabetes and more frequent follow-up with patients who demonstrate inability to comply. Notations in the medical record as to whether the patient is complying will indicate that physicians are routinely monitoring patient behavior and following-up appropriately. The importance of compliance is also addressed in the education program conducted by the Diabetes Center for all diabetic patients.

PLAN FOR DATA ACQUISITION BY USAID

Data Collection Method: Data on each patient registered at the Diabetes Center is collected on a form designed through a collaboration between EMEP and local Russian Academic professors.

Method of Acquisition by USAID: EMEP reports data to USAID as required.

Data Source(s): The Diabetes Center maintains the data for its patients.

Timing/Frequency of Data Acquisition: Data is collected on each patient during mandatory quarterly visits to the Center.

Estimated Cost of Data Acquisition: Data on control of blood sugar, complications of diabetes and physician management of the disease are routinely recorded in the patient's medical record. Subsequently, the data is transferred to a data collection form that lists the entire cohort of patients followed in this project.

Responsible Individual(s) at USAID: Data is reported to Elena Gurvich, USAID/Moscow

PLAN FOR DATA ANALYSIS, REVIEW, & REPORTING

Data Analysis: Data is analyzed by at least three physicians: 1) the EMEP partner, a Russian academic professor, 2) an EMEP US Board Certified physician specializing in diabetes and 3) a US Board Certified specialist in internal medicine.

Presentation of Data:

Review of Data: Data is reviewed quarterly upon submission by Diabetes Center to EMEP.

Reporting of Data: The Diabetes Center reports quarterly to EMEP

DATA QUALITY ISSUES

Date of Initial Data Quality Assessment:

Known Data Limitations and Significance (if any): The data relates to the cohort of patients followed by the study and is representative of the results of the CME training of physicians. It does not measure all patients that are benefiting from the physician training.

Actions Taken or Planned to Address Data Limitations: It is not feasible to follow all patients benefiting from the study. A cohort study is a valid scientific protocol.

Date of Future Data Quality Assessments: Data is reviewed semi-annually by EMEP physician.

Procedures for Future Data Quality Assessments: The chief of the Diabetes Center and a person responsible for data collection in the clinic are trained by EMEP and Russian academics in the data collection methodology for the project. Thereafter, the chief of the Diabetes Center supervises the person who has been trained in data collection and conducts the first level of review of the data.

OTHER NOTES

(e.g., on baselines and targets; key to performance data table; location of data storage; etc.)

Note on Baselines/Targets: Baseline data was collected before the EMEP program was implemented.

Key to data table: Site 1: Ekaterinburg, Site 2: Kharbarovsk, Site 3: Kazan

Data Storage:

THIS SHEET LAST UPDATED ON: 12/17/02

Eurasian Medical Education Program

Performance Indicator Reference Sheet

Strategic Objective: Management of conditions that are the leading causes of death and disability in Russia is improved.

Intermediate Result 1: Physician practice related to diagnosis and treatment of diabetes improved.

IR Indicator 1.2: # diabetic patients hospitalized in two selected sites, percentage of hospitalized patients in third site.

DESCRIPTION

Precise Definition: In the cohort of diabetic patients followed by the project, the number or percentage of patients whose records show they were admitted to an inpatient facility for complications of diabetes.

Unit of Measure: Diabetic patients with complications in two selected sites. Patients with complications divided by total diabetic patients in third site. There is a predetermined cohort of patients registered for treatment at the Diabetes Center.

Disaggregated by:

Justification/Management Utility: Physician management of diabetic patients according to the practice guidelines which are presented in the EMEP program, should result in a decrease in the number of complications from diabetes requiring hospitalization.

PLAN FOR DATA ACQUISITION BY USAID

Data Collection Method: Data on each patient registered at the Diabetes Center is collected on a form designed through a collaboration between EMEP and local Russian Academic professors.

Method of Acquisition by USAID: EMEP reports data to USAID as required.

Data Source(s): The Diabetes Center maintains the individual medical records and aggregated study data for its patients.

Timing/Frequency of Data Acquisition: Data is collected on each patient during mandatory quarterly visits to the Center.

Estimated Cost of Data Acquisition: Data on control of blood sugar, complications of diabetes and physician management of the disease are routinely recorded in the patient's medical record. Subsequently, the data is transferred to a data collection form that lists the entire cohort of patients followed in this project.

Responsible Individual(s) at USAID: Data is reported to Elena Gurvich, USAID/Moscow

PLAN FOR DATA ANALYSIS, REVIEW, & REPORTING

Data Analysis: Data is analyzed by at least three physicians: 1) the EMEP partner, a Russian academic professor, 2) an EMEP US Board Certified physician specializing in diabetes and 3) a US Board Certified specialist in internal medicine.

Presentation of Data:

Review of Data: Data is reviewed quarterly upon submission by Diabetes Center to EMEP.

Reporting of Data: The Diabetes Center reports quarterly to EMEP

DATA QUALITY ISSUES

Date of Initial Data Quality Assessment

Known Data Limitations and Significance (if any): The data relates to the cohort of patients followed by the study and is representative of the results of the CME training of physicians. It does not measure all patients that are benefiting from the physician training.

Actions Taken or Planned to Address Data Limitations: It is not feasible to follow all patients benefiting from the study. A cohort study is a valid scientific protocol.

Date of Future Data Quality Assessments: Data is reviewed semi-annually by EMEP physician.

Procedures for Future Data Quality Assessments: The chief of the Diabetes Center and a person responsible for data collection in the clinic are trained by EMEP and Russian academics in the data collection methodology for the project. Thereafter, the chief of the Diabetes Center supervises the person who has been trained in data collection and conducts the first level of review of the data.

OTHER NOTES

(e.g., on baselines and targets; key to performance data table; location of data storage; etc.)

Note on Baselines/Targets: Baseline data was collected before the EMEP program was implemented.

Key to data table: Site 1: Ekaterinburg, Site 2: Kharbarovsk, Site 3: Kazan

Data Storage:

THIS SHEET LAST UPDATED ON: 12/17/02

Eurasian Medical Education Program

Performance Indicator Reference Sheet

Strategic Objective: Management of conditions that are the leading causes of death and disability in Russia is improved.

Intermediate Result 2: Physician practice related to diagnosis and treatment of cardiovascular disease improved.

IR Indicator 2.1: % of patients with hypertension who are compliant with their medication regime in three selected sites.

DESCRIPTION

Precise Definition: Every hypertension patient is prescribed medication for control of blood pressure and other symptoms of cardiac disease. Hypertension patients are those patients who blood pressure has been over 140/90, resulting in a special treatment program by the physician.

Unit of Measure: The percentage of hypertension patients in three selected sites who have complied with their medication regime. The number of patients with hypertension who have complied with their regime is divided by the total number of hypertension patients in the cohort. There is a predetermined cohort of patients registered for treatment at the selected polyclinics.

Disaggregated by:

Justification/Management Utility. Patient compliance with medication is a proxy for physician management of cardiovascular disease, a leading cause of disability and death in the Russian Federation. Successful physician management of patient medications should result in minimal cases of complications from coronary artery disease. Increasing levels of hypertension patients who are compliant with medication regime is one of the objective of improved physician management.

PLAN FOR DATA ACQUISITION BY USAID

Data Collection Method: Data on each hypertension patient is collected on a form designed through a collaboration between EMEP and local Russian Academic professors.

Method of Acquisition by USAID: EMEP reports data to USAID as required.

Data Source(s): The polyclinics maintain the data for their patients.

Timing/Frequency of Data Acquisition: Data is collected on each patient during physician visits.

Estimated Cost of Data Acquisition: Hypertension patient compliance with medication should be ascertained at the time of physical examination by the physician and routinely recorded in the patient's medical record. Subsequently, the data is transferred to a data collection form that lists the entire cohort of patients followed in this project.

Responsible Individual(s) at USAID: Data is reported to Elena Gurvich, USAID/Moscow

PLAN FOR DATA ANALYSIS, REVIEW, & REPORTING

Data Analysis: Data is analyzed by at least three physicians: 1) the EMEP partner, a Russian academic professor, 2) an EMEP US Board Certified physician specializing in cardiology and 3) a US Board Certified specialist in internal medicine.

Presentation of Data:

Review of Data: Data is reviewed quarterly upon submission to EMEP.

Reporting of Data: The partner institutions report quarterly to EMEP

DATA QUALITY ISSUES

Date of Initial Data Quality Assessment:

Known Data Limitations and Significance (if any): The data relates to the cohort of patients followed by the study and is representative of the results of the CME training of physicians. It does not measure all patients that are benefiting from the physician's new continuing education curriculum.

Actions Taken or Planned to Address Data Limitations: It is not feasible to follow all patients benefiting from the study. A cohort study is a valid protocol.

Date of Future Data Quality Assessments: Data quality is reviewed semi-annually by EMEP physician.

Procedures for Future Data Quality Assessments: The chief of the polyclinic and a person responsible for data collection in the clinic are trained by EMEP and Russian academics in the data collection methodology for the project. Thereafter, the chief of the polyclinic supervises the person who has been trained in data collection and conducts the first level of review of the data.

OTHER NOTES

(e.g., on baselines and targets; key to performance data table; location of data storage; etc.)

Note on Baselines/Targets: Baseline data was collected before the EMEP program was implemented.

Key to data table: Site 1: Ekaterinburg, Site 2: Kharbarovsk, Site 3: Kazan

Data Storage: Primary data from the medical records is stored in the polyclinics. Aggregated data used for reporting to USAID is stored in the academic center.

THIS SHEET LAST UPDATED ON: 12/17/02

Eurasian Medical Education Program

Performance Indicator Reference Sheet

Strategic Objective: Management of conditions that are the leading causes of death and disability in Russia is improved.

Intermediate Result 2: Physician practice related to diagnosis and treatment of cardiovascular disease improved.

IR Indicator 2.2: # of hospital admissions for hypertension patients with an acute episode in three selected sites

DESCRIPTION

Precise Definition: A hospital admission that results in an overnight stay is counted as a hospital admission. A hypertension patient is a patient that has had uncontrolled blood pressure (over 140/90) at some time during the study. An acute episode of hypertension occurs when blood pressure reaches a life threatening level.

Unit of Measure: The number of hypertension patients in three selected sites who have been admitted to the hospital. There is a defined cohort of hypertension patients registered for treatment at the selected polyclinics.

Disaggregated by:

Justification/Management Utility. Hospitalization of patients with hypertension is an indicator of uncontrolled blood pressure, and is a proxy for physician management of cardiovascular disease, a leading cause of disability and death in the Russian Federation. Successful physician management of patients should result in minimal cases of complications from coronary artery disease. Decreasing levels of hospital admissions for hypertension patients is one of the objectives of improved physician management.

PLAN FOR DATA ACQUISITION BY USAID

Data Collection Method: Data on each hypertension patient is collected on a form designed through a collaboration between EMEP and local Russian Academic professors.

Method of Acquisition by USAID: EMEP reports data to USAID as required.

Data Source(s): The polyclinics maintain the data for their patients.

Timing/Frequency of Data Acquisition: Data is collected on each patient during physician visits.

Estimated Cost of Data Acquisition: Hypertension patient treatment in an inpatient setting is routinely recorded in the patient's medical record. Subsequently, the data is transferred to a data collection form that lists the entire cohort of patients followed in this project.

Responsible Individual(s) at USAID: Data is reported to Elena Gurvich, USAID/Moscow

PLAN FOR DATA ANALYSIS, REVIEW, & REPORTING

Data Analysis: Data is analyzed by at least three physicians: 1) the EMEP partner, a Russian academic professor, 2) an EMEP US Board Certified physician specializing in cardiology and 3) a US Board Certified specialist in internal medicine.

Presentation of Data:

Review of Data: Data is reviewed quarterly upon submission to EMEP.

Reporting of Data: The partner institutions report quarterly to EMEP

DATA QUALITY ISSUES

Date of Initial Data Quality Assessment:

Known Data Limitations and Significance (if any): The data relates to the cohort of patients followed by the study and is representative of the results of the CME training of physicians. It does not measure all patients that are benefiting from the physician's new continuing education curriculum.

Actions Taken or Planned to Address Data Limitations: It is not feasible to follow all patients benefiting from the study. A cohort study is a valid protocol.

Date of Future Data Quality Assessments: Data is reviewed semi-annually by EMEP physician..

Procedures for Future Data Quality Assessments: The chief of the polyclinic and a person responsible for data collection in the clinic are trained by EMEP and Russian academics in the data collection methodology for the project. Thereafter, the chief of the polyclinic supervises the person who has been trained in data collection and conducts the first level of review of the data.

OTHER NOTES

(e.g., on baselines and targets; key to performance data table; location of data storage; etc.)

Note on Baselines/Targets: Baseline data was collected before the EMEP program was implemented.

Key to data table: Site 1: Ekaterinburg, Site 2: Kharbarovsk, Site 3: Kazan

Data Storage: Primary data from the medical records is stored in the polyclinics. Aggregated data used for reporting to USAID is stored in the academic center.

THIS SHEET LAST UPDATED ON: 12/17/02

Eurasian Medical Education Program

Performance Indicator Reference Sheet

Strategic Objective: Number of patients completing continuous TB treatment, i.e. the DOTS protocol, in one oblast.

Intermediate Result 3: Medical practice related to TB diagnosis and treatment improved.

IR Indicator 3.1: # of doctors trained in TB standardized protocol (i.e. DOTS), in three sites.

DESCRIPTION

Precise Definition: Specific training of TB physicians in standardized protocol (DOTS) treatment
Unit of Measure: Number of TB physicians trained
Disaggregated by: Recording only TB specialists trained (do all TB treatment)
Justification/Management Utility: Indication of practice change by TB physicians

PLAN FOR DATA ACQUISITION BY USAID

Data Collection Method: Recording attendance and understanding by TB physicians
Method of Acquisition by USAID: EMEP and Russian academic physicians
Data Source(s): Both TB physicians trained by EMEP and by Russians trained by EMEP
Timing/Frequency of Data Acquisition: Annually as part of EMEP activities
Estimated Cost of Data Acquisition: Part of EMEP
Responsible Individual(s) at USAID: Data is reported to Elena Gurvich, USAID/Moscow

PLAN FOR DATA ANALYSIS, REVIEW, & REPORTING

Data Analysis: Demonstration of practice change (i.e. DOTS) by Russians
Presentation of Data: Reporting based on CME programs
Review of Data: Done by Russian academic TB physicians, EMEP consultants and EMEP
Reporting of Data: Reported as a result of specific program activities by EMEP

DATA QUALITY ISSUES

Date of Initial Data Quality Assessment: Policy changes by local government (prekazes)
Known Data Limitations and Significance (if any): Limitation would be completion of therapy
Actions Taken or Planned to Address Data Limitations: Programs developed to provide completion
Date of Future Data Quality Assessments: Expansion of standardized treatment (DOTS)
Procedures for Future Data Quality Assessments: Assessment of treatment protocols

OTHER NOTES

(e.g., on baselines and targets; key to performance data table; location of data storage; etc.)

Note on Baselines/Targets: DOTS was *NOT* taught before EMEP. A major achievement of EMEP has been the introduction and utilization of DOTS in three locations. Russian TB leaders were trained in the US at the National TB Center in Newark, NJ, Johns Hopkins in Baltimore, MD, and National Jewish Medical and Research Center in Denver, CO. Both US visiting professors (TB experts) and Russian TB specialists then taught DOTS to TB physicians (who manage all cases). Standardized Protocols being used (DOTS).
Data Storage: Local TB centers and EMEP

THIS SHEET LAST UPDATED ON: 12/17/02

Eurasian Medical Education Program

Performance Indicator Reference Sheet

Strategic Objective: Number of patients completing continuous TB treatment, i.e. the DOTS protocol, in one oblast.

Intermediate Result 3: Medical practice related to TB diagnosis and treatment improved.

IR Indicator 3.2: # of patients initiating standardized DOTS treatment in one site.

DESCRIPTION

Precise Definition: In a cohort of diagnosed TB patients, followed by the project, the percentage of patients started on standardized DOTS therapy.

Unit of Measure: Percentage of patients that had completion of DOTS therapy

Disaggregated by: City, oblast and prison

Justification/Management Utility: Physician management of TB according to practice guidelines presented by EMEP program should result in an increase in completion of therapy.

PLAN FOR DATA ACQUISITION BY USAID

Data Collection Method: DOTS from the TB registry

Method of Acquisition by USAID: EMEP reports data to USAID required

Data Source(s): TB registry

Timing/Frequency of Data Acquisition: Biannually, as part of EMEP activities

Estimated Cost of Data Acquisition: Cost included in EMEP budget

Responsible Individual(s) at USAID: Data is reported to Elena Gurvich, USAID/Moscow

PLAN FOR DATA ANALYSIS, REVIEW, & REPORTING

Data Analysis: By EMEP partner and TB Director of Sverdlovsk

Presentation of Data:

Review of Data: Upon submission to EMEP by TB specialists

Reporting of Data: Biannually to EMEP

DATA QUALITY ISSUES

Date of Initial Data Quality Assessment: February 2003

Known Data Limitations and Significance (if any): Potentially, transfer from prison to civilian population

Actions Taken or Planned to Address Data Limitations: Specific program to address prison to civilian transfer

Date of Future Data Quality Assessments: August 2003

Procedures for Future Data Quality Assessments: The oblast TB Director has had EMEP training at the National TB Center in Newark, NJ, and the National Jewish Medical and Research Center in Denver, CO

OTHER NOTES

(e.g., on baselines and targets; key to performance data table; location of data storage; etc.)

Note on Baselines/Targets:

Key to data table:

Storage of Data: Local TB centers and EMEP

THIS SHEET LAST UPDATED ON: 12/17/02

EURASIAN MEDICAL EDUCATION PROGRAM

TRIP REPORT

Kazan

October 5-11, 2002

Women's Health Program

In Partnership with:
Kazan State Medical Academy
Ministry of Health, Republic of Tartarstan

Visiting Professors

Sara E. Walker, MD, MACP
Professor of Medicine, University of Missouri
President, American College of Physicians- American Society of Internal Medicine

Henry M. Greenberg, MD, FACP
Associate Professor of Clinical Medicine, Columbia University
Director, Coronary Care Unit, St. Luke's-Roosevelt Medical Center, NY

Eurasian Medical Education Program

Richard G. Farmer, MD, MS, MACP
Medical Director

Background

The Eurasian Medical Education Program (EMEP) is based on the premise of helping Russian physicians and other health care workers deal with the problems that cause approximately 60% of ALL deaths in Russia. Cardiovascular disease causes more than half of all deaths, and is based on unhealthy lifestyle and behavior, but primarily on the prevalence of hypertension in the adult population: more than one-third of all Russian adults have hypertension, and about 90% of the cases are undetected or not treated. This has resulted in the average life expectancy of a Russian male not being 58 years, and a loss of population of 750,000 per year, with a death-to-birth ratio currently of more than two.

The EMEP was begun four years ago and we have conducted 35 programs in Russia, involving more than 4500 Russian physicians, and eight in the US. Our emphasis is on hypertension detection, treatment, follow-up (continuity of care), and prevention of complications. Other programs address diabetes, tuberculosis, digestive disease, arthritis, women's health, and programs directed to the general population. We have worked in Ekaterinburg and Sverdlovsk Oblast, Kazan and the Republic of Tartarstan, Khabarovsk and the Jewish Autonomous Republic, and Tula.

EMEP's philosophy is to partner with Russians at three levels: government, academic, and clinical. All programs have been developed in conjunction with Russian colleagues. Our American partner is the American College of Physicians (ACP), with 115,000 physicians members, the largest specialty organization in the world. Our visiting professors are experienced ACP educators/clinicians who serve on a voluntary basis. We have made multiple visits to each location and have organized and locally co-sponsored Continuing Medical Education (CME) programs for physicians directly responsible for patient care. The vast majority are Primary Care Physicians rather than specialists, but programs regarding treatment of complications are directed to hospital specialists. The third group addressed are those who teach the Russian CME programs, and represent a "train-the-trainer" aspect. We provide written handouts and slides, in Russian, for subsequent use; it is estimated that about four times as many additional physicians are exposed to the EMEP programs and curriculum developed by EMEP.

Although the initial vehicle is CME, EMEP has expanded in each location into related clinical aspects, including specific programs, such as the recent women's health program in which the organization and required social services were addressed.

Public education, in the forms of brochures for TB prevention and education regarding hypertension, cardiovascular disease, and lifestyle have also been in the form of "health fairs" and "hypertension schools" where patients and the public are educated in the problem of cardiac disease prevention.

Trip Report

The current program is the 10th conducted in Kazan; at their request, the major focus was on women's health. A special decree ("prikaz") from the Ministry of Health allowed physicians to be off from work for two days to attend the conference. During this visit, the other major activities were to obtain current data from the data collection programs in diabetes and hypertension that have been ongoing for 2 years.

It was a special pleasure to have as a visiting professor, Dr. Sara Walker, the current President of the American College of Physicians. Dr. Henry Greenberg has been the cardiology consultant for EMEP, and organized the data collection programs.

Monday, October 7, 2002

(Departure from US October 5, arrival in Kazan October 6)

There was a round-table discussion of the cardiovascular/hypertension data collection in two polyclinics begun in March 2000. The overall supervision in Kazan is Professor Galyavich, the chief cardiologist of the Republic of Tartarstan.

A cohort of 185 patients was enrolled in March 2000, and has been followed by the same group of physicians since then. (This is the first time such a program has been carried out.) It is under the direction of the Director of Polyclinic #18, Dr. Chisamutdinov, and was presented in detail. Results are appended to this report; there are monthly visits and emphasis is made on compliance with medications, lifestyle modifications and continuity of care. A dramatic increase in compliance from 11% to 93% was noted. Additionally, women are comparatively far more compliant than men under age 40.

A second cohort of patients is now being followed at Polyclinic #11, and there were representatives from 6 other polyclinics in which future programs may be developed.

The data collection programs were begun following EMEP lectures on the detection and management of hypertension, and represent evidence of the benefit from the CME programs. An important feature of the program is patient education that has enhanced results.

A discussion was held in the Department of Clinical Pharmacology in the afternoon. This is relevant because of the gender differences in drug metabolism, and therefore, dosage of medications used in cardiovascular - and other - diseases. We also met with representatives of Geotar medical publishing and reviewed three publications: Evidence Based Medicine guidelines, drug handbook and disease handbook. These could be incorporated into EMEP programs.

Tuesday, October 8, 2002

There was a round-table discussion at the Endocrinology Center of the data collection program in diabetes with Dr. Zyangirova and her staff. A cohort of 377 patients has been followed prospectively since July 2000. The cohort includes both adults and children, and insulin-dependent and insulin independent diabetes patients. (Diabetes and cardiovascular disease cause more mortality, morbidity and lost work of all the other medical conditions in Russia combined.) Patients are seen and examined every 3 months, with data collected regarding complications.

Emphasis is placed on patient compliance, lifestyle modification and patient education. This program was also begun following the EMEP series of lectures on diabetes and represents the results of the CME programs. There have been no deaths from acute complications (diabetic coma), and hospitalization has decreased from 66% to 18% in adults, and 94% to 26% in children.

Attendance at diabetes school is now 100%, and compliance has increased. Results are appended to this report. These two data collection programs represent important successes for the EMEP lectures, and demonstrate the ability of the polyclinic physicians to follow patients, improve short-term results and decrease complications. Further, the collaboration between EMEP and Russian colleagues has resulted in improved care of patients.

In the afternoon, Drs. Walker, Greenberg, Ziganshina, Ms. Wirth and I met with the Minister of Health of Tartarstan, Dr. Zyatdinov, and Professor Nizamov, Deputy Director of the Academy and responsible for CME programs for the entire Volga region (business cards appended). Dr. Zydatinov complimented the EMEP activities and the positive effect on the quality of care in Tartarstan. He noted, however, that there still is a great over-use of health care services: the average person sees a physician 11 times a year and 1 person in 5 is hospitalized. He listed the following as activities in which he would like EMEP input:

1. Primary Care and the development of an "American Polyclinic", using principles of care from the US experience
2. Assistance in technology development (Dr. Zydatinov cited the US involvement in obtaining equipment for their cardiac center.)
3. Development of Evidence Based Medicine guidelines in Russian (such as those developed by the American College of Physicians)
4. Seminars in the management of health care services (to "change attitudes"), which was the request he emphasized the most.

We responded that each of us had extensive managerial experience and would be pleased to participate with them.

Wednesday, October 9, 2002

This was the first of the two-day conference on women's health, co-sponsored by the Ministry of Health, the Kazan State Medical Academy (KSMA) and EMEP. There were 175 physicians in attendance, virtually all polyclinic doctors and 90% women. As the conference was co-sponsored by the Ministry, the Academy and EMEP, the moderators were Dr. Nail Sadikov, Deputy Minister of Health and Professor Rustem Gazizov, Dean of the Therapeutic Faculty of the Academy.

Handouts, translated into Russian, were given to the audience members, and are appended to this report. The conference program consisted of lectures by Drs. Walker (lupus) and Greenberg (coronary disease in women) and lectures by Russian professors. Roberta M. Wirth, MAS, Director, Finance and Administration, EMEP, discussed the organization and structure of a women's health program. Janice M. Farmer, MSSA, discussed social work as a profession (newly established in Kazan) and role in

women's health. Dr. Ziganshina, EMEP Coordinator, discussed pharmokinetics and drug interactions in women. Each lecture was followed by questions from the audience; there was excellent participation. (Professor Nizamov and people at his Department of Social Medicine and Healthcare Management are planning to include Ms. Wirth's and Janice Farmer's lectures in their curriculum. Prof. Nizamov also stated that they would like to include social medicine and healthcare management into plans for the development of EMEP in Tartarstan. Janice Farmer was invited to visit the social service center, which she did the following day.)

Meeting with Professor Nizamov. He is responsible for this conference from the Academy; he asked to meet with us to discuss an expanded activity by EMEP. The Russian Federation is now divided into seven regions of the Federal Ministry of Health; the center for post-graduate medical education for the Volga region is in the Academy. He is responsible for CME for 130,000 physicians in the Volga region. (There are 608,000 physicians in the entire Russian Federation. This is approximately the same number as in the US, but the Russian Federation has about half the population.) The Volga region encompasses 15 oblasts, and CME programs are being coordinated through the KSMA. We discussed the possibility of an expanded EMEP activity for CME programs throughout the region.

Thursday, October 10, 2002

The conference on women's health continued with lectures by Drs. Walker (arthritis) and Farmer (digestive disease in women) and two Russian professors.

Following conclusion of the conference, there were closing remarks by Professor Nizamov and Dr. Farmer. Professor Nizamov presented certificates of membership in the Eurasian Academy of Medical Sciences to Drs. Walker, Greenberg and Farmer, and Ms. Wirth. We then presented certificates of attendance to all 175 physician participants in the conference. They were given individually and were signed by three Americans representing EMEP and the ACP, and three Russians (President of the Eurasian Academy of Medical Sciences, Minister of Health and President of Academy of Medical Sciences). These are appended.

Three photos are appended – with cardiologists, endocrinologists and Dr. Walker lecturing at the conference.

Summary Comments

This visit to Kazan illustrates the evolution and maturity of EMEP programs. Each is developed in conjunction with our Russian colleagues – governmental, academic and clinical – and expands on previous visits. CME programs are but the initial activity. The direct polyclinic visits, train-the-trainers and discussions regarding detailed information such as dosage and specific complications are examples of evolution. Program development, as illustrated by the women's health conference, demonstrates the expansion of the program based on Russian needs and wishes. The data collection programs over the past two or more years represent documentation of the value of EMEP in improving the health of populations.

We believe that EMEP could be replicated in almost any location in Russia, the diseases addressed could be expanded, and programs could continue to be added. These are all possible because of our experience, our relationship with our Russian colleagues, and the infrastructure we have developed over 4 years.

Richard G. Farmer, MD, MS, MACP
Medical Director, EMEP
November 8, 2002

Hypertension Data
Kazan, October 2002

- Every 8th person in Tartarstan has cardiovascular disease
- 40% of all adults have hypertension
- Hypertension contributes to 55% of all deaths in Tartarstan
- There are three times as many strokes as heart attacks (opposite from US) and 60% of stroke victims are permanently disabled

Two Cohorts of Patients, Followed Prospectively

- 185 patients in Polyclinic #18 now followed for 18 months
  - 117 with hypertension alone
  - 68 with hypertension and diabetes
- Newly developed cohort of patients seen at Polyclinic #11
- Monthly visits – compliance, blood pressure, weight, diet, exercise, smoking, alcohol
- Compliance with medications: 93% (11% for patients not in cohort)
- Poorest blood pressure control/compliance by men underage 40, and by patients who had stroke
- Best blood pressure control by patients with diabetes for 5-10 years (compliance)
- Women have better compliance

Diabetes Data
Kazan, October 2002

- 40,000 endocrinology patients in Tartarstan; population 4.5 million
- 6,000 children (under 18) included
- 17,000 have diabetes; 15,000 Type 1
- Computerized registry developed, with assistance from EMEP
- All patients "registered" and receive free medications

Two Cohorts of Patients, Adults and Children

- 377 followed prospectively since July 2000
  - 165 adults and 167 children with Type 1 (insulin requiring) diabetes
  - 45 patients with Type 2 diabetes
  - Every three months follow-up
  - 100% of patients now attend "school"

Diabetes in Children – Improvements Related to EMEP Involvement

- Hospital treatment decreased from 94% in 2000 to 26% in 2002
- Regular following diet from 41% to 64%
- Use of glucometer (i.e. patient self-control) increased from 54% to 71%
- No significant acute complications and no deaths

Diabetes Data
Kazan, October 2002

Diabetes in Adults (Insulin Dependent) – Improvements Related to EMEP Involvement

- Hospital treatment decreased from 66% in 2000 to 18% in 2002
- Regular following diet from 30% to 49%
- Use of glucometer (i.e. patient self-control) increased from 12% to 40%
- Attendance of diabetes school increased from 81% to 100%
- Few acute complications, low mortality
- Note: only 5 patients obese (BMI over 30)

Type 2 Diabetes - 45 Patients ("Representative")

- Approximately 1/3 are obese
- Diet regulation improved from 34% to 45%
- Hospital treatment decreased from 74% to 27%
- No deaths

Conclusions

- Development of Effective registry system with EMEP assistance
- Measurement of clinical outcomes improvement based on EMEP
- Dramatic decrease in hospitalization in all groups
- Improvement in compliance
- Few complications

9 October (Wednesday)

10.00 – 10.30

Организация программы здоровья женщин: уроки, извлеченные из опыта в США

Organization of Women's Health Program: Lessons From the US Experience

Roberta M. Wirth, Eurasian Medical Education Program, Director, Finance and Administration

10.30 – 11.45

Ишемическая болезнь сердца у женщин

Coronary Artery Disease in Women

Henry M. Greenberg, Director, Coronary Care Unit, St. Luke Roosevelt Hospital, New York, Professor of Medicine, University of Columbia, USA

11.45 – 13.00

Systemic Lupus Erythematosus – Hormone-Induced Auto-Immune Disease

Системная красная волчанка – гормонально обусловленное аутоиммунное заболевание

Sara E. Walker, President, American College of Physicians
Professor of Medicine, University of Missouri, Columbia, USA

Lunch

13.00 – 13.45

Перерыв на обед

13.45 - 14.30

40-летний клинический опыт лечения больных с климактерическим синдромом

40-Years Clinical Experience of Managing Post-Menopausal Patients

L.I. Anchikova, Head of the Department of Endocrinology
Professor, Kazan Medical Academy

14.30 – 14.50

Некоторые вопросы инвалидности и реабилитации женщин старше 45 лет при заболеваниях внутренних органов по Республике Татарстан

Disability and Rehabilitation of Women Over 45 years Old With Internal Diseases in the Republic of Tatarstan

O.V. Puzanova, Deputy Head of the State Service of Medical and Social Expertise in the Republic of Tatarstan

14.50 – 15.20

Profession of Social Worker in the US, Importance for Women's Health

Профессия социального работника в США, значение для здоровья женщин

Janice M. Farmer, Clinical Social Worker, Emeritus
Children's National Medical Center, Washington, DC, USA

15.20 – 15.40

Особенности фармакокинетики и взаимодействия лекарственных средств у женщин.

Pharmacokinetics and Drug Interactions in Women

L.E. Ziganshina, Head, Department of Clinical Pharmacology
Professor, Kazan State Medical Academy

10 October (Thursday)

10.00 – 11.15

Новое в терапии ревматоидного артрита

New Therapies for Rheumatoid Arthritis

Sara E. Walker, President, American College of Physicians
Professor of Medicine, University of Missouri, Columbia, USA

11.15 – 11.40

Клиническое значение мелатонина в развитии симптомов патологического климакса у женщин

Clinical Significance of Melatonin in Symptoms of Pathologies in Post-Menopausal Women

L.I. Maltseva, Head, Department of Obstetrics and Gynecology
Professor, Kazan State Medical Academy

11.40 – 12.25

Заболевания пищеварительного тракта у женщин

Digestive Diseases in Women

Richard G. Farmer, Eurasian Medical Education Program, Medical Director
Professor of Medicine, University of Georgetown, Washington, DC, USA

12.25 – 12.40

Заболевания гепато-билиарной системы у женщин и возможности коррекции

Liver Disease in Women and Possibilities of Treatment

F.G. Shigabutdinova, Associate Professor, Department of Internal Medicine
Kazan State Medical University

12.40 – 13.30

Торжественная церемония вручения сертификатов участникам конференции

Ceremony of Giving out Certificates

Eurasian Medical Education Program

Richard G. Farmer, MD, MS, MACP
Medical Director
Clinical Professor of Medicine, Division of Gastroenterology
Georgetown University Medical Center
Washington, DC

American College of Physicians-
American Society of Internal Medicine

EMEP
Irritable Bowel Syndrome (IBS)

- Most common diagnosis in gastroenterology (19%)
- *Criteria for diagnosis*: abdominal pain, plus frequent bowel movements, often liquid and with mucus, pain relieved by bowel movements, abdominal distension
- Three times more frequent in women, up to 20% prevalence
- Physician visits by women are 3 times more than men

Digestive Diseases and Sciences
47:705, 2002

EMEP
Inflammatory Bowel Disease (IBD)

Crohn's Disease: 20% more common in women

Ulcerative Colitis: 20% more common in men

- Depression and irritable bowel syndrome (more common in women)
- Women are more compliant with medications
- Corticosteroid – induced osteoporosis (more common in women)
- Pregnancy and IBD

Office of Women's Health, 2002
US Dept of Health and Human Services

EMEP
Digestive Diseases in Women

1. Colorectal Cancer – third most common cancer in the US (after lung and breast)
   - 30, 000 deaths among women in US annually, far more than from cervical cancer
   - Slight male preponderance overall
2. Irritable Bowel Disease
   - Affects 15-20% of women in US
   - 3 times more women than men
   - Average loss from work is 13.4 days/year

EMEP
Digestive Diseases in Women (cont.)

3. Gallstone Disease
   - Affects 20 million people in US
   - Twice as common in women
   - 500, 000 cholecystectomies/year
   - Role of estrogens on cholesterol in liver
   - Inhibition of mortality in pregnancy
4. NonSteroidal Anti-Inflammatory Drugs (NSAIDs) and Peptic Ulcers
   - Aspirin and ibuprofin used more by women

EMEP
Digestive Diseases in Women (cont.)

5. Liver Disease

A. *Autoimmune Liver Disease – Primarily Biliary Cirrhosis*
   - 9 times more common in women
   - Most common cause for liver transplant in women
   - Autoimmune hepatitis – 3-4 times more in women

B. *Non-Alcoholic Steatohepatitis (NASH)*
   - Most common liver disease in women
   - Obesity, insulin resistance, diabetes

EMEP

Digestive Diseases in Women (cont.)

6. **Osteoporosis**
   - Affects 25 million people in US
   - 1 million fractures, especially in post-menopausal women
   - IBD and treatment with corticosteroids
   - Chronic Biliary Cirrhosis

7

EMEP

Digestive Diseases in Women (cont.)

7. **Digestive Disease During Pregnancy**

   A. *Chronic Conditions*
   - IBD – Relapse, remission, therapy, diagnostic procedures
   - Gallstones and Pancreatitis

   B. *Pregnancy Symptoms – nausea/vomiting*
   - Acute fatty liver of pregnancy

8

EMEP

Digestive Diseases in Women (cont.)

8. **Motility Disorders**
   - Peptides
   - Visceral hypersensitivity
   - Menstrual cycle
   - Environmental stressors

Agenda for Research on Women's Health
For the 21st Century, US Dept. HHS, 2000 9

EMEP

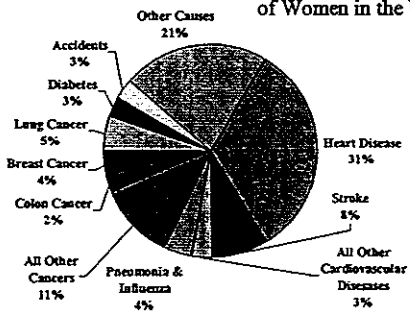
Digestive Diseases in Women (cont.)

9. **Inflammatory Bowel Disease and Pregnancy**
   - Fertility of women with IBD is normal
   - About 1/3 of IBD patients relapse during pregnancy
   - IBD poses no threat to the fetus
   - Mesalamine is safe during pregnancy
   - Pre-term birth (37 weeks) is more common
   - Breast feeding is safe with mesalamine therapy

Society of Women's Health Research, 2002 10

EMEP

Leading Causes of Mortality of Women in the U.S.



National Vital Statistics Report, Vol. 48, No. 11, July 24, 2000

Eurasian Medical Education Program

Organization of a Women's Health Program

Roberta M. Wirth, M.A.S.
Director, Finance and Administration

American College of Physicians-
American Society of Internal Medicine

EMEP

Mission

- Be responsive to the needs of women
- Emphasize the whole patient, body and mind
- Provide easy access to:
  - health care services
  - preventive health care
  - health-promoting activities

US Department of Health and Human Services, The Office of Women's Health, Centers of Excellence in Women's Health

2

EMEP

Core Components

- Clinical
- Education
- Research
- Monitoring and Evaluation

3

EMEP

Multidisciplinary Team Approach

- Physician
- Nurse Practitioner
- Nutritionist
- Physical and Occupational therapists
- Social Worker

4

EMEP

Five Stages of Development Across the Life Span of a Woman

- The Early Years
- The Adolescent Years
- The Reproductive Years
- The Middle Years
- The Older Years

- US Dept of Health and Human Services, CDC

5

EMEP

Physicians

- Primary Care doctors and therapists
- Gynecology
- Endocrinology
- Cardiology
- Gastroenterology
- Rheumatology
- Oncology
- Radiology
- Infectious Diseases

6

EMEP

Nurses

- Organize and manage "schools"– hypertension, diabetes and weight control
- Initial telephone calls (person of first contact)
- Triage – referrals to physicians
- Facilitators – ensure patient gets to next step

7

EMEP

Clinical Programs

- Breast Cancer
- Cardiology
- Continence Care
- Menopause
- Nutrition
- Osteoporosis
- Weight and Exercise

8

EMEP

Evaluation and Monitoring

- Continuity of care
- Satisfaction surveys
- Objective evidence of care

9

EMEP

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10

11D

NEW THERAPIES FOR RHEUMATOID ARTHRITIS

Sara E. Walker MD, MACP
Professor of Medicine
University of Missouri-Columbia

RHEUMATOID ARTHRITIS

- July, 1998 48 yo nurse
- Rheumatoid arthritis 10 years
- Treatment
  - Methotrexate 7.5-15 mg/wk
  - Prednisone 5-20 mg/day
  - Intraarticular steroid injections
- Joint pain/swelling, disability
- Changes in treatment:
  - NSAID, IM methotexate, Plaquenil

CLASSIFICATION CRITERIA RHEUMATOID ARTHRITIS

- Morning stiffness > 1 hour
- Swelling ≥ 3 joints, 6 weeks
- Swelling of hand joints
- Symmetry
- Erosions/decalcification x-ray
- Rheumatoid factor

PATHOGENESIS OF RHEUMATOID ARTHRITIS

- Stage I Antigen presentation to T cells
  No abnormal physical findings
- Stage II T cell, B cell proliferation
  Angiogenesis
  Malaise, mild joint stiffness
  Warm swollen joints

PATHOGENESIS OF RHEUMATIOD ARTHRITIS (2)

- Stage III PMN's in joint fluid
  Proliferation of symovium
  Joint pain and swelling
  Malaise & Morning stiffness
  Warm, swollen joints
- Stage IV Pannus & Enzymes
  Signs and symptoms of inflammation continue

PATHOGENESIS OF RHEUMATOID ARTHRITIS (3)

- Stage V Subchondral bone erosion
  Pannus invades cartilage
  Stretched ligaments
  Loss of function
  Deformity
  Unstable joints
  Flexion contractures
  Extraarticular disease
  Loss of articular cartilage

SIDE EFFECTS OF TRADITIONAL NSAIDS

- Gastric/esophageal irritation
- Peptic ulcer disease
- Anti-platelet activity
- Reversible hepatocellular toxicity
- Decreased creatinine clearance
- Rhinitis, nasal polyposis, asthma
- Headaches, confusion in the elderly

COX-2 INHIBITORS

Celebrex-celecoxib	*Vioxx*-rofecoxib
11 hours	17 hours
RA, OA, FAPoly	OA, pain, I° dys

- As effective as "traditional" NSAIDs
- No platelet effects
- Meta-analysis raises question of stroke, MI risks in RA (JAMA 2001:286:954)
- Rare GI bleeding, dyspepsia
- Not renal or hepatic sparing

TRADITIONAL DISEASE-MODIFYING DRUGS

- Hydroxychloroquine (Plaquenil)
- Sulfasalazine
- Gold salt (Aurolate)
- Methotrexate
- Azathioprine

METHOTREXATE

- Inhibits dihydrofolate reductase
- Dose: 7.5-20 (25) mg/week, PO or IM
- Titrate dose by clinical effectiveness
- Monitor: blood count, mucosa, lungs,liver
- Folic acid (1-2 mg/day) decreases toxicity
- Avoid:
  - probenecid - delays renal excretion
  - trimethoprim-sulfamethoxazole - hematologic tragedy

METHOTREXATE

- LUNGS
  - Acute hypersensitivity pneumonitis
  - Opportunistic infection
  - ? Fibrosis
- LIVER
  - Baseline
    - Enzymes, hepatitis B & C
    - Biopsy if high enzymes, history alcohol/hepatitis
  - Monitor
    - Enzymes q 4-8 weeks, biopsy elevated 5/9 or 6/12 in 12 mos

GOLD

- Gold salts, bound to plasma proteins/RBC
  - Can persist 20 years after the last dose
- Test doses: 10 mg, then 15 mg IM
- 50 mg/week, total 1000 mg; judge efficacy
- Maintenance: 50 mg IM/4-6 weeks
- Monitor: rash, blood count (platelets), urinalysis (albuminuria)

WHO NEEDS NEW DMARDs ?

- Failed/cannot tolerate MTX, others
- Indicators of poor prognosis
  - Early age onset
  - > 20 joints, Extraarticular manifestations
  - High Rheumatoid Factor, CRP, ESR
  - Rheumatoid nodules
  - Erosions, cartilage loss at diagnosis
  - HLA-DR4

ARAVA (leflunomide, Aventis)

- Active rheumatoid arthritis, $3,400/yr
- Inhibits *de novo* pyrimidine synthesis
- 100 mg/day X 3 days, then 20 mg/day
- 41%-49% response
- Slows radiographic progression
- Teratogenic, liver enzymes, alopecia, rash, diarrhea. 9 deaths liver failure

ENBREL

(Etanercept, Immunex/Wyeth Ayerst)

- Adult & juvenile RA, Psoriatic, $12,000/yr
- Fusion protein, p75, human, inhibits TNF alpha & beta binding to receptors
- 25 mg SQ twice/wk
- 60-80% response, enhanced by MTX
- Injection site reactions, infections, demyelinating disease (4), anti-DNA

REMICADE (Infliximab, Centocor)

- Rheumatoid arthritis, Crohn's $21,000/yr
- Human/mouse chimeric anti-TNF alpha
- IV: 3 mg/kg IV, repeat after 3 & 8 wk, then every 8 wk; +MTX; 79% response
- Headache, rash, hypersensitive reactions
- Infection, tuberculosis, worsening CHF
- Demyelination;Anti ds-DNA 10%, rare SLE

PROSORBA COLUMN (Cypress Bioscience)

- Rheumatoid arthritis, $12,000 plus filtration/vascular access costs
- Single-use immunoadsorption, protein A
- One/week X 12, may repeat, 43% respond
- Contraindications: ACE inhibitors, hypercoagulation, thromboembolism
- Anemia, hypotension, fatigue

KINERET(Anakinra, Amgen)

- Approved Nov., 2001
- Unresponsive, moderate to severe rheumatoid arthritis
- Recombinant human IL-1r antagonist
- Competitive inhibitor, blocks IL-1 alpha & beta
- 100 mg/day SQ, refrigerate, with or without MTX
- 5 randomized trials
  - ACR20 response rates 38-42% vs controls 22%
  - ACR70 response 10-20%
- Side effects:
  - Injection site reactions, infections (1.5-2%), Leukopenia

MANIFESTATIONS OF SLE

USUAL	*LESS USUAL*
Positive FANA	Leukopenia, Anemia
Joint & muscle pain	Anti-phospholipid Ab
Skin	High immunoglobulin
Low complement	Pleural/pericar effusion
Cognitive impairment	Pleurisy
Fever	Proteinuria
High anti-DNA	Lymphadenopathy

SLE *vs* STEROID PSYCHOSIS

- SLE Psychosis
  - Seizures, Abnormal neurological exam
  - Active SLE, Cytoid bodies
  - Vasculitis, Anti-P-ribosomal protein
- Steroid Psychosis
  - Develops soon after increase in prednisone
  - Dose often above 40 mg/day

TREATMENT

- Prednisone
- Cyclophosphamide
- Imuran
- Experimental
  - Cyclosporine-A
  - IV immunoglobulin
  - Mycophenolate mofetil

PREMATURE CORONARY ARTERY DISEASE IN SLE

- CAD - 30% deaths in Baltimore Lupus Cohort (average age 38 years)
- Independent risk factors CAD
  - Older at dx, Hypertension, Hi cholesterol, Obesity, Duration SLE, Duration steroids
- 53% $\geq$ 3 risk factors
- 10 mg prednisone deleterious (Ch/BP/wt)

OSTEOPOROSIS IN SLE

- Daily intake Ca 1000-1500 & Vit D 800U
  - Increase D to keep 25-OHD high normal range
- Follow bone density, especially with frequent flares & glucocorticoids
- ERT if SLE quiescent, not contraindicated
  - High IgG ACL, High BP, Breast CA
- Thiazide, Alendronate, Calcitonin, NaFl

LONGTERM MANAGEMENT

- Education, Social and psychological support, Financial planning
- Collaboration among experts: Primary physician, Rheumatology, Nephrology, Infectious disease, Mental health
- Long term health maintenance: Cancer, Hypertension, Coronary artery disease

MYCOPHENOLATE MOFETIL (CellCept - Roche) TREATMENT

- Hydrolyzed to mycophenolic acid, active immunosuppressant
- Reversible inhibitor of inosine monophosphate dehydrogenase, a rate-limiting enzyme in *de novo* synthesis of purines
- Inhibits lymphocyte proliferation and antibody production

MYCOPHENOLATE MOFETIL (CellCept) TREATMENT[2]

- Improved:
  - 4/5 CTX-resistant SLE patients, diffuse proliferative glomerulonephritis
    - *Arthritis Rheum 40:S58, 1997*
- Improved: 22 SLE
  - lupus activity, C4, anti-ds DNA, prednisone
    - *Arthritis Rheum 42:S303, 1999*
- Improved: 13 SLE nephritis
  - *M. A. Dooley, unpublished*

MYCOPHENOLATE MOFETIL (CellCept) TREATMENT[3]

- Treatment regimen
  - 500 mg BID X 1 week
  - 750 mg BID X 1 week
  - 1000 mg BID X 1 week
  - May increase to 1000 mg TID
- Side effects
  - Nausea, vomiting, diarrhea
  - Leukopenia, Infections

BREAKTHROUGHS IN TREATMENT

- Alter gonadal, pituitary hormones
- Manipulate cytokines, growth factors, idiotypes, endothelial cell/PMN function
- Absorb circulating antibodies
- Cytotoxic drugs specific for lymphocytes
- Stem cell transplantation

LUPUS NEPHRITIS

- Prednisone
- Azathioprine (Imuran, Glaxo Wellcome)
- Cyclophosphamide (Cytoxan, Bristol-Myers Squibb)
- Experimental therapy
  - Cyclosporine-A (Sandimmune, Neoral, Novartis)
  - Mycophenolate mofetil (CellCept, Roche)

LYMPHOCYTES - A SOURCE OF CIRCULATING PROLACTIN?

- Hyperprolactinemic acute myeloid leukemia patient; cells contained immunoreactive PRL
- Unstimulated SLE PBMC secrete PRL
- Cultured sfRamos B cell line produced PRL-like protein; Nb2 cell growth factor

PROLACTIN

- Lactotropic polypeptide hormone
- Hypothalamic dopamine inhibits secretion
- Receptors on T-cells, B-cells, monocytes, thymic epithelium
- Prolactin receptors are in a novel family that includes receptors for:
  - IL-1 beta, IL-3, IL-4, IL-6, IL-7, erythropoietin, growth hormone

PROLACTIN -- A CYTOKINE?

- Prolactin shares properties with hematopoietic growth factors
  - Comparable structural motifs
  - Multiple sites of synthesis
  - Ubiquitous distribution of receptors
  - Homologous receptor structure
  - Similar signal transaction pathways
    - Reviewed in *Endocrine Rev* 17:639, 1996

Dehydroepiandrosterone (DHEA) Treatment for SLE

- Abundant mildly androgenic adrenal hormone
- 10 Women with SLE improved with 3-6 months of treatment
- Prednisone dose was decreased
  - *Arthritis and Rheumatism* 1994

LONG-TERM DHEA THERAPY FOR SLE

- 50 women with SLE
- Open label DHEA 50-200 mg/day
- 29 (58%) dropped out
  - no efficacy 30%, androgenic (& other) side effects 16%, remission 6%, other 6%
- 21 (42%) completed one year
- Improvement: SLEDAI, global assessments, prednisone dose
  - *J Rheumatology* 25:285, 1998

IMMUNOLOGIC PROPERTIES OF DHEA

- Mice
  - Increased IL-2 secretion
  - Decreased IL-4, IL-5, IL-6 production
  - Improvement in SLE B/W mice
- Humans
  - Increased IL-2 production by activated T-cells in healthy and SLE subjects
  - ? supplements low circulating DHEA in SLE

CASE

35 year old woman, +FANA, +anti-platelet aB, +anti-phospholipid aB

Normal pregnancy, breast fed baby

Aching, fatigue, weight loss, red malar rash, alopecia. SLE diagnosed.

Recovered days after started prednisone, Plaquenil, weaning the baby

Second pregnancy: twins, to breast feed?

PLASMA LEVELS 17-BETA-ESTRADIOL (pg/ml)

- Menstrual cycle 40-500
- Pregnancy 16,000-30,000
- Ovulation induction 1,000
- Menopause 5-20
- Estrogen replacement
  - Premarin 0.625, 6 mo 40-100
  - Transdermal, 6 mo 40-100

* Adapted from *Buyon J, Dubois' Lupus Erythematosus, 5th Ed, p. 819*

SYSTEMIC LUPUS ERYTHEMATOSUS

CLINICAL FEATURES

- Skin and mucous membranes
- Joints
- Pleurisy, pericarditis
- Kidney
- Brain
- Blood
- Autoantibodies

SYSTEMIC LUPUS ERYTHEMATOSUS

EPIDEMIOLOGY

Prevalence: 15-50 cases/100,000

1985: National Arthritis Data Workgroup

- 131,000 cases in the USA
- 72,000 white and 41,000 African American women
- 7,000 white and 7,000 African American men

SYSTEMIC LUPUS ERYTHEMATOSUS

PATHOGENESIS

- Loss of tolerance to self
- Antigen-driven anti-DS DNA
- Polyclonal B cell activation
- Key role of CD4+ T helper cells
- Defective apoptosis
  - Longlived stimulated lymphocytes
  - Antigen presentation bypasses normal self tolerance

SYSTEMIC LUPUS ERYTHEMATOSUS

PREDISPOSING FACTORS

- 10% have affected first- or second-degree relatives
- HLA-DR2, HLA-DR3
- C2, C4 deficiencies
- C4a null alleles
- Deficient C3b/C4b receptors

SLE AUTOANTIBODIES

- Fluorescent antinuclear antibody (FANA) test
- Anti-DS DNA
- Anti-Sm(B B' D E)
- Anti-Ro/SSA
- Anti-histone

ANTI-Ro/SSA

- Antibodies against RNA-protein conjugates
- SLE, Sjogren's syndrome
- Clinical associations
  - "ANA" negative lupus
  - Neonatal lupus
  - Subacute cutaneous LE
  - C2- and C4-deficient lupus

CASE

- 45 yr old woman, SLE diagnosed age 35 (rash, alopecia, arthritis, nephritis)
- IV cyclophosphamide for 2 1/2 years
- Continuous prednisone for 10 years
- SLE clinically inactive
- Premature menopause, high cholesterol, high blood pressure, osteoporosis
- Recent onset of chest pain with effort

MYCOPHENYLATE MOFETIL (CellSept) TREATMENT

- Reversible inhibitor of inosine monophosphate dehydrogenase
- Inhibits lymphocyte proliferation and antibody production
- Given to 5 cyclophosphamide-resistant patients with diffuse proliferative GN
- 4/5 had improved renal status and SLE scores
  - *Arthritis Rheum 40:S58, 1997*

POSTMENOPAUSAL HORMONE REPLACEMENT

DECISIONS IN SLE

- Use hormones when benefits outweigh the risks
- Don't push the estrogen dose to high levels to improve preservation of bone mass
- Bisphosphonates and nasal calcitonin are alternatives in the patient with active disease

DIFFUSE PROLIFERATIVE GLOMERULONEPHRITIS

- Therapy is based upon prospective studies at NIH; SLE patients were randomized to treatment groups
- IV cyclophosphamide (CY) reduced risk of renal failure in SLE patients with moderate renal scarring
- Hemorrhagic cystitis = 0; Cancer = 0
- Regimen: 0.5-0.75 gm/M2 BSA IV q mo X 6; repeat q 3 mos X 2 years

AUTOANTIBODIES IN SLE

	COMMON	*SPECIFIC*
FANA	++++	+
ANTI-DS DNA	+++	++++
ANTI-Sm	+	++++

"Some increase in plasma cells. Peculiar, rather structureless globular bodies taking purple stain (artifact?). This is not diagnostic."
This was 5 years before our first publication describing the LE cell!

MM Hargraves: Mayo Clinic Proc. 44:579, 1969

ORAL CONTRACEPTIVES Guidelines for use in SLE

- Stable or inactive disease
- No venous or arterial thrombosis
- No antiphospholipid antibodies
- No cigarettes
- Normal blood pressure
- OC tablet contains $\leq$ 35 micrograms synthetic estrogen

HYPERPROLACTINEMIC LUPUS

- 4 women, aged 22-39 years
- Symptomatic hyperprolactinemia 4/4
- Pituitary microadenoma 3/4
- High prolactin 27-120 mos before SLE
- All had malar rash, photosensitivity, arthralgias, positive FANA
- CNS symptoms 1/4, Renal 0/4
- 2/4 flared after stopping bromocriptine

HORMONAL INFLUENCES ON SLE IN NZB/NZW MICE

- Estradiol
  - Shortens life
    - Accelerated autoimmune nephritis
    - Toxicity (obliterated bone marrow, endometritis)
    - Stimulates hyperprolactinemia and pituitary adenomas
- Testosterone
  - Protects from autoimmune disease, even after onset of proteinuria

HORMONE REPLACEMENT THERAPY AND SLE RISK

- Nurses' Health Study Cohort
- 45/120,000 developed SLE 1976-1990
- HRT increased risk for SLE from 1.8- to 2.5-fold
- Increased occurrence of SLE was associated with duration of HRT
  - *Liang MH: Proc AAP 108:25, 1996*

PROLACTIN STIMULATES SLE IN AUTOIMMUNE MICE

- Hyperprolactinemic NZB/NZW females with 2 pituitary transplants had prolactin increased 3-18X controls
  - Results: Increased albuminuria, IgG, mortality
- NZB/NZW females treated with daily injections of bromocriptine
  - Results: Delayed anti-DNA, mortality
    - *J Immunol* 147:3780-3787, 1991

PROLACTIN AND SLE

- Accelerated SLE in hyperprolactinemic NZB/NZW mice
- "Hyperprolactinemic lupus"
  - SLE in patients with prolactinomas
- Hyperprolactinemia in men, women, and pregnant women with SLE, may correlate with disease activity
- Improvement with bromocriptine therapy

DIFFERENT EFFECTS OF ESTROGEN AND PROLACTIN

- Ovariactomized NZB/NZW mice, high or low estrogen with high or low PR
- HIGH E/HIGH PR had early albuminuria and anti-DNA (65% + at 16 wks of age), and early mortality
- HIGH E/LOW PR had late-onset albuminuria and anti-DNA (10% at 16 wks), and later mortality
  - *Elbourne et al. Lupus* 7:420, 1998

HYPERPROLACTINEMIA AND RHEUMATOLOGIC DISEASES

- Hyperprolactinemia preceded Graves' disease, dermatomyositis
- High mean serum prolactin in FANA + girls with juvenile arthritis
- Hyperprolactinemia
  - 65% Primary Sjogren's syndrome
  - 59% Scleroderma
  - 16 - 28% SLE

Systemic Lupus Erythematosus

A hormonally influenced autoimmune disease

Sara E. Walker MD, MACP
Professor of Internal Medicine
University of Missouri-Columbia

Autoimmune Diseases - Why women?

- Immune-stimulating X-linked genes?
- Suppressive Y-linked genes?
- Mary Lyon effect
  - Female heterozygotes for X-linked gene are mosaics
- Exposure to circulating fetal cells/HLA
- Intrauterine imprinting of immune system
- Cultural: viral exposure, cosmetics

» *Lupus 6:625, 1997*

Systemic Lupus Erythematosus and the Card Game Analogy

- HEARTS - Hormones
  - Estrogen, Prolactin, Testosterone
- CLUBS - Genetic factors
  - HLA, C4AO null allele, T cell receptor genes
- DIAMONDS - Antigens, antibodies
- SPADES - Infectious, environmental agents

– *J Rheumatol 48:62, 1997*

Raloxifene

- Benzothiophene with high-affinity binding to estrogen receptor
- Selective estrogen receptor modulator (SERM)
- Agonist in bone and cardiovascular tissue
- Antagonist in reproductive tissue

Raloxifene

- Autoimmune MRL *lpr/lpr* mice
  - 50% succumb to glomerulonephritis, arteritis at 6 mos
- Treatment with raloxifene
  - diminished LN weight, glomerulonephritis
  - no changes in anti-DNA antibodies
  - longevity prolonged

» *Cellular Immunology 173:55-63, 1996*

OVULATION INDUCTION and *IN VITRO* FERTILIZATION IN SLE

- ➢3 new SLE cases with ovulation induction
  - ➢6-10 cycles
  - ➢Estradiol concentrations 1,560-2,850 pm/L
    - ➢*Arthritis Rheum* 37:1614, 1994
- ➢Fatal SLE exacerbation
  - ➢IVF/embryo transfer
    - ➢*J Rheumatol* 24:1639, 1997
- ➢3/7 SLE patients had flare with OI/IVF
  - ➢*Arthritis Rheum* 43:550, 2000

ANTI-ESTROGENS IN NZB/NZW MICE

- Tamoxifen (estrogen receptor blocker)
  - – Suppressed IFN-gamma
  - – Stimulated natural killer cell activity
- 4-hydroxyandrostenedione (aromatase inhibitor)
  - – Decreased thymic weight
  - – Limited renal inflammation
- Norgestrel (19-nor-testosterone, progestogen)
  - – Suppressed anti-ds DNA
  - – Prolonged life
    - » Reviewed in *Dubois' Lupus Erythematosus*, 5th Ed., Ch. 18

ANDROGEN TREATMENT OF NZB/NZW MICE

- Te, 5-OH testosterone (potent androgens)
  - – Beneficial
- DHEA (weakly androgenic steroid)
  - – Delayed onset of disease
  - – Reduced mortality
- Nandrolone decanoate (attenuated androgen)
  - – Beneficial
- Danazol (attenuated androgen)
  - – No benefit
    - » Reviewed in *Dubois' Lupus Erythematosus*, 5th Ed., Ch. 18

ANDROGEN TREATMENT-HUMAN SLE

- Testosterone for Klinefelter's syndrome/SLE
  - – Clinical remission
    - » *J Clin Endocrinol Metabol* 64:3236, 1987
- Danazol (attenuated androgen)
  - – Treated mild active disease
  - – Decreased anti-DNA, increased platelets, and increased serum complement
    - » *J Rheumatol* 10:682, 1983
- 19-nor-testosterone
  - – Not effective in women, men had lupus flares
    - » *J Rheumatol* 19:547, 1992

BROMOCRIPTINE THERAPY OF SLE

- CNS lupus responded to BC (1)
  - » *Arthritis Rheum* 33(Suppl):R22, 1990
- Prolactinoma (1)
  - – Anti-DNA correlated with prolactin
  - – Flare after BC stopped
    - » *Clin Exp Rheumatol* 16:479, 1998
- Hyperprolactinemia (4)
  - – 3 adenomas
  - – 1 responded to BC
  - – 2 flared after BC stopped
    - » *J Rheumatol* 21:843, 1994

BROMOCRIPTINE THERAPY OF SLE (2)

- Open label, mild active SLE (7)
  - – BC 3.75-7.5 mg/day (prolactin ≤ 3 ng/ml)
  - – SLAM, SLEDAI lower after 6 mos, all active post-BC
    - » *J Rheumatol* 22:2044, 1995
- Double-blind, active & inactive SLE (66)
  - – BC 2.5 mg/day or placebo, 2-17 mos
  - – Fewer flares/patient/month in BC patients
    - » *Lupus* 7:414, 1998
- Blinded, mild active SLE (24)
  - – SLAM, SLEDAI lower after 1 yr, BC=OHchloroquine
    - » *Arthritis Rheum* 42:S282, 1999

NEW TREATMENTS FOR RHEUMATOID ARTHRITIS

Sara E. Walker MD, MACP

A CASE OF RHEUMATOID ARTHRITIS

- July, 1998. Initiated care of 48 year old registered nurse
- Rheumatoid arthritis diagnosed 10 years earlier on basis of persisting and painful swelling of small joints of hands and fingers, morning stiffness, positive test for rheumatoid factor
- Treated with methotrexate, initially oral doses 7.5 mg, progressing to 15 mg once a week + prednisone 5-20 mg/day (dose self-adjusted) and intermittent injections of depot glucocorticoids
- Physical examination: Limited range of motion of both shoulders, swollen wrists, warm and swollen metacarpophalangeal and proximal interphalangeal joints
- Subsequent treatment: Nonsteroidal antiinflammatory drugs (NSAIDs), increased methotrexate to maximum dose of 20 mg/week, gave methotrexate IM instead of po, added hydroxychloroquine 200 mg BID

I. CLINICAL MANIFESTATIONS OF RHEUMATOID ARTHRITIS

Pain, usually of insidious onset, appears over a period of weeks or months. Characteristic stiffness lasts longer than one hour after awakening in the morning and recurs after inactivity. Joint involvement is polyarticular and symmetrical. This is a systemic illness and there are many extraarticular findings, including weight loss, pleurisy, rheumatoid nodules, popliteal cysts, and (in 5% of patients), vasculitis.

II. CLASSIFICATION CRITERIA FOR RHEUMATOID ARTHRITIS

1. Morning stiffness > 1 hour
2. Swelling, 3 or more joints, 6 weeks
3. Swelling in hand joints
4. Symmetric joint swelling
5. Erosions/decalcification on radiograph of hand
6. Rheumatoid nodules
7. Rheumatoid factor

III. DISTRIBUTION OF RHEUMATOID ARTHRITIS

Cervical spine, shoulders, elbows, wrists, MCP/PIP finger joints, hips, knees, ankles, MTP joints

IV. PATHOGENESIS OF RHEUMATOID ARTHRITIS

The synovial lining of joints becomes vascular and is invaded by immunologically active cells. The synovium can eventually resemble an ectopic lymph node. Cytokines regulate and perpetuate many aspects of the inflammatory process, including production of metalloproteinases, recruitment of new cells to the joint, and cell proliferation. The resulting pannus invades and destroys cartilage and bone.

V. STAGES OF DISEASE

Stage I	Antigen presentation to T cells. No symptoms or abnormal physical findings.
Stage II	T cell and B cell proliferation, angiogenesis in synovium. Malaise, mild joint stiffness. Swelling/pain in small joints.
Stage III	PMN's in joint fluid, proliferation of synovial cells. Joint pain and swelling. Morning stiffness. Malaise. Warm, swollen joints.

Stage IV	Pannus formation, enzyme activation. Joint pain and swelling. Morning stiffness. Malaise. Inflammation of joints continues. Limited range of motion. Periarticular osteopenia. Proliferation of pannus can be seen on MRI.
Stage V	Subchondral bone erosion, pannus invades cartilage, stretched ligaments. Loss of function, deformity. Instability of joints, flexion contractures, extraarticular disease, erosions, loss of articular cartilage with narrowing of joint space seen on radiographs.

VI. THERAPY FOR RHEUMATOID ARTHRITIS

In many cases, loss of articular cartilage begins within months of the onset of disease and in most cases within a year of onset of continuously active disease. 50% of the maximum damage to joints occurs within the first 5 years. The patient most at risk is the one who has continuously active synovitis. It can be argued that the long-term outcome will be better in patients who are treated early and aggressively in the course of their disease. Patients with rheumatoid arthritis need long term treatment with a NSAID, often given at maximum dose, and a disease modifying agent (DMARD).

A. NONSTEROIDAL ANTIINFLAMMATORY DRUGS (NSAIDs)

Side effects of traditional (COX-1 and COX-2 inhibitor) NSAIDs:

- Gastric/esophageal irritation
- Exacerbation of peptic ulcers
- Anti-platelet activity
  - Stop ASA 2 weeks preoperatively
  - Stop other traditional NSAIDs long enough for complete excretion before surgery
- Reversible hepatocellular toxicity
- Fluid retention
- Decreased creatinine clearance
- ASA: Rhinitis, nasal polyposis, asthma syndrome
- Headaches and confusion in the elderly

:

NSAIDs work by inhibiting prostanoid synthesis through cyclooxygenase (COX) blockade. COX has at least 2 isoforms, termed COX-1 and COX-2. All traditional NSAIDs inhibit both isoforms. New NSAIDs are available that are selective COX-2 inhibitors. Examples of these new NSAIDs are Celebrex (celecoxib, Searle/Pfizer)and Vioxx (rofecoxib, Merck).

Rationale: COX-1 is expressed constitutively in most tissues. Inhibition of COX-1 suppresses formation of beneficial prostaglandins and may lead to ulceration of the mucosa of the upper gastrointestinal tract and acute renal insufficiency. Therefore, its inhibition is responsible for most of the side effects of the traditional NSAIDs, because these drugs inhibit both COX-1 and COX-2. COX-2 is highly expressed in cells of the immune system where it is induced by a number of factors such as cytokines to produce prostanoids that modulate the inflammatory response. It is believed that drugs which inhibit almost exclusively the COX-2 pathway should control inflammation without inducing adverse gastric effects.

Special indications for Cox-2 inhibitors may include:

- Treating the elderly, because they are more susceptible to gastrointestinal bleeding caused by traditional NSAIDs.
- Treating patients on anticoagulants. Traditional NSAIDs displace coumadin and so do the COX-2 inhibitors. However, the COX-2 inhibitors offer the advantage of not having platelet inhibiting properties. If bleeding were to occur in an anticoagulated patient, it might theoretically be less severe if the patient were taking a COX-2 inhibitor compared to a

traditional NSAID. In addition, the COX-2 inhibitors are less likely to initiate gastrointestinal bleeding.

- Treating patients with a history of gastrointestinal bleeding.
- **Celebrex (celecoxib, Pfizer, Searle)**
  - Structure - Diaryl substituted pyrazole
  - Sulfonamide- ***contraindicated in sulfonamide-allergic patients*** (Bactrim, Pediazole, Septra)
  - For treatment of osteoarthritis and rheumatoid arthritis; familial adenomatous polyposis
  - Half life 11 hours; metabolized mainly through cytochrome P450 2C9
  - 200 mg in one dose, or 100 mg po BID (osteoarthritis); 100 or 200 mg po BID (rheumatoid arthritis)
  - Gastrointestinal bleeding reported, but rare. Two out of 5,285 patients treated with celecoxib in doses $\geq$ 200 mg/day had significant upper gastrointestinal bleeding, 14 and 22 days after starting treatment. The usual occurrence of ulcers in patients treated with traditional NSAIDs is estimated at 1-4%, depending upon length of treatment. Endoscopy of 1,149 patients who received either celecoxib or placebo or naproxen revealed ulcers in 26% of the naproxen patients compared to 4-6% of the celecoxib and placebo-treated patients.
  - Platelet aggregation - No effect.
  - Renal effects - Elevated BUN in 1.5% treated with celecoxib, *vs* 2.8% in patients receiving other NSAIDs. Nevertheless, celecoxib is NOT considered renal sparing.
  - Hepatic effects - Transient elevations of liver enzymes, 1%
  - Efficacy>placebo and = traditional NSAIDs
- **Vioxx (rofecoxib, Merck)**
  - Structure - Methylsulfonyl phenyl furanone
  - Sulfone
  - For treatment of osteoarthritis, acute pain in adults, primary dysmenorrhea
  - Half life 17 hours; metabolized through reduction by cytosolic enzymes
  - 12.5-25 mg/day (osteoarthritis); no recommended dose for rheumatoid arthritis; maximum daily dose 50 mg
  - Side effects: Similar to celecoxib
    Gastrointestinal side effects: Endoscopy after 12 weeks of treatment: 5% ulcers (rofecoxib) *vs* 7% ulcers (placebo) *vs* 28% ibuprofen
  - Efficacy > placebo and = naprosyn and ibuprofen in osteoarthritis

B. TRADITIONAL DISEASE-MODIFYING DRUGS (DMARDs)

- Hydroxychloroquine (Plaquenil)
- Sulfasalazine
- Gold salt (Aurolate) - 50 mg IM/week until total of 1000 mg, then judge efficacy. May continue maintenance (50 mg IM every 4-6 weeks) for years. Monitor for rashes, blood count for suppression especially thrombocytopenia, urinalysis for albuminuria.
- Methotrexate - 5 - 20 mg PO or IM, one day each week. Titrate by clinical effectiveness. Monitor blood count, mucosa, lungs, liver. Addition of ***folic acid*** 1 mg/day protects against toxicity. Avoid: probenecid (delays renal excretion); Bactrim, Septra (trimethoprim-sulfamethoxazole) (associated with hematologic toxicity).
- Azathioprine (Imuran) - 25-200 mg/day. Deficiency of the degradative enzyme, ***thiopurine S-methyltransferase,*** places the patient at risk for serious side effects, especially aplastic marrow. Reduce dose to about 1/3 of usual dose for patients taking allopurinol.

- Combination treatment (example: hydroxychloroquine plus methotrexate)

C. NEW DISEASE-MODIFYING DRUGS (DMARDs)

Who needs them?

- Failed, cannot tolerate other disease-modifying agents
- Early switch in patients with indicator of poor prognosis
  - Early age onset
  - Involvement of more than 20 joints
  - Extraarticular manifestations
  - High titer rheumatoid factor, elevated CRP, high ESR
  - Rheumatoid nodules
  - Erosions, cartilage loss at time of diagnosis
  - HLA-DR4

- **Arava (leflunomide, Aventis)**
  - $3,400./year
  - Prodrug, metabolized in intestine and liver to active form, A77 1726. Inhibits dihydroorotate dehydrogenase, an enzyme involved in *de novo* pyrimidine synthesis. Antiproliferative and anti-inflammatory.
  - Half life 2 weeks
  - For treatment of active rheumatoid arthritis
  - Rationale: Novel immunomodulatory drug, effective in graft-*vs*-host disease in experimental models, inhibits T-cell and B-cell proliferation. Augments the immunosuppressive cytokine, TGF-beta1, and suppresses the immunostimulatory cytokine, IL-2.
  - 100 mg/day X 3 days loading dose, thereafter 20 mg/day
  - Hepatotoxicity (increased with concurrent use of methotrexate) 4-10%
    American College of Rheumatology Hotline August, 2001: 15 leflunomide-treated patients died with hepatic abnormalities; 9 had liver failure.
    Others: diarrhea, dyspepsia, rash, hair loss, hypertension, weight loss, anemia
  - Teratogenic. If pregnant, detoxify with cholestyramine 8 gm po 3 times/day for 11 days.
  - Monitoring: CBC/SGOT/SGPT/alkaline phosphatase
  - Efficacy: 41-49% respond

- **Enbrel (etanercept, Immunex, Wyeth-Ayerst)**
  - $12,000./year
  - Genetically engineered fusion protein consisting of 2 identical chains of the recombinant extracellular human tumor necrosis factor (TNF) receptor p75 monomer fused with the Fc domain of human IgG1. Etanercept effectively binds to TNF alpha and TNF beta and inhibits their activity by inhibiting binding of the cytokines to TNF cell surface receptors.
  - For treatment of moderately to severely active rheumatoid arthritis in patients with inadequate response to one or more DMARDs, treatment of psoriatic arthritis.
  - Rationale: TNF is a cytokine that has a major role in stimulating inflammation in rheumatoid arthritis. It is present in synovium and stimulates synoviocyte proliferation and production of inflammatory mediators.
  - 25 mg SQ injection twice a week
  - Injection-site reactions
  - ***Infections:*** Increased upper respiratory tract infections (29% *vs* 16% placebo)

0.12-3% were serious infections.
Do not start with active, chronic, or localized infections and discontinue in serious infections. Special concern in patients with past history of tuberculosis or exposure to tuberculosis; TNF is important in immune defense against tuberculosis.

- ***Autoantibodies:*** 15% anti-ds DNA by RIA
- ***Demyelinating disease:*** New onset 4 patients
- Efficacy: 60-80% response rate. Improvement may begin within 2 weeks. Concomitant methotrexate treatment may improve favorable response. Symptoms return within one month after it is stopped.

Etanercept Treatment of Other Diseases

Beneficial effects of etanercept have been demonstrated in polyarticular juvenile arthritis and psoriatic arthritis. In a randomized, double-blind, placebo-controlled study, either etanercept or placebo was given for 12 weeks to 60 patients with psoriatic arthritis and psoriasis. Criteria for arthritis improvement were met in 87% of etanercept-treated patients, and 5/19 had 75% improvement in psoriasis. In the placebo group, arthritis improved in 23% and psoriasis improved in 0 patients. (*Lancet* 356:385-390, 2000)

- **Remicade (infliximab, Centocor)**
  - $21,000./year
  - Chimeric human (constant region)/mouse (variable region) IgG1 anti-TNF monoclonal antibody. It binds to TNF alpha, which is then unable to bind to cell surface receptors.
  - For treatment of rheumatoid arthritis, Crohn's disease
  - Rationale: Neutralization of TNF alpha and subsequent reduction of inflammation
  - IV infusion. 3 mg/kg is given IV, then additional infusions of 3 mg/kg IV 3 and 6 weeks later, then 3 mg/kg IV every 8 weeks thereafter. Use in-line, sterile, non-pyrogenic, low-protein-binding filter with pore size 1.2 microm or less; infuse slowly over at least 2 hours).
  - Headache, rash, hypersensitivity reactions (fever, chills, urticaria, dyspnea, hypotension)
  - ***Infections:*** Definite risk, ranging from upper respiratory to fatal tuberculosis
  - ***Autoantibodies:*** 10% anti-ds-DNA, lupus-like syndrome
  - ***Demyelinating disease:*** Exacerbation of MS, concern about new-onset disease
  - ***Special precautions:*** Congestive heart failure, tuberculosis
  - Efficacy: 79% response rate. Improvement often occurs within 2-3 weeks and disease reappears within 1 month of stopping treatment.

American College of Rheumatology Hotline September, 2001:

Etanercept (104,000 patients), infliximab (170,000 patients)
M. tuberculosis, Atypical mycobacterium (E), Histoplasmosis, Listeria monocytogenes, Pneumocystis carinii, Aspergillosis, Candidiasis, Pancytopenia, Aplastic anemia (E), Multiple sclerosis, Optic neuritis, Seizures, Lupus, Colonic perforations, Lymphoma

- **Prosorba Column (Cypress Bioscience)**
  - Column $1,000. (total of 12 columns needed for full course of treatment) plus costs of filtration procedure and vascular access
  - Single-use immunoadsorption devise, 6 inches long and 3 inches in diameter, used in conjunction with therapeutic apheresis. Contains protein A from Staphylococcus aureus covalently bound to an inert silica matrix
  - For treatment of rheumatoid arthritis
  - Rationale: Protein A binds IgG and circulating immune complexes
  - Work with pheresis center (Red Cross) to set up one treatment a week for 12 weeks. Course of treatment may be repeated.

- Contraindications: Use of ACE inhibitors (72 hour withdrawal period recommended), hypercoagulability, recent history of thromboembolic events
- Side effects: Anemia, hypotension, fatigue.
- Efficacy: 42% respond; Duration of response 20-84 weeks.

Newer Treatments for Rheumatoid Arthritis

Kineret (anakinra, Amgen)

- Active rheumatoid arthritis, failed at least one DMARD
- Recombinant human IL-1r antagonist
- Blocks IL-1alpha and beta on cells
- 100 mg/day subcutaneously
- Infections (1.5-2%)
- Leukopenia
- 38% ACR 20 response (control=22%)

REFERENCES

Much of this material is covered in *Harrison's Textbook of Medicine, Rheumatology, Second Edition,* Klippel and Dieppe, Editors, and *Textbook of Rheumatology*, Sixth Edition, edited by Kelley, Ruddy, Harris, and Sledge. Some was derived from product information provided by the pharmaceutical manufacturers, and from reports of research that was supported by pharmaceutical companies.
A highly recommended reference is the ***Primer on the Rheumatic Diseases***, published by the Arthritis Foundation (1330 West Peachtree Street, Atlanta, GA, 30309).

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SYSTEMIC LUPUS ERYTHEMATOSUS

Sara E. Walker, MD, MACP

Systemic lupus erythematosus (SLE) is a chronic, inflammatory disease of unknown etiology. The most common clinical manifestations are fever, arthralgia, arthritis, and skin lesions. However, any organ system may be involved. Depression and disabling fatigue shadow the SLE patient. The spectrum of disease ranges from mild (skin rash, arthralgias, pleurisy) to severe (life-threatening involvement of brain or kidney). Therapy, which should be individualized and directed at specific clinical problems, ranges from moderate doses of aspirin to aggressive immunosuppression.

Clinical questions:

1. What are the most important points in making the diagnosis of SLE?
2. What new treatments are available?
3. What are the most important factors in health maintenance for the patient with lupus?

History

"Lupus" = Latin for "wolf"

1810 - Bateman classified destructive or ulcerative lesions of face and nose as "lupus".

1833 - Biett/Cazenave described round red facial patches on young women: 1st SLE description.

1845 - Von Hebra described "butterfly" malar rash. His *Atlas of Skin Diseases* illustrated lupus.

1902 - Sequeira/Balean, London Hospital, published case of 18-year-old woman with malar rash, malaise, headache, abdominal pain, edema, hematuria. Glomerulonephritis was found at autopsy. This is thought to be the first published case of disseminated LE. Two years later, Osler published 2 cases with facial erythema and renal failure.

1948 - Hargraves (Mayo Clinic) described the LE cell and made it possible to diagnose SLE pre mortem. Corticosteroids were recognized as anti-inflammatory agents.

1954 - Shulman published the classic modern description and defined multisystem SLE in *Medicine*.

1957 - Friou used direct immunofluorescence to demonstrate antinuclear antibodies. Anti-ds DNA antibodies were reported, and soon thereafter Dixon and Kunkel introduced the concept that lupus glomerulonephritis is mediated by immune complex deposition.

1974 - 1991 - Steinberg/Decker reported benefits of treating severe glomerulonephritis with CY.

Epidemiology

- 15-50 cases/100,000. 1985 National Arthritis Data Workgroup: 131,000 cases in USA; 72,000 Caucasian females, 41,000 African American females.
- 90% are female. SLE is rare before puberty.

Pathogenesis

- Loss of tolerance to self; makes antibodies to self antigens, also makes antibodies to "normal" antigens.
- B-cells: Antigen-driven induction of antibodies to ds DNA; Polyclonal activation.
- T-cells: CD4+ cells are important. Eliminating these cells or blocking their interactions with B cells prevents SLE in animal models.
- Cytokines: Th1 cytokines (example: IFN-gamma) initiate SLE and Th2 cytokines

(examples: IL-4, Il-6) promote and perpetuate B-cell activity.

- **Apoptosis** is programmed cell death. Mutations in apoptosis-producing molecules or over expression of molecules that cause lymphocytes to live longer limit apoptosis and lead to lymphadenopathy. These changes may allow stimulated cells to survive for long periods during which they could produce harmful antibodies. Fas mutations have been identified in humans, and there may be reduced macrophage engulfment of apoptotic cells. These cells build up: they may selectively modify self antigens and present antigens in such a way that they bypass normal mechanisms of self tolerance.

Genetic factors

- 10% of SLE patients have 1 or more first- or second-degree relatives with SLE.
- 15 - 70% monozygotic twins are concordant; 9% dizygotic twins are concordant.
- HLA-DR2, HLA-DR3
- SLE associated with complement deficiencies; C2 or C4 hetero- or homozygote deficient
- C4A gene deletion decreases C4A, the "good C4" that binds and hastens metabolism of certain immune complexes. The deletion is found in 13-15% of SLE patients *vs* <1% in normals.
- Complement type 1 C3b/C4b receptors on erythrocytes are involved in erythrocyte processing of immune complexes (IC) and permit attachment of IC through C3b to erythrocytes. The IC are transported to the liver and spleen, transferred to macrophages, and eliminated. There is a deficiency of these receptors in SLE patients.
- 52 pairs of siblings with SLE were analyzed; 5 markers were identified in the 1q41-q42 region, an area analogous to the telomeric end of mouse chromosome 1. Glomerulonephritis and IgG antichromatin were mapped in this region in mouse models of SLE.

Clinical features

Lists derived from 2,000 patients/7 studies/1975-1997:

- MORE COMMON: Positive FANA, arthritis, arthralgias, myalgia, skin, low serum complement, cognitive impairment, fever, anti-ds DNA
- LESS COMMON: Leukopenia, pleurisy, proteinuria, anemia, anti-phospholipid antibodies, high level immunoglobulins, pleural/pericardial effusion, lymphadenopathy

Autoantibodies

- FANA - Not specific for SLE, found in at least 6% of women 18-30 years old.
- Anti-ds DNA - Specific: Indirect immunofluorescence using *C. luciliae* substrate; RIA.
- Anti-Ro/SSA - 40% SLE patients, also "ANA-negative lupus," neonatal SLE (dermatitis, complete congenital heart block), and subacute cutaneous lupus eyrthematosus. Also associated with primary Sjogren's syndrome
- Immunoblotting: Sensitive means of detecting autoantibodies. Nuclear extract is electrophoresed to separate the antigens by molecular weight. Antigens are transferred to paper and reacted with patient serum in a system that stains antigen-reactive immunoglobulins. The result is a narrow strip of paper with various visible transverse bands. The bands are compared to bands made by sera with known antibody specificities. Patterns of bands relevant to SLE and associated diseases are:
  - snRNP proteins B, B', and D, representing anti-Sm and highly specific for SLE.
  - U1RNP proteins 70kd, A, and C, found in mixed connective tissue disease.

- **Antiphospholipid antibody syndrome** - Antibodies against negatively charged phospholipids are associated with fibrin plugging of small vessels, clots in veins and arteries, recurrent fetal loss, thrombocytopenia. Antibodies are detected by positive tests for lupus anticoagulant or positive ELISA tests for IgG and/or IgM antibodies to cardiolipin or other phospholipid. The antigen that binds antiphospholipid antibodies may actually be a complex formed by beta2-glycoprotein-1 and phospholipid. The hypercoagulable state in these patients may result from inhibition of protein C activation and activated protein C neutralization of factors Va and VIIIa, or activation of platelets by antibodies that bind phospholipids and protein complexes in platelet membranes.

Hormones in SLE

- In the NZB/NZW mouse model of SLE, estrogen and prolactin accelerate disease and testosterone is protective.
- Old-style oral contraceptives with $\geq$ 50 micrograms synthetic estrogen/tablet were associated with development of positive FANA tests and rheumatoid factor, SLE flares, and new-onset SLE. Progestogens do not stimulate SLE.

- Guidelines for oral contraceptives in SLE:
  - Stable or inactive disease
  - No history venous or arterial thrombosis
  - No antiphospholipid antibodies
  - Not a smoker
  - Normal blood pressure
  - $\leq$ 35 micrograms estrogen/pill
  - Avoid desogestrel and gestodene
  - Consider progestogen-only contraceptive

- Advantages of postmenopausal estrogen replacement in SLE:
  - Premature menopause with cyclophosphamide therapy
  - Longterm corticosteroid use predisposes to osteoporosis, hyperlipidemia, hypertension = increased risk of fractures, premature coronary artery disease

- Caution: Nurse's Health Study (>69,000 women) revealed that women who had taken hormone replacement had increased risk of SLE, related to duration of treatment.
- Use estrogen replacement/progesterone when benefits outweigh risks, especially when disease is inactive and patient has osteoporosis and cardiac risk factors. Avoid "pushing" high-dose estrogen to improve bone mass preservation.

SLE and pregnancy

- Pregnancy is contraindicated if disease is active, anti-ds DNA is elevated, creatinine clearance is <50 ml/min, patient is receiving methotrexate or cyclophosphamide.
- Appropriate patient management includes acceptance of high risk status of the mother (risk of SLE flare) and the fetus (high fetal wastage, increased premature births).
- Anti-ds DNA is useful to monitor for active disease.
- Serum complement levels are increased in normal pregnancy, decreased in active SLE and preeclampsia.
- Nonsteroidal antiinflammatory drugs (NSAIDs) should be avoided because of possible

premature constriction of the ductus arteriosus and predisposition of premature infants to intracranial hemorrhage.

- Active disease should be treated aggressively with prednisone. This steroid, as well as prednisolone and hydrocortisone, are inactivated by placental enzymes and have little potential to affect the fetus. Cover delivery with stress-dose corticosteroid. Breast feeding is permitted in women who take prednisone.
- In pregnant patients with lupus anticoagulant/antiphospholipid antibodies who have had miscarriages or vascular thrombotic episodes, treatment may include daily low dose aspirin plus low dose self-administered SQ heparin or low molecular weight heparin.

Neuropsychiatric SLE

- A major cause of morbidity in SLE.
- Diagnostic points: Cerebrospinal fluid changes are abnormal in 1/3 of affected patients and not specific for SLE. Oligoclonal bands may be present. Lumbar puncture is useful to rule out infection.
- Computerized Tomography - In acute, catastrophic CNS disease in SLE patient, useful to look for atrophy, infarcts, hemorrhage, dilated ventricles.
- MRI - May detect fresh focal lesions associated with abnormal neurological examination or seizures. Follow-up MRI may help assess resolution of lesions and response to therapy.
- Nonprogressive transient cognitive defects ("lupus lapses") - no specific treatment.
- Depression and lupus headaches - treat symptomatically.
- Psychosis (possibly associated with anti-ribosomal P antibodies) - severe organic changes, seizures, coma, and other severe complications such as cranial nerve palsy, aseptic meningitis, transverse myelitis, chorea, cerebellar ataxia, cortical blindness, and intracerebral hemorrhage require aggressive anti-SLE therapy.

Renal SLE

- A major determinant of disease outcome.
- Lupus Survival Study Group (1103 patients, 1965-1978) - Proteinuria $\geq$2+ predicted 56% 10-year survival; serum creatinine >3 mg/dl predicted 12% 10-year survival.
- Standard renal function tests may underestimate the extent of nephron damage because of compensation by hemodynamic adjustments and hypertophy of the kidney.
- Renal biopsy - Estimates prognosis, allows planning of a rational therapeutic program.

- World Health Organization classification of lupus nephritis:
  - Class I - Normal or minimal change
  - Class II - Mesangial glomerulonephritis
  - Class III - Focal proliferative glomerulonephritis
  - Class IV - Diffuse proliferative glomerulonephritis
  - Class V - Membranous glomerulonephritis

- Diffuse proliferative glomerulonephritis (Class IV) has the poorest outlook; 30% develop end-stage renal failure within 10 years of the diagnosis. Younger age at diagnosis confers especially poor prognosis. Treatment is offered with high-dose prednisone and IV cyclophosphamide (Cytoxan) (CY).

Treatment of SLE

- Rest, avoid agents that can trigger an exacerbation (UV light, infection, certain drugs, stress, fatigue), educate patient and family, refer to local support group, Lupus Foundation of America (www.lupus.org).
- NSAIDs: Frequently necessary. ASA may be associated with increased SGOT and SGPT and ibuprofen has produced idiosyncratic reactions (aseptic meningitis syndrome, rash, fever, abdominal pain). NSAIDs have the propensity to elevate serum creatinine in patients with mildly impaired renal function.
- Photosensitivity and skin rashes - Sun avoidance, sunscreens. Hydroxychloroquine (Plaquenil) is usually given in doses of 200 - 400 mg/day and has a low incidence of retinal toxicity if the daily dose is <6.0-6.5 mg/kg/day. Nevertheless, ophthalmologic examinations at 6-month intervals are recommended.
- Low-dose prednisone (0.5 mg/kg/day or less)
  - Fever, skin rashes, arthritis, serositis
  - Given in 1 or 2 daily doses. Alternate day corticosteroids seldom suppress symptoms but may be used as maintenance after disease activity is controlled.
- High-dose prednisone, 1.0 mg/kg/day, or intravenous Solu-medrol
  - Lupus crisis, neuropsychiatric disease, severe hematologic disease (hemolytic anemia, thrombocytopenia), severe lupus nephritis
  - Split doses initially, give a dose q 6-12 hours.
  - Taper after 4-6 months, maintenance doses <10 mg/day desirable, may not be able to discontinue prednisone completely.
- Consider high-dose pulses of Solumedrol, up to 1 gm IV daily for 3 successive days, for "rescue" of the SLE patient in crisis.
- In some patients, oral methylprednisolone is more effective than oral prednisone.
- Cyclophosphamide (Cytoxan, CY) or azathioprine (Imuran)
  - Life-threatening disease not responsive to high-dose corticosteroids
  - Major organ disease which recurs with reduction of corticosteroid dose
  - Intolerable complications of corticosteroids
- Use of CY to treat severe membranoproliferative or diffuse proliferative glomerulonephritis - rationale
  - In prospective long-term studies at the NIH, patients received daily high dose oral prednisone only OR one of the following regimens combined with daily low-dose prednisone to suppress extrarenal disease: daily oral azathioprine, daily oral CY, daily oral azathioprine plus CY, or IV CY. Best response was in the relatively small number of subjects who received IV CY. The best responders to IV CY had moderate renal scarring at the start of treatment.
  - Fewer infections occurred in oral CY and IV CY groups *vs* prednisone-only group.
  - 15% hemorrhagic cystitis in oral CY group *vs* 0 in IV CY group.
  - 17% cancer (hematologic, bladder transitional cell carcinoma, skin cancer) in oral CY group *vs* 0 in IV CY group.
  - Inferior preservation of renal function in prednisone-only group.
- IV CY regimen:
  - 6 monthly boluses of CY (0.3 - 0 0.5 gm/M2 for Ccr 10-20 ml/min, higher dose of 0.75 gm/M2 for patients with better renal function). CY is given in 100 ml NS over 30-60 minutes with pre-treatment and post-treatment hydration, Mesna, and

antiemetics with follow-up blood count after 14 days. All doses take into account the previous WBC nadir.

- Maintenance IV CY is offered every 3 months for 2 years.
- Consider previous malignancy, possible development of malignancy, contraception, possible gonadal failure, patient compliance, infection

Other treatments for SLE

DHEA (Aslera, synthetic dehydroepiandrosterone, Genelabe Technologies

- Orphan drug status, not FDA-approved
- Abundant, mildly androgenic adrenal hormone.
- Consider as a long term steroid-sparing agent for the patient with mild disease
- Decreases IL-4, IL-5, IL-6 production in mice
- Available over-the-counter
- Improvement has occurred with dose of 200 mg/day, and prednisone dose has been decreased.
- Side effects: acne (70%), hirsutism

Mycophenylate mofetil (CellCept-Roche)

- Not FDA-approved for SLE
- Consider as an expensive alternate to continued high dose prednisone, azathioprine, and/or CY for the patient with severe disease; "Cytoxan rescue"
- Hydrolyzed to mycophenolic acid, active immunosuppressant
- Reversible inhibitor of inosine monophosphate dehydrogenase, a rate-limiting enzyme in *de novo* synthesis of purines
- Inhibits lymphocyte proliferation and antibody production
- Treatment regimen used by some rheumatologists: 0.5 gm po BID X 1 wk, 0.75 gm po BID X 1 wk, 1 gm po BID X 1 wk, may increase to 1 gm po TID.
- Improvement of lupus activity, C4, anti ds-DNA, prednisone requirement has been observed in active SLE.
- Improvement in renal status has been observed in CY-resistant diffuse proliferative glomerulonephritis
- Side effects: nausea, vomiting, diarrhea, leukopenia, infections.
- Not approved by FDA for this indication.

- Experimental therapies
  - Columns: Phenylalanin, immunoglobulin adsorption with sheep antihuman IgG, C1q ligand coupled to polyhydroxymethacrylate
  - Hematopoietic stem cell transplantation
  - Future treatment directions: Alter gonadal and pituitary hormone levels, manipulate cytokines, growth factors, idiotypes, endothelial cell/neutrophil function, induce tolerance to DNA, peptides, Ig.

Health maintenance for the SLE patient

- Prevent and treat hypertension, coronary artery disease, osteoporosis, cancer
- Osteoporosis
  - Stop smoking. Start exercising regularly.

- Daily calcium 1000-1500 mg & 800 U vitamin D
- Follow bone density especially with flares and glucocorticoid treatment.
- Consider postmenopausal estrogen replacement
- Supplement vitamin D to keep serum 25 OH vitamin D at high normal level
- Thiazides, alendronate, calcitonin, NaFl
- Premature coronary artery disease
- 30% of deaths in the Baltimore Lupus Cohort (average age 38 years)
- Independent risk factors: older at diagnosis, hypertension, hypercholesterolemia, obesity, SLE duration, steroid therapy duration
- Prednisone dose $\leq$ 10 mg/day deleterious. Prednisone contributes to high cholesterol/high blood pressure/excess weight.

Suggested reading

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SEW/ss

7/27/02

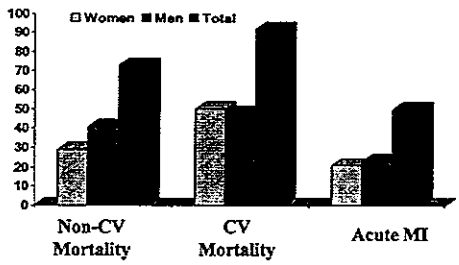
Coronary Artery Disease in Women

Women and CAD

- About 2.5 million women hospitalized annually for cardiovascular problems
- About 500,000 women die annually from cardiovascular diseases
- About 250,000 deaths from CAD
- About equal number of men and women die of CAD annually

US Cardiovascular Mortality

From AHA: 1991 Heart and Stroke facts
(in Thousands per year)



AMWA Education Project on CHD in women

What do Women Think?
American Heart Association Survey

Today
- 62% of women believe cancer is the greatest threat for women
- <10% of women perceive heart disease as greatest threat

Since 1997
- Knowledge of heart disease has increased from 34% to 40%
- Knowledge of stroke has increased from 28% to 35%

Robertson *Circulation* May 2001

Women and men are different!!!

- Prevalence of risk factors/ comorbidites
- Presentation
- Coronary anatomy
- Outcomes/Complications

Sex Differences

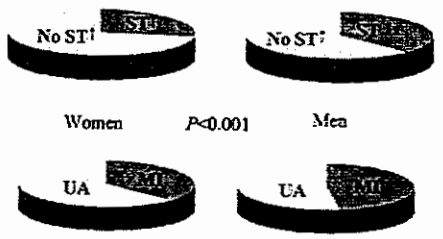
Greater
- Age
- Diabetes
- Hypertension
- History of congestive heart failure
- Atypical symptoms

Less
- Cigarette smoking
- Prior MI

SexDifferences in Presentation

- Late Presentation
- Atypical Symptoms
- Hypertension
- Tachycardia
- Heart failure
- ECG changes

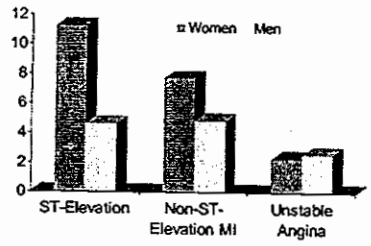
Sex Differences in Presenting Clinical Syndrome GUSTO IIB



Hochman et al. *N Engl J Med.* 1999;341:226-232.

GUSTO II-B

30-Day Mortality Stratified by Presenting Coronary Syndrome

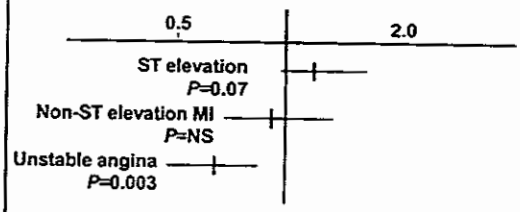


Hochman et al. *N Engl J Med.* 1999;341:226-232.

Adjusted 30-Day Mortality and Nonfatal Infarction

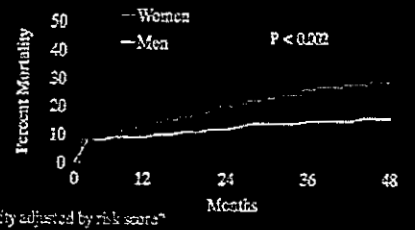
Odds Ratio: Women vs Men

GUSTO IIB



Hochman et al. *N Engl J Med.* 1999;341:226-232.

Mortality curves for women and men after myocardial infarction taken from a meta-analysis of 816 patients

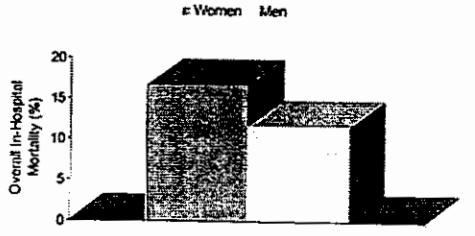


Mortality adjusted by risk score*

*Feller GH, Stone PH, Muller JE, et al J. Am Coll Cardiol. 1987;9:473-482. Variables included in risk score were age, hypertension, diabetes, smoking, congestive heart failure, family history of MI before age 60 years, level of education, Karnofsky score, cardiac arrhythmias, use of diuretics in the 3 weeks before admission, transmural ischemia/infarction, presence of ST elevation at randomization, hypotension on admission, and left ventricular ejection fraction on admission.

National Registry of Myocardial Infarction-2

Overall Mortality



Vaccarino et al. *N Engl J Med.* 1999;341:217-225.

National Registry of Myocardial Infarction-2

Baseline Characteristics

Odds ratio: Women vs Men

	30-59	60-69	70-79	80-89
Diabetes	2.14	1.67	1.30	1.11
Hypertension	1.45	1.46	1.53	1.66
Cigarette Smoking	0.96	0.96	0.90	0.59
Prior MI	0.80	0.72	0.70	0.73
Prior CHF	1.95	1.54	1.23	1.17
Prior CVA	1.73	1.23	1.02	0.91

Vaccarino et al. *N Engl J Med.* 1999;341:217-225.

National Registry of Myocardial Infarction-2

Presenting Symptoms and Signs

Odds ratio: Women vs Men

	30-59	60-69	70-79	80-89
No Chest Pain	1.52	1.32	1.15	1.04
Heart Rate>100	1.62	1.47	1.20	1.14
SBP <90 mm Hg	1.72	1.27	1.20	1.14
CHF	1.51	1.35	1.16	1.06
Shock	1.67	1.32	1.11	0.95
Nonspecific Changes	1.29	1.14	1.06	1.02
ST Elevation	0.77	0.89	1.04	1.17

Vaccarino et al. *N Engl J Med.* 1999;341:217-225.

National Registry of Myocardial Infarction-2

Treatment

Odds ratio: Women vs Men

	30-59	60-69	70-79	80-89
Aspirin	0.63	0.77	0.88	0.95
Thrombolysis	0.75	0.84	0.94	0.98
IV β-blockers	0.77	0.90	0.94	1.03
Angiography	0.90	0.84	0.82	0.77
CABG	0.72	0.74	0.68	0.65
PTCA	0.83	0.90	0.94	0.86

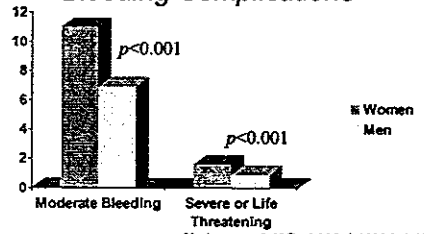
Vaccarino et al. *N Engl J Med.* 1999;341:217-225.

Hypotheses to Explain Higher Risk in Women

- More aggressive disease
- Less treatment with established therapy
- Differences in pathophysiology of MI
- Differences in coagulation/fibrinolysis
- Less extensive coronary artery disease
- Less collateral development
- Differences in symptoms and signs

Gender Differences in Complications from Thrombolytic Therapy

Bleeding Complications



Hochman et al. *N Engl J Med.* 1999;341:226-232.

Chest Pain and Insignificant CAD

Inaccuracies of coronary angiography

Syndrome X

Variant angina

GI etiology

Other

Trials of HRT

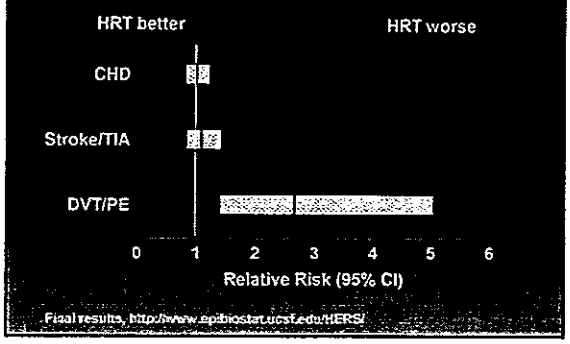
- PRIMARY PREVENTION
  - Risk Factors
    - PEPI
  - Carotid IMT:
    - EPAT (estradiol decreased IMT)
  - Clinical:
    - WHI (CEE, CEE+MPA, early excess vascular events, final results 2005)
    - WISDOM (CEE, CEE+MPA, results 2010)
    - RUTH (raloxifene, results ?2006)

Trials of HRT

- Secondary Prevention
  - Coronary angiography:
    - ERA (CEE, CEE+MPA, no effect on progression)
    - WELL-HART (estradiol, estradiol+MPA, results expected 2001)
    - WAVE (CEE+/-MPA, results expected 2002)
    - EAGAR (estradiol, IVUS, results expected 2004)
  - Clinical:
    - HERS (CEE+MPA, no effect overall on CHD, excess CHD first year, excess VTE)
    - PHASE (transdermal estradiol +/-NETA, small trial, nonsignificant excess CHD)
    - WEST (estradiol in patients with prior stroke, no overall effect on recurrent stroke, some early excess in estradiol group)

Selected Cardiovascular Outcomes in HERS

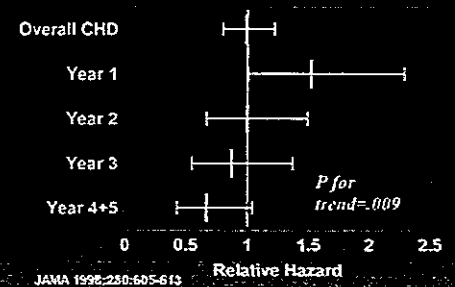
RCT of Estrogen/progestin vs. Placebo in Women with CHD



Final results, http://www.epibiostat.ucsf.edu/HERS/

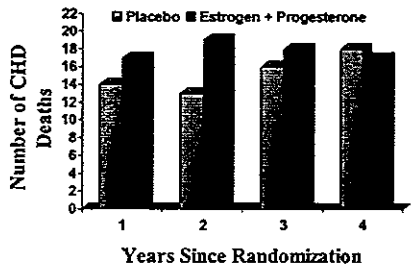
Heart and Estrogen/Progestin Replacement Study (HERS)

CHD by Year Since Randomization



JAMA 1998;280:605-613

HERS: Number of CHD Deaths



Heart and Estrogen/Progestin Replacement Study (HERS)

Venous Thromboembolic Events by Year Since Randomization

JAMA 1998;280:605-613

Estrogen after Ischemic Stroke: the Women's Estrogen for Stroke Trial (WEST)

Viscoli et al, Stroke 2001;32:329 (abstr)

- RCT of oral 17- beta estradiol 1 mg versus placebo
- primary outcome nonfatal stroke and all-cause death
- 652 postmenopausal women with stroke or TIA in previous 90 days
- mean age 71 (46-91)
- mean follow up 2.7 years
- 76% on study drug at one year

How Does HRT Cause Venous Thrombosis?

HRT Effect + Synergism with Thrombotic Abnormalities

HRT	= 4x risk
Thrombotic abnormality*	= 3x - 4x risk
HRT+ACP-r	= 13x risk

* high factor IX, low antithrombin, or activated protein C resistance

Lowe et al, Thromb Haemost 2000; 83:530-5 (66 cases, 163 controls age 45-64)

Sex differences in early and long term result of angioplasty

- The gender influenced the outcome of PTCA , early results were compared in 705 women and 2374 men.
- Women were older ($p< 0.01$) and had more unstable angina ($p < 0.01$), class 3 or 4 angina ($p<.01$).
- Women had lower angiographic success rate (60.3vs 66.2%; $p <.01$) and had lower clinical success rate (56.6% vs 62.2%; $p<.01$)
- Women had more complications (27.2% vs 19.4%; $p<.01$)
- Overall frequency of major complications (death, MI, emergency surgery) was not deferent 9.8%vs9.3%.
- Women had higher incidence of coronary dissection ($p<.05$) and higher hospital mortality(1.8% vs 0.7%; p,.01)
- PTCA related mortality is 6 times higher in women.

TIMI III Study

- Women were less likely to smoke than men.
- Women were more likely to have history of arterial hypertension and diabetes mellitus and family history of premature coronary disease.
- Women were less likely to have had prior MI as well as prior cardiac procedures(catheterization or revascularization).
- Women present with angina in similar way as men.
- Women were less likely to receive intensive ischemic therapy for their qualifying episode of angina.
- Women were less likely to have a high risk exercise thallium test response .They underwent exercise testing at the same rate but less likely to undergo coronary angiography compared with men $P< .001$, they were found to have less severe or extensive coronary disease.

TIMI III Study

- Women had lower incidence of treatment with beta-blocker, asprin, heparin and nitroglycerin.
- Women less likely to undergo revascularization procedure than men, they experience similar outcome in terms of death, MI, or recurrent ischemia by 42 days.

THE ROLE OF A SOCIAL WORKER IN A MEDICAL SETTING

An Overview

Janice Farmer, BA, MSSA, LICSW
Clinical Social Worker, Emeritus
Children's National Medical Center
Washington, DC

Purpose of Social Work as a Profession

A focus on individual / families in a specific situation

Action is to help individuals/ families meet the demands/cope with the crises in their lives

Manage crises caused by unexpected events

Identify strengths of the individual / family

Identify resources in the community

Goal is to integrate their reality and adapt

Resume normal function of their lives

Type of Social Work Specialties in Health Care

Hospital based:

Pediatric; Adolescent; Adult

Outpatient / Clinic based

Alcohol / Substance Abuse Treatment Centers

Mental Health – Inpatient and Outpatient facilities

Pediatric and Adult

Hospice

HIV / AIDS Clinics / Outreach

Geriatrics / Long-term care facilities

Hospital Social Workers

Specialty Based

Part of the Interdisciplinary Team: Physician, Nurse, Psychologist, Nutritionist

Cardiology

Dialysis

Pulmonary

Hematology / Oncology

Neonatal Intensive Care Unit / Intensive Care Unit

Endocrinology

Hematology / Oncology

Referral to Social Worker from Interdisciplinary Team Member

Social Worker interviews patient / family and completes an assessment to identify problem and establish treatment plan

Crisis secondary to diagnoses and hospitalization

Issues: Shock of Diagnoses;

Anxiety about hospitalization

Child fears diagnostic tests, multiple "strange" people, hospital routine, treatment

Losses – health, separation from family

Reality Issues: care of other children, economic, insurance

Oncology Patient

Impact of diagnoses on patient / family

Assess level of understanding of diagnoses and treatment plan

Communicate with Interdisciplinary team

Oncology Patient / Family

Need to cope with repeated hospitalizations

Ongoing diagnostic tests and treatment regime

Side effects of chemo-therapy treatment

Fear and anxiety of remission / exacerbation of disease

Loss to child of normal activities, role in family, school, play

Fear of death

Hematology

Hemophilia

Outpatient diagnosis and treatment

Diagnosis usually at birth of child

Referral to Social Worker

Assessment / Counseling / Education

Significant impact on parents, particularly the mother

Feelings of guilt

Anxiety about the future for the child

Hemophilia Patient

Outpatient Treatment by Interdisciplinary Team: Nurse, Physician, Physical Therapist, Genetics Counselor, Social Worker

Education and Counseling critical

Need for "normal" growth and developmental experiences in a "safe" environment

Need for patient / family to identify bleeding episodes

Understand of Emergency Room routines

Parents need to learn to infuse factor replacement product

Goal for patient to learn to be independent and manage condition

Concern of costs of factor replacement products

Hospice

Patient, Family, Physician make decision for Hospice Care

Interdisciplinary team: Nurse, Physician, Clergy, Volunteer, Social Worker

Hospice Care for patients with limited life expectancy

Plan is to stop all active medical treatment

Focus on comfort care

End of life issues

Role of Social Worker in Hospice Setting

Hospice Care usually home based

Hospice Facilities for Respite or "final days"

Assessment interview of patient and family

Determine patient and family member's understanding

Of Hospice Care

A time to grieve

Counseling of patient – goal to permit patient to complete life tasks

Counseling of family to "complete" relationship / closure

Substance Abuse / Alcohol Abuse Treatment

Referral by family, courts, self (patient)

Inpatient or Outpatient

Detox is Inpatient only

Intensive group and individual counseling

Conduct regular urine tests to assure sobriety

Involve community agencies and AA

Counseling and support for families

Job / employment issues

Need for life-long commitment of sober life-style

Long-Term Care

Social Worker Interviews all admissions

Significant impact on patient

Loss of health, former life style, separation from family, and former activities

Adjustment to environment and new routine

Importance of maintaining hopeful, positive environment with appropriate stimulating activities

Counseling with focus on helping patient / family adapt

End of life issues / closures

Assist families with loss of their loved one and funeral arrangements

In Summary

Social Workers in Health Care Settings

Goal is to support patients / families as they integrate a new reality

Respect the individual needs and family autonomy

Support the patient and family negotiate the health care system

For example: Multiple specialties, frequent hospitalizations and out-patient clinic appointment

Support communication between patient / family and Health Care Providers

EURASIAN MEDICAL EDUCATION PROGRAM

TRIP REPORT

Khabarovsk and Moscow, Russia

October 23 – November 6, 2002

Visiting Professors

Bruce K. Lloyd, MD
Associate Professor, Georgetown University

Charles Christianson, MD
Associate Professor, University of North Dakota

Eurasian Medical Education Program

Edward J. Burger, Jr., MD, Sc.D.
Director

Wednesday, 10/23/02

Immediately upon arrival in Moscow I met with Mr. George Russell who was in that city for a meeting of the East-West Institute. Included in the Meeting were Nikolai V. Kapranov, Country Director for Russia, East-West Institute, and Vasil Hudák, Senior Vice-President, East-West Institute, Prague Centre. The purpose of my meeting was to discuss a broad initiative for health assistance for Russia in the context of his evolving program for the Russian Federation.

Dr. Charles Christianson, Dr. Bruce Lloyd and I arrived in Khabarovsk on the afternoon of Thursday, October 24.

Friday, 10/25/02 Khabarovsk (The itinerary for the trip and for the Khabarovsk portion of the travel are found in Appendix A)

A. Dr. Lloyd met with patients at the Khabarovsk Regional Hospital in the morning

B. Dr. Christianson and I met at 10:00 AM with Dr. Boris Kogut, Rector, Far Eastern Medical University, and with his five deputy rectors:

Dr. Natalia Varonina, Prorector for Postgraduate Medical Education and Chairman of the Department of Therapy

Professor Rud, Prorector for Cultural Issues and Chairman of the Department of Pediatrics

Professor Michael I. Petrichko, Prorector, Science and Research and Chairman, Nephrology and Urology

Professor Vladimir P. Molotchnyi, M.D., Ph.D., Prorector, Medical Sciences and Chairman, Department of Infectious Diseases

Dr. Larissa Zhitinikova, Chairperson, Family Medicine

This session was devoted to an acknowledgment of the accomplishments of the Eurasian Medical Education Program in Khabarovsk, particularly for hypertension and cardiovascular disease, and proposals for further work.

Dr. Kogut described in general terms his aspiration for furthering the Family medicine initiatives to additional parts of the Far East – especially Sakhalin, Khabarovsk and the Jewish Autonomous Region. This discussion was somewhat general and did not appear to be as clearly linked to population shifts and trends in economic development as might have been expected. Dr. Kogut's conception includes the establishment of privately-funded family practice units, available on a fee-for-service basis.

Dr. Christianson made three proposals:

- Study and take advantage of the parallels between rural North Dakota and rural areas of the Russian Far East

- Develop creative programs to further professional education

- Search for opportunities for cooperative research – including comparative studies of international experience

Dr. Petrichko replied that cooperative projects of this sort were very appealing in the face of changing economic development. On the one hand, the Russian Far East is experiencing a net loss of population (although Khabarovsk City remains stable). On the other, there are rapid economic changes anticipated in Sakhalin and in adjacent Khabarovsk krai.

Dr. Petrichko proposed three project areas:

- Opportunities for primary and secondary prevention for persons who work in remote areas. He emphasized particularly non-infectious diseases. (Dr. Petrichko acknowledged the substantial contribution made by our program for hypertension and diabetes.)

- Opportunities for secondary prevention of cancer

- Problems of the elderly in the face of a growing population of the aged. It would be useful to take advantage of U.S. experience in gerontology.

Dr. Kogut passed on a concern from the Governor's office of the hazards to health and complication resulting from chronic exposure to long-burning forest fires (smoke, carbon dioxide, etc.), which is common in the Far East. Any U.S. experience would be helpful. (Dr. Molotchnyi expressed his skepticism about this problem).

Dr. Christianson offered to inquire of useful experience and resources from the American Academy of Family Practice.

I encouraged this discussion but indicated a dependence on adequate funding.

C. At noon, we all met with an additional group at the Regional Hospital:

Dr. Sergei Pudikov, Head Physician and Hospital Director

Dr. Vladimir Bondar, Head Surgeon, Cardiovascular Disease.]

Dr. Tatyana Polykova, Head Physician and Medical Director

Dr. Petrichko, representing the Far East Branch of the Russian Medical Association

Dr. Polykova's son

A surgeon, member of the Board of the Federal Medical Assocation.

Once again, Dr. Petrichko was a very strong supporter of our program and a source of constructive ideas for further cooperation.

Some of this discussion turned around development of further professionalism and professional organizations.

Dr. Bondar announced plans for a new regional cardiovascular center. (See Appendix B). Initially, this center is to serve Khabarovsk City and surrounding areas with eventual coverage of larger (Far East) areas.

We were furnished with a list of "needs" for the field of interventional ccardiology (Appendix C). These were grouped under the headings of education, research and administration.

Finally, Dr. Polykova and others inquired about the possibility of a liaison of some sort with the American College of Physicians.

D. Meeting with Dr. Sirotin

Dr. Sirotin proposed that exchanges for education purposes had perhaps reached its useful limit but strongly encouraged finding topics suitable for cooperative research. (See Appendix D and E). Dr. Sirotin was particularly interested in the possible comparative study of diabetes among the Nanai tribe in Khabarovsk Krai relative to other, comparable tribes in the United States (Alaska). According to a study recently completed by one of his students, there is no diabetes found among Nanai males. (Ryabova, T.I., "Distribution of type II diabetes among native and recently arrived people in Khabarovsk." Dissertation Thesis, 2002.)

Dr. Sirotin presented us with a copy of a recent monograph (Sirotin, B., Merenetsky, K.B., and Onshakova, O.V., "Dalogin in a combination drug for ulcer lesions in the diabetic stop syndrome." Khabarovsk, 2002.) The forward was written by Dr. Gerald Bernstein.

E. Later that afternoon I met with Dr. Karpenko to review the status of the tuberculosis program. Dr. Karpenko was especially complementary about the contribution our program had made to the thinking about tuberculosis, especially through the visits to the United States. He appeared particularly candid regarding the deficits he faced in dealing with tuberculosis:

- There are one-third fewer TB physicians than needed

- He lacks funds for transportation, for x-ray equipment and for laboratory equipment

I relayed as much information as was available about the currently estimated possibility of a World Bank loan. I indicated to him the possibility of an Ex-Im Bank loan guarantee for laboratory equipment and summarized the somewhat complicated process for seeking these funds.

Saturday, 10/26/02

All of us took part in the Rotary-sponsored health fair ("Day for Family Health") held at School No. 80. The decision to hold this fair in a school setting and deal with teachers and pupils was apparently reached after a year-long, difficult series of negotiations. The general subject was prevention of disease and promotion of health for school-aged populations.

While this was not what we would have favored for our contribution, in fact, I believe we did make a useful contribution. The audience was an estimated 700 students, teachers and some parents. (The audience could have been much larger, but was limited by restricting participation.)

Taking part were local Rotarians, members of the Khabarovsk krai Duma, Dr. Dwight L. Snyder representing a Rotary Club in Arizona and representatives from the Far Eastern Medical University. Particularly outstanding were the President of the Khabarovsk Rotary Club and member of the Duma, Mrs. Khukova, and the school principal.

The morning was devoted to ceremonial activities and demonstrations for the students. In the afternoon, each of Drs. Christianson, Lloyd and Burger delivered hour-long lectures to teachers and students:

- Seminar - "Role of the family in promoting a healthy way of life" – Christianson

- Roundtable on problems and programs for prevention of disease, and promotion of health in the U.S. – Burger

- Lecture on prevention of cardiovascular disease – Lloyd

Following the health fair, we met at length with Dr. Zhitnikova and Dr. Svetlana Pavlova to discuss possible collaborations in family medicine and to plan for further data collection for hypertension. Dr. Christianson offered two proposals, both of which were accepted:

- A joint publication discussing family practice and family practice training in the Russian Far East. Authors are to include Boris Kogut, Larissa Zhitnikova, and Charles Christianson. Dr. Zhitnikova is to supply details of the training of family physicians in Khabarovsk. Charles Christianson will be responsible for the writing.

- Brief exchanges to the U.S. of family practice physicians to the University of North Dakota

- Dr. Zhitnikova agreed to further data collection, following the pattern of Dr. Bistrovsky

Monday, 10/28/02

A planned trip to Birobijan was canceled because of 3-day-long snow and windstorm.

We met a second time with Dr. Sirotin who agreed to continue the gathering of data on registered diabetics from both the Regional Hospital and the whole of the Khabarovsk City.

Late in the afternoon we met with Dr. Oteva, Chief Rheumatologist. When shown the slides prepared for a talk by Dr. Sara Walker in Kazan, she became very enthusiastic over the prospect of one or several exchanges on rheumatology issues in Khabarovsk. She would be pleased to see one each in the spring and next November.

Tuesday, 10/29/02

At 9:00 AM we met with Sergei Chichanalskiy, Vice-Chairman for Social Affairs, and the Governor of the Khabarovsk krai, Viktor Ishaev. Mrs. Irina Strelkova apparently arranged this meeting. Mr. Chichanoskiy, an engineer by training, has been in this position about six months. His office set the agenda for this meeting, which consisted of two items, tuberculosis and the extension of our program. He described the new postgraduate training program and refurbished facility and invited us to work with that institute. I replied that we would be pleased to work with both institutions. He requested a detailed prospective program of our activities.

Between 10:00 AM and 2:00 PM, Charles Christianson gave a series of talks on family medicine and saw patients at the family medicine clinic under the direction of Dr. Larissa Zhitnikova and her colleagues.

During this period, Bruce Lloyd and I undertook a similar exercise at one of 5 polyclinics associated with Hospital #10. This complex serves a surrounding catchment area of 16,000 persons.

The Hospital Director described a number of creative efforts designed to reduce hospitalization and length of stay.

Dr. Natalia Varonina is Prorector for Education and Chairman of Therapy.

Before an audience of about 50 persons, Bruce Lloyd delivered a very straightforward lecture on cardiovascular risk factors and how to prevent them, followed by a discussion of appropriate therapy.

At 3:00 PM, we met over lunch with Dr. Strelkova. This included a candid conversation about our continuing relationship with the Far Eastern Medical Center in an uncertain environment. We also touched on tuberculosis.

Mrs. Strelkova was particularly concerned with tuberculosis. I left with her a copy of the letter-report from our colleagues in Ekaterinburg. On the subject of further cooperation, Mrs. Strelkova indicated the importance of continuing these exchanges and promised her continuing support.

At 4:00 PM, Anatoli Fomine, Dr. Boris Kogut and I met with Uri Timofeevich Averianov, Deputy to the Regional Representative of President Putin for the Russian Far East, General Konstantin Mulikovsky. Mr. Averianov was accompanied by two of his colleagues, Dr. Kapitomenko and Mr. Prigornev. This was an important meeting as it represented Dr. Kogut's responsibilities as Deputy Minister of Health for the Federal Ministry of Health. We were strongly encouraged to extend our program to additional areas of the Russian Far East. Finally, Mr. Averianov made note of a forthcoming meeting in January 2003 of all of the governors of the Russian Far East focused particularly on economic development and political issues.

That evening, we met with Boris M. Kogut for dinner. The subjects for discussion included:

- Relationships between the Khabarovsk krai health leadership and the Far Eastern Medical University
- Further expansion of our programs in the Russian Far East
- Possible month-long residence in the United States of Dr. Kogut's daughter

Wednesday, 10/30/02 and Thursday, 10/31/02

Both of these days were devoted to a conference ("Third Scientific-Practical Conference") for continuing medical education in the Russian Far East. (Appendix F). This 2-day meeting was dedicated to a revered gastrointestinal specialist. Professor L.I. Gellera. Sponsorship was divided between the Far Eastern Medical University and the Khabarovsk krai Ministry of Health. Accordingly, on the first day, the meeting was held at the university, and on the second, it took place in the newly refurbished conference facility of the Khabarovsk krai Regional Hospital.

Each of Drs. Christianson, Lloyd and Burger delivered lectures to an assemblage of approximately 250 attendees. The subjects of these talks corresponded to requests made by the organizers of the meeting:

- Charles Christianson - family medicine training and practice
- Bruce Lloyd - cardiovascular disease
- Edward Burger - American policies and programs for financing medical care and for controlling expenditures

During the afternoon of October 21, we met with Dr. Oteva, Chief Rheumatologist, Khabarovsk krai. She had earlier expressed interest in encouraging continuing medical education programs dealing with arthritis and rheumatology. She had had the opportunity to review the visual educational material prepared by Dr. Sara Walker for the latter's presentation earlier in Kazan. As a result, she strongly urged that we make possible a similar series of presentations in Khabarovsk. Her desire was for two separate visits over the next year.

We departed Khabarovsk at 7:00 PM for return to Moscow.

Monday, 11/4/02

9:00 AM Had an abortive attempt to meet with Tatyana Loginova, Operations Officer, World Bank

10:30 AM I met for a half hour with Ambassador Alexander Vershbow. Joining the meeting were:

Kerry Pelzman, Chief, Health Division, US AID
Jeffrey A. VanDreal, First Secretary
Melissa Sanderson, Science and Technology

We discussed three principal issues:

I took the opportunity to acquaint Ambassador Vershbow with the details and accomplishments of the Eurasian Medical Education Program over the past 4½ years.

I invited the Ambassador to visit one of the regions covered by our program during the course of one of our visits.

I summarized our current involvement in the development of a broad, public-private initiative for health for Russia ("Program for Health and Security"). This elicited a good deal of interest and offer of assistance.

In addition, I acquainted him with the proposed NIH-funded project to determine the implications of the HIV/AIDS epidemic on the TB epidemic. We also discussed the prospect for borrowing upon selected biological warfare resources in Russia for tuberculosis.

12:30 PM I met for an hour with Andrew B. Somers, President, American Chamber of Commerce in Russia, and with Tatiana Raguzina, Senior Director, Strategic Planning and Policy. Andrew Somers was very enthusiastic about the prospect of a public-private effort for health in Russia. He offered the offices of his organization and introductions to some key individuals and firms he believed would be important contributors. I was furnished a series of names for further contacts.

2:00 PM I met with Ricardo Cabeza de Vaca, Country Manager, Merck Sharp and Dohm Idea, Inc., and with Tatiana V. Serebriankova, MD, Ph.D. (clinical pharmacology), Product Manager. We discussed two levels of collaboration:

- The dovetailing of the distribution of cardiovascular drugs and information about those drugs with our CME activities

- Contribution to a longer-term, broad public-private program for health assistance in Russia. Included in this discussion was a reference to the recently concluded (7/31/02) agreement between Secretary Tommy Thompson and Health Minister Yuri Shevchenko

4:30 PM I met with Hugo Erikssen, Director, International Information Department, Yukos Oil Co. According to Hugo Erikssen, Yukos is the largest single contributor to charitable giving in Russia, supplying 30% of all charitable funding. Yukos is interested in furthering this effort, particularly kin the geographic regions where it operates. Yukos would like to have partners in this matter.

I was asked to provide a prospectus for the Program for Health and Security proposal in Russian to which he promised a rapid reply.

Tuesday, 11/5/02

I spent essentially the entire day with Boris N. Topornin, Director, Institute of State and Law, Russian Academy of Sciences. Boris Topornin has been serving as the key Russian representative for the Future of Russia Program and its Balashika Project in the Moscow Oblast suburb. We discussed at length the combining of the efforts of the Future of Russia Project and the Eurasian Medical Education Program in the evolving Program for Health and Security.

Wednesday, 11/6/02

I met in the evening with Dr. Andrei Kozlov, Head, Biomedical Center, St. Petersburg. Andrei Kozlov spent two years at the NIH working with Robert Gallo. He heads a research program, partly funded by NIH, devoted to the development of a successful AIDS vaccine. We discussed his collaboration in two projects:

- An NIH (NIDA)-funded project designed to determine the effect of the Russian HIV/AIDS epidemic on the TB epidemic

- The planned Program for Health and Security

Itinerary for Khabarovsk Visit
October 24 – 31, 2002

Thursday 24

15:05	Meeting at the airport
16:00	Checking in the Parus Hotel

Friday25

09:30 11:45	Dr. Lloyd works at Regional Hospital with patients-
10:00 – 11:30	Meeting with Dr. Kogut
12:00 – 13:00	Meeting with Dr. Pudovikov, Director Regional Hospital, Dr. Polyakova, Medical Director and Dr. Bondar Chief Cardio-Surgeon
13:00 –14:15	Lunch
14:30 – 15:30	Dr. Sirotin
15:45 – 16:30	Dr. Karpenko
Dr. Lloyd	Vladimir Yurievich, 372-958, 701-646, (m) 779977
09:30 – 12:00	(interpreter provided by clinic)

Saturday 26

09:00 – 14:00	Hypertension Health Fair
After Health Fair	Meeting with Drs. Kogut, Zhitnikova, Pavlova and Lebedev discuss the Family Medicine development between EMEP, UND and FESMU

Sunday27
Trip to Petrogliphs Welcome 305603, 329679.783344

Monday 28
Visit to JAR

08:30	Departure for Biro
10:30	Arrival at Biro
11:00 – 12:00	Dr. Lloyd's Lecture
12:15 – 13:15	Dr. Christianson's Lecture
13:30 – 14:30	Meeting with Dr. Andreev

Tuesday 29

09:00 – 09:45	Meeting with Mr. Sergei Alexeeveich Chahonatskiy, Deputy Governor on Social Issues

Family Medicine Clinic

10:00	Lecture
10:00 – 12:00	Patients
13:30 – 14:00	Lecture and discussions

CVD

10:30 – 13:30	Lecture, patients, discussions.
14:30- 15:30	Lunch with Ms. Strelkova

Wednesday 30
Conference for Drs. Burger, Lloyd, Christianson
Far Eastern Medical University
09:30 – 14:00

11:20 – 12:00	Dr. Christianson's presentation on Family Medicine Gastroenterological Aspects

Thursday 31
CME Institute Conference for Drs. Burger, Lloyd, Christianson
10:00 – 14:30

11:10 – 11:20	Dr. Christianson's presentation on HP
13:20 – 13:40	Dr. Lloyd's presentation on Cholesterol: management and treatment
12:00 –12:30	Meeting with Rotarians
	Wrap up and departure

Proposed meetings with: Meeting with Dr. Oteva, Chief rheumatologist

THE MANAGEMENT OF HELICOBACTER PYLORI DISEASE IN FAMILY PRACTICE

Charles E. Christianson, M.D., Sc.M.
Department of Family Medicine
University of North Dakota School of Medicine

Dyspepsia

- A very common complaint
- Epigastric pain, often burning
- Nausea, gas
- Relation to meals
- May be caused by ulcer or gastritis
- Cannot accurately identify cause from symptoms
- Cannot perform endoscopy on all

Helicobacter pylori

- Present in 30% to 50% of adult U.S. population
- Prevalence increases with age
- More prevalent in minorities, lower socioeconomic status
- More prevalent in people born in developing countries

Diagnostic tests

- Endoscopy with biopsy
- Urea breath test
- Serum antibodies
- (Stool antigen)

Patient with dyspepsia

- Consider immediate referral: bleeding or cancer
- Consider other diseases
- Medications, especially NSAID's
- Treat with H2-blocker or proton pump inhibitor

Treatment regimes

- Proton pump inhibitor twice a day
- Two antibiotics:
- Clarithromycin 500 mg twice a day
- Amoxicillin 1 gm twice a day
- Tetracycline 500 mg twice a day
- Metronidazole 500 mg twice a day
- May add bismuth subsalicylate 525 mg four times a day

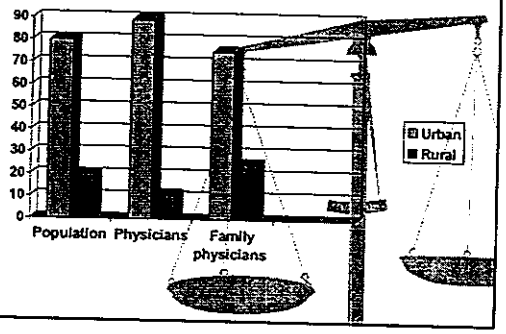
RURAL FAMILY PRACTICE

Charles E. Christianson, M.D.,Sc.M.
University of North Dakota

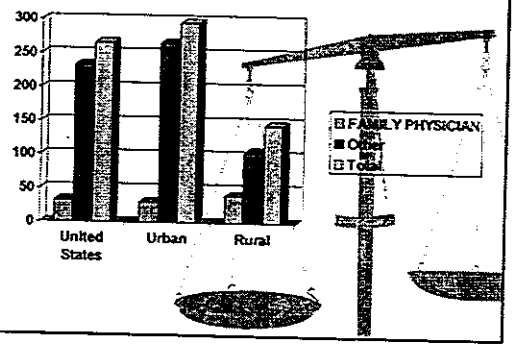
Family practice is the main source of care in rural areas

- Specialists concentrate in large cities, near hospitals and technology
- Areas with low population can only support a few doctors, not a group of specialists

U. S. Urban and rural population and physicians



Physician/population ratios



Medical problems seen in rural family practice

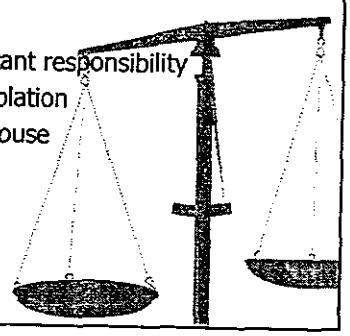
- More acute injuries, trauma: agricultural accidents, motor vehicle accidents
- More obstetrics and surgery
- More elderly
- Public health

Attractions of rural practice

- Wide range of practice
- More independence
- Small town life
  - Lower cost of living
  - Less crime
  - Good for children
  - Outdoor activities

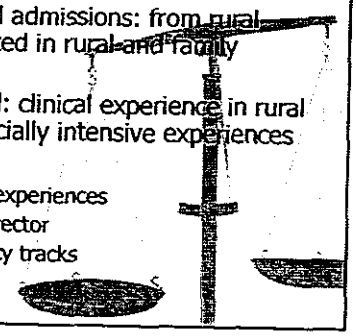
Problems

- Stress of constant responsibility
- Professional isolation
- Problem for spouse
  - Job
  - Cultural life
  - Shopping



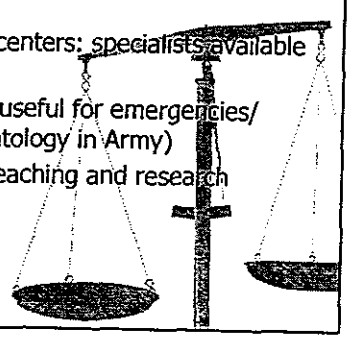
Policies to increase physicians in rural areas

- Medical school admissions: from rural areas, interested in rural and family practice
- Medical school: clinical experience in rural practice, especially intensive experiences
- Residency:
  - Rural clinical experiences
  - Supportive director
  - Rural residency tracks



Support for rural doctors

- Rural medical centers: specialists available part-time
- Telemedicine: useful for emergencies/ trauma (dermatology in Army)
- Networks for teaching and research
- Internet



THE ROLE OF THE FAMILY PHYSICIAN

Charles E. Christianson, M.D., Sc.M.
Department of Family Medicine
University of North Dakota
School of Medicine and Health Sciences

FAMILY MEDICINE IN THE UNITED STATES

- Development
- Training
- Role in health care system
- Relations with consultants

THE PRIMARY PHYSICIAN

The Folsom Commission, 1966

- Integration and continuity
- Preventive medicine
- Partnership
- Factors influencing health
- Render care or refer
- Concern for patient as a whole
- Continuing relationship

GROWTH OF RESIDENCY TRAINING

YEAR	RESDENCIES	RESIDENTS
1975	250	2671
1985	378	7489
2000	472	10503

RESIDENCY TRAINING

- BLOCK TIME IN SPECIALTIES
- OFFICE PRACTICE
- FAMILY PRACTICE CURRICULUM

SPECIALTY MONTHS

- 8 TO 12 – INTERNAL MEDICINE
- 4 TO 6 – PEDIATRICS
- 3 TO 4 – OBSTETRICS AND GYNECOLOGY
- 1 EACH – EMERGENCY, ORTHOPEDICS, ENT, DERMATOLOGY
- 4 TO 6 – ELECTIVE

FAMILY MEDICINE CURRICULUM

- DIAGNOSIS AND MANAGEMENT OF ACUTE AND CHRONIC DISEASES
- PREVENTIVE MEDICINE
- COMMUNITY MEDICINE
- HUMAN BEHAVIOR AND MENTAL HEALTH

Provide primary care

- First Contact
- Comprehensive
- Preventive
- Continuing

PERCENT OF VISITS FOR COMMON DIAGNOSES

- 7.4% Hypertension
- 4.8% Upper respiratory infection
- 3.2% Adult preventive examination
- 3.0% Diabetes
- 2.9% Sinusitis
- 2.3% Child preventive examination
- 1.8% Bronchitis

ACTIVITY IN HOSPITAL

- 86% admit to hospital
- 76% newborn care
- 56% coronary care
- 45% fracture care
- 37% assist in surgery
- 32% routine deliveries

Consultant care

- Provided on referral from family physician
- Limited to area of expertise of consultant
- Usually does not include preventive services
- Usually for a limited time

Reasons for consultation

- Advice about diagnosis and/or treatment
- Confirmation
- Procedure
- Second opinion
- Rarely, ongoing management of a complex condition

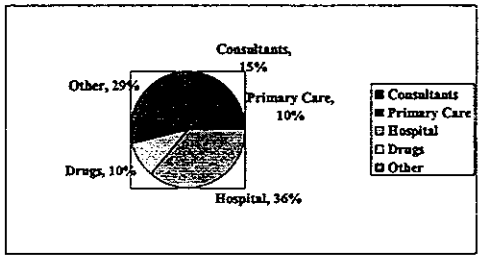
Responsibilities of family physician

- Refer appropriately: not too quickly, not too slowly
- Provide medical information to consultant
- Provide reason for consultation
- COMMUNICATE WITH CONSULTANT

Responsibilities of consultant

- Review clinical data and reason for consultation
- Provide appropriate diagnostic and therapeutic care
- Answer the questions of the family physician
- COMMUNICATE WITH FAMILY PHYSICIAN AND PATIENT
- Send patient back to family physician at appropriate time

U.S. Health care expenditures: 120,000 rubles per person per year



Conclusion

- Family practice is a growing and vital part of American health care
- Three year residency provides skills to meet most of patients needs
- Family physicians provide primary care and some hospital services
- Family physicians refer only 5% of patients
- Relations with consultant are usually cordial, especially when communications are good

ERRORS IN FAMILY PRACTICE

Charles E. Christianson, M.D., Sc.M.
University of North Dakota
School of Medicine

Medical error: a major concern now in the United States

- Estimated to be responsible for 50,000 to 100,000 deaths a years in hospitals
- Errors often a result of complex systems
- A systems approach to error reduction is usually more effective than blaming individuals
- Little is know about errors in family practice

Practice-based research networks

- A group of practicing physicians make practices available for research
- Allows a larger patient base, greater generalizability of results
- Practicing physicians can be involved in research:
  - Professional stimulation
  - Community with colleagues

Results

- 42 family physicians reported 342 errors
- 42% individual error
- 58% system error

Individual errors

- 23% treatment errors
  - 6% other
  - 17% medication
- 5% failure to respond to abnormal test result
- 14% lack of knowledge or skill

Process of care

- 31% administrative tasks
- 20% laboratory and other investigations
- 6% communications

Consequences

- 56% None
- 22% Care delayed or extended
- 18% Costs increased
- 25% Health consequences
  - 12% Patient angry, lost trust
  - 9% Patient became or stayed ill
  - 3% Patient hospitalized
  - 0.3%Patient died (N=1)

Eurasian Medical Education Program (EMEP)

Trip Report

Ekaterinburg
January 26 - 31, 2003

Visiting Professor:
Joseph E. Johnson, III, MD, MACP
Advisor to Chief Executive Officer,
American College of Physicians
Formerly, Dean, School of Medicine University of Michigan

Richard G. Farmer, MD, MS, MACP
Medical Director, EMEP
Clinical Professor of Medicine
Georgetown University Medical Center, Washington, DC

Harvey I. Sloane, MD
Director, Public Health, EMEP
Formerly, Commissioner of Health
District of Columbia, USA

The purpose of the visit was to conduct two seminars for continuing medical education (CME): Infectious Disease and Digestive Disease. This was a result of requests from the Urals State Medical Academy (USMA), with which EMEP has had a professional relationship since 1998, and, in conjunction with USMA, has conducted nine previous seminars. Focus subjects have included cardiovascular disease, diabetes, and tuberculosis (TB).

Russian colleagues have visited the US on four occasions for TB seminars, including four laboratory physicians who spent on one month in Denver in March 2002, learning laboratory techniques. In addition, our Russian colleagues have adopted Directly Observed Therapy (DOTS) programs for TB treatment by official decree, and they have emphasized treatment to conclusion and transition of TB care from prisons to civilian medical facilities.

Data collection is ongoing in cardiovascular disease, with emphasis on early detection, treatment, and follow-up of patients with hypertension. Increased compliance with medications, lifestyle modification, and blood pressure control have been demonstrated.

In diabetes, demonstration of improvement of care for patients with ketoacidosis (the most serious complications of diabetes) was documented following CME programs. In addition, there was -- and continues to be -- excellent transition care between pediatric and adult diabetic medical services.

Because of close collaboration between EMEP and USMA, discussions have occurred concerning changing medical problems over the past five years. Specifically, increases in prevalence of HIV/ AIDS and hepatitis caused requests for the current CME program. There were requests for discussions of common digestive diseases, plus requests for presentations regarding public health and medical education in the U.S. Accordingly, the two seminars were developed.

EMEP acknowledges the close cooperation of Rector Jasterov and Vice Rector Chugaev of USMA in the continuing of the EMEP program.

EMEP also acknowledges the presence of Elena Gurvich, PhD, representative of USAID - Moscow, who attended the entire seminar programs.

Monday, January 27, 2003

Infections Disease Conference, USMA

Attendance: 102 Russian physicians

Lectures: The New York Experience with the management of a TB epidemic, Dr. Sloane
Emerging Infectious Diseases, Dr. Johnson
"The Russian Cross", Dr. Sloane
The decrease in births and the increase in deaths, leading to a loss of population of 750,000 people a year.

Dr. Sloane discussed the TB epidemic in New York City in the early 1990s. A massive effort, including the news media and the government, was mobilized. The epidemic came under control with the use of DOTS and legislation enabling the detention of persons who did not comply with therapy. Completion of therapy increased from 50% to 93% during this program.

Dr. Johnson discussed "new" and "emerging" infectious diseases in recent years, including HIV/AIDS, Legionnaire's disease, the ebola virus, "mad cow" disease and West Nile virus. In addition, "old"

infections - TB, malaria, cholera -- have become more frequent. There are now concerns regarding possible bio-terrorism and use of anthrax, plague, and smallpox as weapons. Factors creating these problems include immuno-suppressed patients, antibiotic overuse (resistance), environmental factors and decline in Public Health systems. Bacteria are now resistant to some antibiotics, especially pneumonia and enteric bacteria. The West Nile virus is the most recent example of an organism that has "migrated" to other areas in the world.

Dr. Sloane discussed the "Russian Cross" and factors creating decrease in births and premature deaths -- the mean age of death of a Russian male is less than 60 years.

Meeting with Rector Jasterov; he is Representative of the Federal Ministry of Health for the Ural Region; and Vice Rector for CME, Prof Yuri Chugaev; he moderated and supervised the current EMEP seminars.

The Rector emphasized that USMA and EMEP "developed the programs together" and considers important focal points currently to be hypertension and infectious disease. There are 13 million people in the Ural region and he is pleased that they have "adopted the US experience" for treatment of certain diseases. He is interested in further programs regarding HIV/AIDS because of the increasing prevalence, and also "genetic" diseases. He is also concerned over the need for primary care / family physicians, "health organization" and public health issues, and CME for polyclinic physicians. We discussed all of these questions and expressed enthusiasm in continuing EMEP collaboration.

Tuesday, January 28, 2003

Infectious Disease Conference - Day 2

Lectures: TB in Russian Prisons, Dr. Sloane
Antibiotic Resistance, Dr. Johnson
Medical Education in the U.S., Dr. Farmer

Dr. Sloane described his experience during visits to prisons in Sverdlovsk, Tatarstan, and the Jewish Autonomous Republic. He observed that the major problems encountered were:

1. Resources / facilities
2. Drug availability
3. Infection control within the prisons
4. Quality of the laboratory.

He noted that about 10 % of prisons have TB and that 25 % of those are drug resistant. Completion of therapy and transfer to civilian medical facilities are significant impediments to successful treatment.

Dr. Johnson discussed antibiotic resistance and hospital-acquired infections, which are related problems. Failure of hand washing is the most common cause; also needle sterilization deficiency, infected catheters and IV tubes, and lack of isolation of patients. This is a worldwide problem that must be addressed in each hospital; empiric antibiotic therapy is quite appropriate but should be based on frequency of organism responsible for the infection. Target patient audiences for special attention include children, elderly patients, and those who are immuno-compromised.

Dr. Farmer described the medical education process in the U.S., from undergraduate to CME and discussed the differences and similarities with Russian education. There was considerable interest by audience members.

Meeting with Russian physicians who studied in the TB laboratory in Denver in 2002. They are responsible for bacteriologic control in the Ural region as well as education of other microbiologists. They described an organized course with syllabus and "hands on" laboratory work. They developed standards for culture, sensitivity, and infection control. They have published an article based on their experience. Drug resistant TB is about 5 % in civilian patients and about 15 % in prisons.

Dr. Chugaev noted that he has now trained more than 500 physicians in DOTS treatment.

All expressed gratitude to EMEP.

Meeting with Prof. Archipov regarding data collection in hypertension. Following completion of three series of lectures by EMEP visitors, data was collected to determine effectiveness of CME. In addition, Prof. Archipov developed "hypertension schools", that are seminars for patients, discussing lifestyle modifications and compliance
with therapy. There are now 6 schools in the city, using a similar format. There are 8 lectures by physicians, with 8 - 15 patients in each class. Each lasts 2 hours. There are also lectures that are given to patients and include up to 150 in audiences. Emphasis is on diet, exercise, alcohol, smoking and cholesterol lowering. They have been following 150 patients for more than one year and data are included in this report. Blood pressure control and compliance with medications have dramatically improved. An interesting aspect is "hypertensive crisis" this is unusual in the U.S., but there are 20,000 ambulance calls a year in Ekaterinburg (population 1.5 million) for this condition.

In the evening we met with Dr. Lev Grinberg, who was involved in the anthrax accident in 1979, He and Dr. Johnson had a very interesting discussion of this event

Wednesday, January 29, 2003

Gastroenterology Conference - 1st day

Audience attendance - 94 physicians

Lectures: Inflammatory Bowel Disease, Dr. Farmer
Hepatitis, Dr. Johnson

Both lectures were in-depth discussions of important chronic illnesses and there was considerable discussion from the audience. Prof Tamara Postnikova and Dr. Sergy Kuzmin, Head of Colonproctology, were prominent discussants. Dr. Farmer discussed current treatment, medical and surgical, for inflammatory bowel disease. Dr. Johnson described the evolution of knowledge regarding various forms of hepatitis and that chronic hepatitis C was now three times more common than B in the U.S., as many as 75 % of cases. Treatment of hepatitis C is complex but there is a vaccine for hepatitis B. Hepatitis A in the U.S. is much less of a problem than those forms which are blood bourne, and therefore related to IV drug use and HIV /AIDS. Dr. Sloane also commented on this aspect of transmission and public health efforts in prevention.

Meeting with Dr. Irina Zaikova, chief physician for pediatric diabetes.
She noted that EMEP lectures had been very helpful and that they were still using the materials from EMEP, given 3-4 years ago, as an example of "sustainability" of the program.
She described pediatric CME needs relating to growth delays, genetic diseases and reproductive problems. She would be interested in visiting professors with these interests.

Meeting with Prof Shilko, Vice Rector of Scientific Research.
He discussed the need for a hospital dedicated to care of HIV / AIDS patients and the organization of such services. He is also interested in "ecological factors" in disease and would like visiting professor input. In addition, emphasis on cardiovascular diseases (the leading cause of death) is important.

Thursday, January 30, 2003

Gastroenterology Conference - 2nd day

Lecturer: Gender differences in digestive disease, Dr. Farmer
Upper Gastrointestinal inflammation, Dr. Farmer
Public Health in the U.S., Dr. Sloane
Comments, Dr. Johnson

There has been great interest in the differences in frequency, clinical characteristics, and response to therapy among men and women with digestive diseases, particularly chronic inflammation. With the development of the office of Women's Health Research at the U.S. National Institutes of Health (NIH) 10 years ago, there has been much more research, particularly relating to safety and efficacy of drugs in women, including pregnancy and breast feeding.

Upper gastrointestinal inflammation affects 15-20 million people in the U.S. and is of great interest, because of the frequent presence of Helicobacter pylori as cause of inflammation, as well as pre-cancerous changes that may occur. There was considerable discussion regarding the most effective form of therapy and much audience participation.

Dr. Sloane described the 10 most significant public health successes in the U.S. in the 20th century - including infection control and vaccination / immunization, use of seat belts, anti-smoking programs and public education.

Dr. Johnson commented from his perspective as an infectious disease specialist and educator.

At the completion of the program, evaluation questionnaires were distributed to audience members (both programs). These were collected and will be tabulated in order to assess effectiveness of the program and for future improvements.

Meeting with Olga Nechaeva, chief of TB for Sverdlovsk Oblast and Yuri Chugaev, director of TB education. They discussed the very significant impact of EMEP programs and visits to the U.S. They now use DOTS, 500 TB physicians have been trained, and completion of therapy for TB has increased from 40 % to 70 %. Drug-resistant TB had increased but now has come to a plateau, both believe due to EMEP program. TB in prisons has decreased slightly. There are now 200 patients with HIV / AIDS and TB. They both were highly complimentary of EMEP and its contributions.

Meeting with Dr. Chugaev and Dr. Gurvich regarding future plans for EMEP. Dr. Gurvich emphasized the importance of "sustainability" and the long-term benefits of CME from EMEP programs. She wishes more involvement of "healthcare leaders" and public health leaders. She also encouraged EMEP to be "involved in their educational programs" as we have with USMA. She is interested in EMEP curriculum material that could be available for more widespread use in CME. It is her opinion that "sustainability" will result from "training the trainers" and involving medical and public health "decision makers."

Dr. Chugaev emphasized "collaboration" between USMA and EMEP and noted that the concept of "trainers" visiting the U.S. could be expanded to other subjects besides TB. We discussed this suggestion in detail. He believes CME priorities are cardiology, diabetes, TB, HIV / AIDS, public health and rural health.

Comment: This visit, from EMEP perspective, was excellent. The organization by EMEP coordinator, Dr. Maria Syrochkina, was superb. The involvement by Dr. Elena Gurvich was of great value to the program, and the collaboration of Dr. Chugaev was excellent. From EMEP perspective, the lectures were very appropriate and Dr. Johnson made a great contribution.

Richard G. Farmer

Richard G. Farmer, MD
Medical Director

УВАЖАЕМЫЕ ДОКТОРА!

Уральская государственная медицинская академия
и
Евразийская медицинская образовательная программа

приглашают Вас на конференцию

«Актуальные вопросы диагностики, лечения и профилактики туберкулеза и инфекционной патологии»

которая будет проходить

27-28 января 2003 года

в

Уральской государственной медицинской академии
3й учебный корпус, актовый зал
ул. Ключевская, 17

Начало регистрации 9.00
Начало конференции в **9.30**

170

Уральская государственная медицинская академия
Евразийская медицинская образовательная программа

ПРОГРАММА КОНФЕРЕНЦИИ

«Актуальные вопросы диагностики, лечения и профилактики туберкулеза и инфекционной патологии»

Екатеринбург, 27-28 января 2003 года

27.01.2003	9.00–9.30	Регистрация участников Конференции
	9.30-11.30	ВИЧ-инфекция/СПИД *Д-р Х. Слоан, ЕМОП*
	11.30-13.30	Вновь возникающие инфекционные болезни. *Д-р Д. Джонсон, ЕМОП*
	13.30-14.00	Перерыв
	14.00-16.00	Российский перекресток *Д-р Х. Слоан, ЕМОП*
28.01.2003		
	9.30-11.30	Туберкулез среди Российских заключенных *Д-р Х. Слоан, ЕМОП*
	11.30-13.30	Последипломное медицинское образование в США *Д-р Р. Фармер, ЕМОП*
	13.30-14.00	Перерыв
	14.00-16.00	Последипломная подготовка для Российских врачей в рамках ЕМОП *Д-р Х. Слоан, ЕМОП*

УВАЖАЕМЫЕ ДОКТОРА!

Уральская государственная медицинская академия
и
Евразийская медицинская образовательная программа

приглашают Вас на конференцию

«Актуальные вопросы диагностики, лечения и профилактики заболеваний желудочно-кишечного тракта»

которая будет проходить

29-30 января 2003 года

в

Уральской государственной медицинской академии
3й учебный корпус, актовый зал
ул. Ключевская, 17

Начало регистрации 9.00
Начало конференции **9.30**

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Уральская государственная медицинская академия
Евразийская медицинская образовательная программа

ПРОГРАММА КОНФЕРЕНЦИИ

«Актуальные вопросы диагностики, лечения и профилактики заболеваний желудочно-кишечного тракта»

Екатеринбург, 29-30 января 2003 года

29.01.2003	9.00–9.30	Регистрация участников Конференции
	9.30-11.30	Воспалительные заболевания кишечника: болезнь Крона и язвенный колит *Д-р Р. Фармер, ЕМОП*
	11.30-14.00	Гепатиты — современный взгляд *Д-р Д. Джонсон, ЕМОП*
30.01.2003		
	9.30-11.30	Синдром раздраженного кишечника *Д-р Р. Фармер, ЕМОП*
	11.30-12.00	перерыв
	12.00-14.00	Гастродуоденит, язвенная болезнь и геликобактериоз *Д-р Р. Фармер, ЕМОП*

JANUARY VISIT PROGRAM

Date	Time	Events
26.01.2003	22.00	Arrival day: arriving from Frankfurt; going to the hotel; dinner, resting in the hotel
	2.00 (27.01)	Dr. Sloane's arrival from Moscow
27.01.2003	8.00-9.00	Breakfast and picking up at the hotel
	9.30-16.00:	First day of the ID conference (Kluchevskaya, 17; Act-hall):
	9.30-11.30	✓ AIDS/HIV. *Dr. Sloane*
	11.30-13.30	✓ New infection diseases. *Dr. Johnson*
	13.30-14.00	Lunch
	14.00-16.00	✓ Russian Cross. *Dr. Sloane*
	16.30-18.00	Meeting with Prof. Chugaev and Rector (Repina, 3, the Main building of the USMA educ. centre)
	19.00-21.00	Dinner with Dr. Chugaev and Dr. Grinberg at the restraint
	21.00	Back to the hotel
28.01.2003	8.00-9.00	Breakfast and picking up at the hotel
	9.30-16.00:	Second day of the ID conference (Kluchevskaya, 17):
	9.30-11.30	✓ Tuberculosis in Russian prisons. *Dr. Sloane*
	11.30-13.30	✓ Postgraduate education in USA. *Dr. Farmer*
	13.30-14.00	Lunch
	14.00-16.00	✓ Continuing medical education of Russian physicians. *Dr. Sloane*
	16.30-17.30	Meeting with Prof. Archipov (Hospital 33)
	17.30-18.30	Rest at the hotel
	18.30-21.00	Opera or ballet or concert (classical music)
	21.00	Back to the hotel

29.01.2003	8.00-9.00	Breakfast and picking up at the hotel
	9.30-13.30:	First day of the GI conference (Kluchevskaya, 17, Act-hall):
	9.30-11.30	✓ Inflammatory Bowel Diseases: ulcerative colitis and Crone's disease. *Dr. Farmer*
	11.30-13.30	✓ Hepatitis — the overview. *Dr. Johnson*
	13.30-14.00	Lunch
	14.30-15.30	Meeting with Prof. Postnikova (the GI person)
	15.30-16.30	Meeting with Zaikova (the children diabetes person)
	16.30-17.30	Meeting with Prof. Sokolov (?)
	17.30-18.30	Rest at the hotel
	18.30-21.00	Opera or ballet or concert (classical music)
	21.00	Back to the hotel
30.01.2003	8.00-9.00	Breakfast and picking up at the hotel
	9.30-13.30:	Second day of the GI conference (Kluchevskaya, 17):
	9.30-11.30	✓ Irritable Bowel Syndrome. *Dr. Farmer*
	11.30-13.30	✓ Gastroduodenitis, ulcer disease and helicobacteriosis. *Dr. Farmer*
	13.30-14.30	Lunch
	15.00-16.30	Meeting with Chugaev and Nechaeva for further planning
	17.00-18.30	Rest at the hotel
	18.30-23.00	All-come dinner at the restraint
	23.00	Back to the hotel
31.01.2003	14.00	Leaving day. To the Airport.

Eurasian Medical Education Program

Continuing Medical Education for Russian Physicians

American College of Physicians-
American Society of Internal Medicine

Richard G. Farmer, M.D., MACP
Medical Director

1

Medical Education in the United States

1. **Undergraduate - College or University**
   - Ages 18-22 (4 years)
   - Science courses, history, literature, math, language, writing; AB, BS degree
   - Apply to medical school (125 in US – average size about 100/year)
     - Acceptance based on grades in college and standardized test, plus experience, interviews
     - Approximately 1 in 6 accepted
     - Cost about $25,000 per year

2

Medical Education in the United States

2. **Medical School (MD degree)**
   - Ages 22-26 (4 years)
   - Often different location from undergraduate
   - First 2 years basic science – lectures, laboratory work, introduction
   - 3rd and 4th years – "clinical" in hospital and outpatient settings
   - Progressive patient responsibility (with supervision)
   - Exams, standardized national testing

3

Medical Education in the United States

3. **Internship and Residency (4 years)**
   - Ages 26-30
   - Internal medicine and sub-specialties
   - Family medicine
   - Surgery and sub-specialties
   - Pediatrics and sub-specialties
   - Radiology
   - Pathology
   - Anesthesiology
   - Neurology
   - Psychiatry
   - Dermatology

4

Medical Education in the United States

Medical Residency Features (3 years)

- Hospital (In-patient)
  - Attending (faculty) rounds
  - Case presentations
  - Seminars (subject-oriented)
  - Interactive role-playing
  - Grand Rounds (lectures)
  - Critical Care (ICU)
- Ambulatory (Out-patient)
  - Continuity clinic (same patient, over time)
  - Core Curriculum (24 month cycle)

5

Medical Education in the United States

Medical Residency Features . cont.

- Elective Programs: Specific Diseases or Clinical Situations
  - Procedures (flexible sigmoidoscopy, testing, treadmill)
- Conferences
  - Journal Club
  - CPC
- Sub-specialty Rotations
  - Cardiology, gastroenterology, endocrinology, infectious disease, hematology/oncology, rheumatology, etc.
- Bioethics
- Clinical Investigation/Research
- Affiliated Hospitals

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Medical Education in the United States

4. **Surgical Specialties**

- Duration: 4-7 years (ages 27-34)
  - General surgery
  - Thoracic surgery
  - Cardiovascular
  - Neurosurgery
  - Orthopaedics
  - Gynecology
  - Urology
  - Opthamology
  - Otolaryngology

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Medical Education in the United States

5. **Medical Specialties (Fellowship)**

- Duration: 2-4 years (ages 30-34)
  - Cardiology
  - Gastroenterology
  - Pulmonary/Critical Care
  - Hematology/Oncology
  - Nephrology
  - Endocrinology
  - Infectious Diseases
  - Rheumatology

8

Medical Education in the United States

6. **Continuing Medical Education**

- Conferences, lectures, seminars
- Duration: days or weeks
- Requirement generally 50 hours over a 2 year period

9

Medical Education in the United States

Regulation

1. **Licensure – to practice medicine**
   - Given by individual states and renewed every 2-3 years
   - Pass exam; obtain CME
   - Ethical standards (license can be revoked by state board)
   - Supervision by Medical Board of Physicians and others

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Medical Education in the United States

Regulation, cont.

2. **Certification of Specialty**
   - National exam by specialty organizations (NOT government)
   - All specialties, including general practice, family medicine, primary care, as well as traditional specialties
   - Time limited; renew with exam

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Medical Education in the United States

Regulation, cont.

3. **Medical Schools and Residency**
   - Programs are accredited by national organization – private, NOT government
   - Standards are developed and reviewed
   - 425 programs in Internal Medicine

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Core Clinical Competence in Internal Medicine

1. **Patient Care**
   - Health promotion, disease prevention, treatment
2. **Medical Knowledge**
   - Critical evaluation, basic and clinical science
   - Critical problem-solving and decision-making
3. **Interpersonal and Communication Skills**
4. **Professionalism**
   - Ethical practices, compassion, sensitivity
5. **Practice-Based Learning and Improvement**
6. **Systems-Based Practice**
   - Continuity of care

Inflammatory Bowel Disease

Eurasian Medical Education Program

Inflammatory bowel disorders:
Crohn's disease and Ulcerative colitis

American College of Physicians-
American Society of Internal Medicine

Richard G. Farmer, M.D., MACP
Medical Director

Inflammatory Bowel Disease

Epidemiology of IBD

- 1-2 million IBD patients in the U.S.
- Equal incidence of ulcerative colitis and Crohn's disease
- Approximately 10,000 new cases diagnosed annually*

*Hanauer S. Inflammatory Bowel Disease. *N Engl J Med.* 1996;334(13):841-8

Inflammatory Bowel Disease

Epidemiology of IBD

- Peak onset: 15 to 25 years of age
- Second peak incidence: 50 to 65 years of age
- Approximately equal between males and females
- Incidence increased in industrialized nations from 1970 to 1990

Inflammatory Bowel Disease

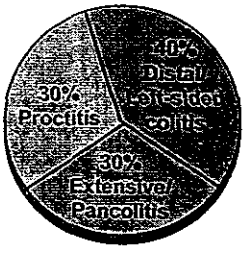
Genetics of IBD

- 10-30% of patients have a positive family history of IBD
- IBD is likely a complex, non-Mendelian genetic disorder
- Monozygotic twins – often share disease pattern and age of onset
  - Concordance – CD (58%) > UC (6%)
- Genome search – loci on chromosomes 12 and 16 confirmed*

*Satsangi, et al. *Nature Genetics*, 14:199, 1996
Hugot, et al. *Nature*, 379:821, 1996

Inflammatory Bowel Disease

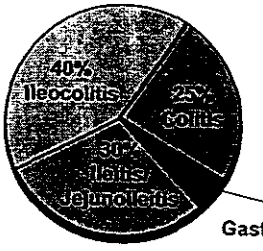
UC: Location and Extent



Percentages based on extent of disease at diagnosis

Inflammatory Bowel Disease

CD: Location and Extent



Inflammatory Bowel Disease

Colon Cancer in IBD

- Increased risk for colon cancer in UC and CD
  - surveillance if >8-10 yr. duration
  - uniform distribution, multiple areas involved
  - higher grade malignancy when detected
- Confirmed dysplasia
  - in flat mucosa – "high grade" should resect; "low grade" may progress to cancer[1]
  - in polyps – can be resected and managed conservatively[2]

[1]Woolrich AJ, et al. *Gastroenterology*. 103:431, 1993
[2]Rubin PH, et al. *Gastroenterology*. 117: 1295, 1999

Inflammatory Bowel Disease

Natural Courses of CD – The Facts

- Nearly 80% of patients require surgery within 20 years of onset[1]
- Recurrence within 6 years of surgery: 90% endoscopic/radiologic, 58% symptomatic[2]
- 20% of patients treated with steroids fail to respond after 1 year
- 36% of patients are unable to discontinue steroids due to rapid recrudescence[3]

[1]Mekhjian HS, et al. *Gastroenterology*. 77:898: 1979
[2]McLeod RS, et al. *Gastroenterology*. 113:1523; 1997
[3]Munkholm P, et al. *Gut*. 35:360; 1994

Inflammatory Bowel Disease

Refractory IBD

- Definition: Persistence of clinical, endoscopic or histologic manifestations despite adequate doses of oral (4.8 gm/d) and topical 5-ASA and steroids (40-60 mg/d prednisone) – includes patients who are unable to taper steroids after initial remission[1]
- Considerations: Stenosis, fistula, abscess, cancer, infection, drug hypersensitivity
- Prognosis: 60% of steroid-resistant patients require surgery
  30% of steroid-dependent patients require surgery[2]

[1]Hanauer S. Inflammatory Bowel Disease. *N Engl J Med*. 1996;334(13):841-8
[2]Munkholm P, et al. Gut. 35:360; 1994

Inflammatory Bowel Disease

Differential Diagnosis of UC

- Infection
- Ischemia
- Diversion, pseudomembranous, or radiation colitis
- Physical agent
- Immunologic etiologies
- Systemic disease
- CD
- Irritable bowel syndrome

Inflammatory Bowel Disease

Differential Diagnosis of CD

- Lymphoma
- Infectious etiologies
- Appendicitis
- Diverticulitis
- Carcinoma
- UC
- Celiac disease

Inflammatory Bowel Disease

5-ASA Summary

- First line therapy for IBD
- More 5-ASA is better: Optimize dose
  - Asacol - 4.8 gm/d
  - Pentasa - 4.0 gm/d
- Combination therapy improves response
- Dose needed for remission may equal dose needed for maintenance

Inflammatory Bowel Disease

Principles of Corticosteroid Therapy

- Corticosteroids are rarely used as monotherapy
- If clinical response to initial therapy is inadequate, add corticosteroids early
- Do not underdose corticosteroids
- If oral corticosteroids fail, change to intravenous corticosteroids
- Corticosteroids are not maintenance drugs

Inflammatory Bowel Disease

Osteoporosis in IBD

- Incidence 20% to 30%
  - Corticosteroid use, dose, and duration important
  - May occur in absence of corticosteroid use
  - Pathophysiologic considerations (smoking, amenorrhea, exercise status, etc.)
- Corticosteroid-associated bone loss occurs early
- All IBD patients should have bone density scanning
- Prophylactic use of calcium, vitamin D, bisphosphonates, nasal calcitonin

Inflammatory Bowel Disease

Azathioprine/6-Mercaptopurine

Toxicity: 6-MP

• Overall toxicity	15%
– Pancreatitis	3.3%
– Bone marrow depression	2%
– Allergic reactions	2%
– Drug hepatitis	0.3%
– Infectious complications	7.4%

Present, *Ann Intern Med*, 1989

Inflammatory Bowel Disease

Surgery in UC – Indications

- Urgent indications: massive hemorrhage, perforation or medical failure
- Non-emergent indications:
  - Suspected carcinoma or confirmed dysplasia
  - Debility and intolerable steroid side effects
  - Growth failure in children
  - Distal colitis with poor quality of life on maximal therapy
  - Extra-intestinal complications (rare)
    - Intractable hemolytic anemia
    - Pyoderma gangrenosum (resistant to steroids or CsA)

Inflammatory Bowel Disease

Surgery in UC – Procedures

- Subtotal colectomy with ileostomy – nutritionally deprived, elderly, high risk
- Elective second stage
  1. Proctectomy (completion)
  2. Ileal pouch-anal anastomosis
     - 5% pouch failure
     - 50% pouchitis (10-15% become resistant to antibiotics)
     - Surveillance for dysplasia needed
  3. Ileo-rectal anastomosis (rare) if poor surgical risk

Inflammatory Bowel Disease

Surgery in CD: Indications

- Failure to respond to medical therapy
- Management of complications
  - Strictures
  - Fistulae
  - Perforations
  - Perianal disease
  - Cancer or precursors

Inflammatory Bowel Disease

Anti-TNF for Fistulizing Crohn's Disease

- Randomized controlled trial of cA2 vs placebo in 94 patients with fistulizing Crohn's
- Endpoint: >50% closure of open fistulae (90% perianal, 10% abdominal)
- Infusion of study drug at 0, 2, and 6 wks

Present D, et al. N Eng J Med, 1999

Eurasian Medical Education Program

Gastroduodenitis, Ulcer and Helicobacter pylori

American College of Physicians-American Society of Internal Medicine

Richard G. Farmer, M.D., MACP
Medical Director

1

Treatment of Gastroduodenal Ulcers

Active ulcer

H_2-receptor antagonists
- Cimetidine 800mg
- Ranitidine/nizatidine 300 mg
- Famotidine 40 mg
- All administered between the evening meal and bedtime

PPIs
- Omeprazole 20 mg
- Lansoprazole 30mg
- Rabeprazole 20 mg
- Patoprazole 40 mg
- All administered daily before breakfast

2

Treatment of Gastroduodenal Ulcers (cont.)

Prevention of NSAID-induced ulcers
- Misoprostol
  - At least 200 µg 3 times/day
- PPIs
  - Omeprazole 20 mg
  - Lansoprazole 30mg
  - Rabeprazole 20 mg
  - Patoprazole 40 mg
  - All administered daily before breakfast

In general, duodenal ulcers should be treated for 4 weeks and gastric ulcers for 8 weeks.

3

Antisecretory Drug Regimens for Treatment of GERD

H_2-receptor antagonists
- **Nonerosive GERD**
  - Cimetidine 400mg twice/day
  - Ranitidine/nizatidine 150 mg twice/day
  - Famotidine 20 mg twice/day
  - Therapy should be individualized to fit patient requirements; often effective when administered between breakfast and lunch, and between the evening meal and bedtime
- **Erosive GERD**
  - Cimetidine 400mg every 6 h
  - Ranitidine/nizatidine 150 mg every 6 h
  - Famotidine 20 mg 12 h

4

Antisecretory Drug Regimens for Treatment of GERD (cont.)

PPIs
- **Nonerosive or erosive GERD**
  - Omepraxole 20 mg daily or 20 mg twice/day
  - Lansoprazole 30 mg daily or 30 mg twice/day
  - Rabeprazole 20 mg daily or 20 mg twice/day
  - Pantoprazole 40 mg daily or 40 mg twice/daily
  - All administerd daily before breakfast; second dose, if necessary should be given before evening meal.

5

Preferred Therapies for *H. pylori* Infection

Twice a day PPI or ranitidine bismuth citrate (RBC) triple therapies[a]
- A PPI or RBC
- Plus 2 of: amoxicillin 1 g, clarithromycin 500 mg, or metronidazole 500 mg

[a]The data suggest that there is no difference between RBC and PPI triple therapies when the *H. pylori* are sensitive. There may be a slight advantage for RBC triple therapies when resistant *H. pylori* are present.

6

Barrett's Esophagus

- Frequency: 10% to 15% of patients with GERD symptoms who have endoscopic examinations
- Pathogenesis: GER injures squamous epithelium and promotes repair by columnar metaplasia

7

EPIDEMIOLOGY
Risk Factors for H. pylori Infection

- Low socio-economic status
- Birth in a developing country
- Crowded living conditions
- Sharing a bed as a child
- Absence of hot water tap in home
- Poor sanitary conditions

8

H. Pylori infection

Irritation/inflammation

↓

Metaplastic epithelium

↓

Dysplasia

↓

CANCER

9

GASTRIC MALT LYMPHOMA

MALT: Mucosa-Associated Lymphoid Tissue

- A benign reactive process consisting of lymphoid follicles

MALT LYMPHOMA: monoclonal proliferation of neoplastic B-lymphocytes infiltrating gastric glands (lymphoepithelial lessons)

10

Barrett's Esophagus
Cancer Risk

- Barrett's exophagus is major risk factor for esophagal adenocarcinoma
- Cancer risk associated primarily with intestinal metaplasia
- Incidence of adenocarcinoma in patients with Barrett's esophagus: ~1% per year

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NCCDS
Crohn's Disease Activity Index (CDAI)

- Diarrhea
- Abdominal pain
- General well-being
- Extra-intestinal complications
- Use of opiates/lomotil for diarrhea
- Abdominal mass
- Hematocrit
- Body weight

12

Demographic Features of Inflammatory Bowel Disease

- World wide, especially Western populations
- Infrequent: Underdeveloped countries
  Inf. Dysentery High Incidence areas
- Incidence: Crohn's disease increasing*
  Ulc. Colitis stable
- More urban, Industrialized than rural
- More white than colored (but all races)
- All ages -- esp. children, teenagers
- More Jewish – but all groups
- Familial incidence – ulc. C. 20%, Crohn's d. 40%

*? Decreasing in Abereen, Stockholm

13

Indications for Surgery in Crohn's Disease

Ileocolic pattern
- Intestinal obstruction
- Internal fistula and abscess
- Perianal disease, severe

Small bowel pattern
- Intestinal obstruction
- Internal fistula and abscess

Colonic pattern
- Toxic megacolon
- Internal fistula
- Stricture with obstruction
- Perianal disease, severe
- Poor response to medical therapy and chronic disability; malnutrition

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Management of Crohn's Disease in Adults: Mild-moderate active disease

- Ileal, ileocolonic or colonic disease is treated with an oral aminosalicylate (sulfasalazine 3-6g daily or mesalamine 3.2-4.8g daily in divided doses)
- Alternatively, metronidazole 10-20mg/kg/d can be administered and may be effective in a proportion of patients not responding to sulfasalazine

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Moderate to Severe Disease

- After infection or abscess are excluded, patients with moderate-severe presentation are treated with predenisone 40-60mg/d administered until resolution of symptoms and resumption of weight gain (generally 7-8 days)
- Infection or abscess requires appropriate antibiotic therapy or drainage (percutaneous or surgical)
- Elemental diets may be an affective alternative to steroid therapy

16

Maintenance Therapy

- Corticosteroids should not be used as long-term agents to prevent relapse of Crohn's disease
- Mesalamine or azathioprine/6 mercaptopurine do provide maintenance benefits and should be considered for patients responding to acute medical intervention
- Mesalamine should also be considered to reduce the likelihood of recurrence of surgical resection

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Prognosis for Patients with Inflammatory Bowel Disease

1. Time from symptoms to diagnosis
2. Age at onset: childhood, prepubertal, adolenscs, adult
3. Severity of onset: acute, insidious
4. Location of disease: proctitis, pancolitis; ileitis, ileocolitis
5. Symptoms: diarrhea, bleeding, pain, weight loss, fever, arthritis

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Prognosis for Patients with Inflammatory Bowel Disease

6. Duration of disease and complications: chronicity, fistulae, obstruction, etc.
7. Dysplasia/cancer
8. Medical therapy and response: type, duration, side effects
9. Surgery: type, frequency, amount resected, recurrence
10. Quality of life

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Eurasian Medical Education Program

Richard G. Farmer, MD, MS, MACP
Medical Director
Clinical Professor of Medicine, Division of Gastroenterology
Georgetown University Medical Center
Washington, DC

American College of Physicians-
American Society of Internal Medicine

EMEP
Irritable Bowel Syndrome (IBS)

- Most common diagnosis in gastroenterology (19%)
- *Criteria for diagnosis*: abdominal pain, plus frequent bowel movements, often liquid and with mucus, pain relieved by bowel movements, abdominal distension
- Three times more frequent in women, up to 20% prevalence
- Physician visits by women are 3 times more than men

Digestive Diseases and Sciences
47:705, 2002

2

EMEP
Inflammatory Bowel Disease (IBD)

Crohn's Disease: 20% more common in women
Ulcerative Colitis: 20% more common in men

- Depression and irritable bowel syndrome (more common in women)
- Women are more compliant with medications
- Corticosteroid – induced osteoporosis (more common in women)
- Pregnancy and IBD

Office of Women's Health, 2002
US Dept of Health and Human Services 3

EMEP
Digestive Diseases in Women

1. Colorectal Cancer – third most common cancer in the US (after lung and breast)
   - 30, 000 deaths among women in US annually, far more than from cervical cancer
   - Slight male preponderance overall
2. Irritable Bowel Disease
   - Affects 15-20% of women in US
   - 3 times more women than men
   - Average loss from work is 13.4 days/year

4

EMEP
Digestive Diseases in Women (cont.)

3. Gallstone Disease
   - Affects 20 million people in US
   - Twice as common in women
   - 500, 000 cholecystectomies/year
   - Role of estrogens on cholesterol in liver
   - Inhibition of mortality in pregnancy
4. NonSteroidal Anti-Inflammatory Drugs (NSAIDs) and Peptic Ulcers
   - Aspirin and ibuprofin used more by women

5

EMEP
Digestive Diseases in Women (cont.)

5. Liver Disease
   A. *Autoimmune Liver Disease – Primarily Biliary Cirrhosis*
      - 9 times more common in women
      - Most common cause for liver transplant in women
      - Autoimmune hepatitis – 3-4 times more in women
   B. *Non-Alcoholic Steatohepatitis (NASH)*
      - Most common liver disease in women
      - Obesity, insulin resistance, diabetes

6

EMEP

Digestive Diseases in Women (cont.)

6. **Osteoporosis**
   - Affects 25 million people in US
   - 1 million fractures, especially in post-menopausal women
   - IBD and treatment with corticosteroids
   - Chronic Biliary Cirrhosis

7

EMEP

Digestive Diseases in Women (cont.)

7. **Digestive Disease During Pregnancy**

   A. *Chronic Conditions*
   - IBD – Relapse, remission, therapy, diagnostic procedures
   - Gallstones and Pancreatitis

   B. *Pregnancy Symptoms – nausea/vomiting*
   - Acute fatty liver of pregnancy

8

EMEP

Digestive Diseases in Women (cont.)

8. **Motility Disorders**
   - Peptides
   - Visceral hypersensitivity
   - Menstrual cycle
   - Environmental stressors

Agenda for Research on Women's Health
For the 21st Century, US Dept. HHS, 2000 9

EMEP

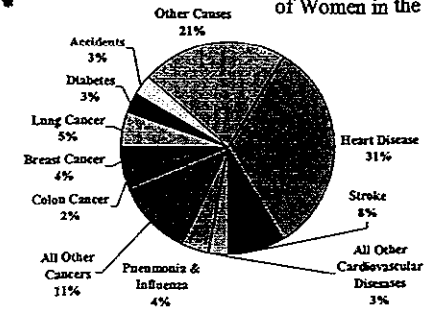
Digestive Diseases in Women (cont.)

9. **Inflammatory Bowel Disease and Pregnancy**
   - Fertility of women with IBD is normal
   - About 1/3 of IBD patients relapse during pregnancy
   - IBD poses no threat to the fetus
   - Mesalamine is safe during pregnancy
   - Pre-term birth (37 weeks) is more common
   - Breast feeding is safe with mesalamine therapy

Society of Women's Health Research, 2002 10

EMEP

Leading Causes of Mortality of Women in the U.S.



National Vital Statistics Report, Vol. 48, No. 11, July 24, 2000

Safety of IBD Medications During Pregnancy and Breast-Feeding

	Pregnancy Category	Safety During Breast-Feeding
• Sulfasalazine	B	Safe when indicated
• Mesalamine	B	Safe when indicated
• Corticosteroids	B	Safe when indicated
• Metronidazole	B	Avoid if possible (safe if used after the first trimester)
• Infliximab	C	Few available data
• Ciprofloxacin	C	Avoid if possible
• Cyclosporine	C	Contraindicated
• Azathioprine/6-Mercaptopurine (AZA/6-MP)	D	No available data
• Methotrexate	X	Contraindicated

1

Safety of IBD Medications During Pregnancy and Breast-Feeding, cont.

Category definitions:

A. Controlled studies in women do not show a risk to the fetus in the 1st trimester, and the possibility of fetal harm appears remote.

B. Animal studies do not show a risk to the fetus and there are no controlled studies in pregnant women, or animal studies do indicate a fetal risk but controlled studies in pregnant women do not.

C. Either animal studies show a fetal risk and there are no controlled studies in women, or there are no available studies in women or animals.

D. There is a positive evidence of fetal risk, but there may be certain situations where benefit may outweigh the risk.

X. There is a definite fetal risk based on studies in animals or humans, or based on human experience. The risk clearly outweighs the benefit in pregnant women.

*Briggs GG, Freeman RK, Yaffe SJ. Drugs in Pregnancy and Lactation: *A Reference Guide to Fetal and Neonatal Risk*. 5th ed. Baltimore, MD: Lippincott, Williams & Wilkins, 1998.

2

Inflammatory Bowel Disease

Inflammation mediated by alpha-4-integrins

- Treatment with selective adhesion-molecule inhibitor natalizumab
- Infusions 3-6mg/kg four weeks apart
- Use of CDAI for response
- Results similar to tumor necrosis factor inhibitor (infliximab)

*NEJM, January 2003

3

Eurasian Medical Education Program

Continuing Medical Education for Russian Physicians

American College of Physicians-
American Society of Internal Medicine

Harvey I. Sloane, MD
Director, Public Health

1

Public Health Approach to TB Control in US has had a Significant Effect on TB Reduction

2

THE NEW YORK EXPERIENCE

- For the last 100 years, New York City has been the center of the United States for tuberculosis control because of a larger concentration of tuberculosis
- Since tuberculosis was well-controlled in the 1960s and 1970s, TB hospitals, sanitoriums, clinics and staff were greatly reduced in the 1980s
- By 1989, less than half of the patients who began treatment were cured

3

THE NEW YORK EXPERIENCE

- In 1991: *New York*
  - 3% of the US population
  - 15% of tuberculosis in US
  - 61% of MDRTB in the US
- This New York Experience is presented as an example of how the United States' largest city abated its tuberculosis epidemic. There are many similarities to the Russian experience with tuberculosis

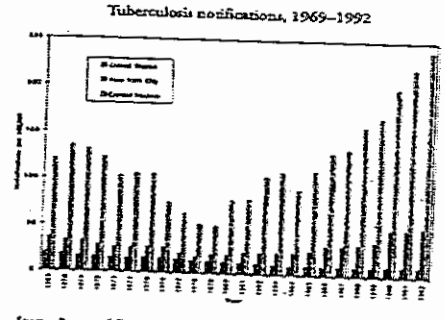
4

THE NEW YORK EXPERIENCE

The tuberculosis experiences in New York City and Russia have similar "U" curves of incidence

5

Tuberculosis notifications, 1969–1992



Source: Bureau of Tuberculosis Control, New York City Department of Health, Information Summary 1993.

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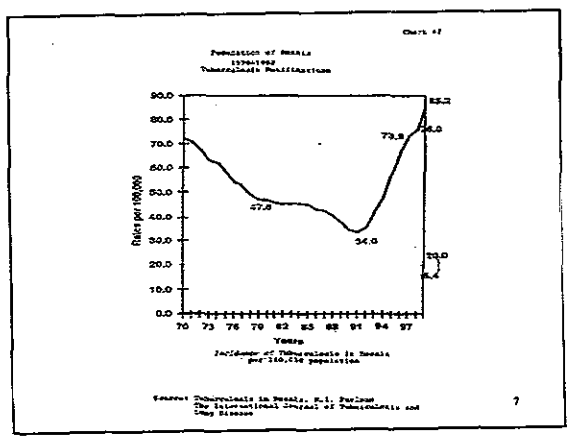


The Cause of the Resurgence of TB in New York City in the 1980s

- Reduced public health efforts & financial support to control tuberculosis
- HIV epidemic – TB co-infection with MDRTB
- Rising poverty, drug abuse, homelessness
- Overcrowded conditions in prisons & homeless shelters
- Immigrants from countries with high prevalence of tuberculosis
- Similar to conditions in Russia

THE NEW YORK EXPERIENCE

- Devastating effect of MDRTB on HIV patients
- Mortality: 70-90%
- Median time from diagnosis to death: 4 weeks
- Over 80% nosocomially acquired (hospitals, prisons, shelters)

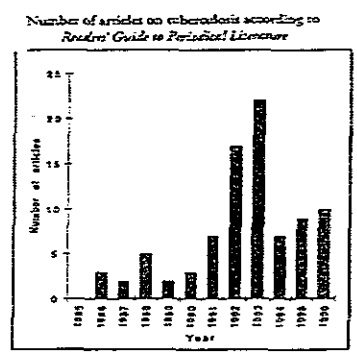
Response to the TB Epidemic: Importance of the Media

- National and City
  - *Public health officials* increased public awareness of the epidemic through the media
- Headlines
  - New York Times
    "Deadly Strain of Tuberculosis is Spreading Fast!"
  - New York Post
    "Highly Contagious Tuberculosis Close to Epidemic Levels in the City"

Response to the TB Epidemic: Importance of the Media

The emphasis of the media was on the:

A) Under-funding of the tuberculosis public health system
B) The failure of health systems to respond
C) The abdication of personal responsibility by patients
D) The likelihood that many people in the general population could acquire TB



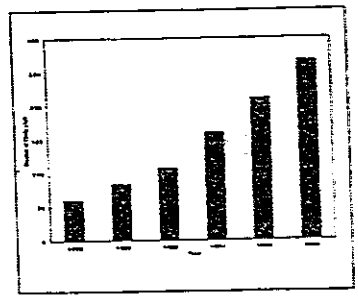
The public awareness of tuberculosis & its threat of contagious spread to the general public created public support to help initiate the following:

- The Mayor significantly increased funds for tuberculosis control
- The Governor of New York increased funding and support for New York City
- The federal government, through the Center for Disease Control and Prevention, needed to provide expert staff & laboratory support

13

Action Taken

Growth in New York City Department of Health tuberculosis clinic staff



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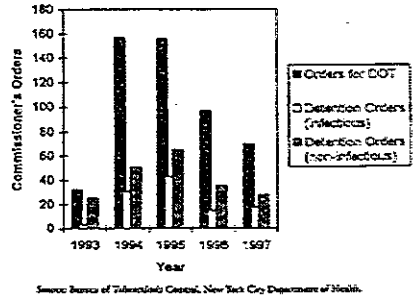
Action Taken, cont.

- Amending the New York City Health Law that stated:
  1. The Commissioner my issue any orders he or she deems necessary to protect public health."
  2. Amended to specify: "To specifically allow the Commissioner of Health to detain a person for:
     - Failure to take medication
     - Refusal to keep appointments for TB treatment
     - Failure to complete treatment
     - Disregard of contagious precautions
  3. The rest of detention I was a deterrent against non-compliance of the tuberculosis regime

15

Commissioner's orders for DOT and detention in New York City



Source: Bureau of Tuberculosis Control, New York City Department of Health.

16

Results of Action Taken

- Reduction of nosocomial infection
  - The city renovated the Rikers Island Correctional Facility (held 120,000 prisoners annually) and constructed a communicable disease unit with effective respiratory isolation
- City shelters for homeless were downsized (formerly 800 or more men in a single room)
- Hospitals constructed respiratory isolation units
- Substantial decrease in TB due to infection control

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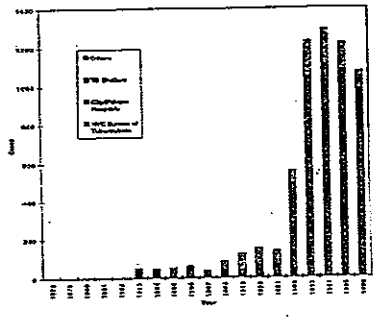
Actions Taken

- Directly Observed Therapy
- With an expanded TB bureau, staff, and funds, directly observed therapy was implemented
- Outreach program for directly observed therapy
- Outreach workers traveled to:
  - Patient homes
  - Work Places
  - Bridges and subway stations
  - "Crack Dens" in abandoned buildings
- All of this was done to ensure treatment
- Completion of treatment improved from 50% in 1980s to 93.2% in 1996

18

Cases of directly observed therapy in New York City



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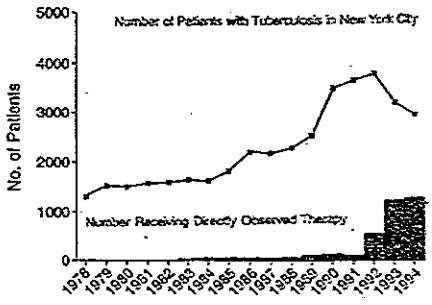
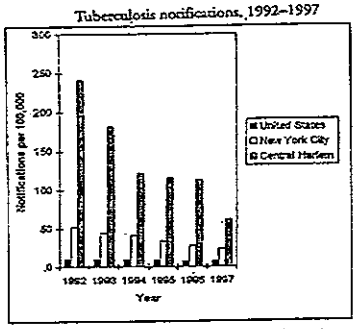


Data are from the New York City Department of Health.

20

Tuberculosis notifications, 1992–1997



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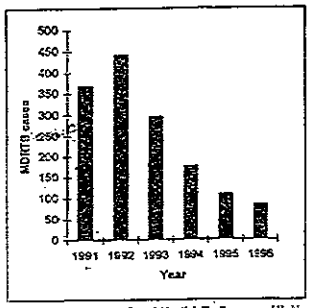
- The decrease in drug-resistant tuberculosis is convincing evidence that links reduced numbers of tuberculosis cases with programmatic experiments

22

Cases of multidrug-resistant tuberculosis in New York City



23

- By the use of DNA finger printing, public health officials documented that:

1. The decrease in tuberculosis incidence is most likely from recently transmitted infections
2. Not a reactivation of old infections
3. In fact, the tuberculosis rate in elder (over 69) and foreign-born patients did not go down

24

Prevention Advice for All Physicians (Private and Public)

1. Physicians should think TB when any patient has chronic cough and fever, regardless of result of TB skin test even if radiographic findings are not typical
2. After diagnosis, physicians should ensure prompt, effective directly observed therapy
3. Physician should work with local health department to conduct drug sensitivity and complete contact training

25

Prevention Advice for All Physicians (Private and Public)

4. Physicians should encourage effective infection control in congregate setting (hospitals, correctional facilities and shelters)
5. Preventative Chemotherapy
   - HIV infected
   - High-risk contacts to recent infectious cases
   - Recent immigration from regions with high tuberculosis prevalence
6. Greatest priority
   - Early and effective case detection
   - Lab diagnosis and drug-susceptibility
   - Prompt treatment for cure

26

- To help bring this epidemic under control, the TB officials recommended an intense regimen of at least 4 drugs for all active TB patients
  - Isoniozid
  - Pyrayinaniole
  - Rifanpin
  - Ethanbutol
- This drug regimen reduced the likelihood that treatment of drug-resistant TB would be ineffective, and also shortened the infectious time

27

- Improved and more rapid laboratory diagnosis and drug susceptibility
- Preventative therapy in high-risk groups, especially persons with HIV infection. INH treatment used except when MDRTB infection was suspected.

28

The following methods were very important in arresting the epidemic in New York:

1. Direct Observed Therapy
2. Legal authority to ensure completion of therapy
3. Expand outreach program with positive incentives
4. Authority to follow-up on released prisoners
5. Improved infection control in hospitals, shelters and correctional facilities
6. Put whole health community on high alert for tuberculosis
7. Good data

29

Cost

- The arrest of this epidemic required a lot of public money, particularly for the control of nosocomial infection (new ventilation systems, isolation rooms) and for an increased tuberculosis staff
- However, the cost of treating one MDRTB patient will pay for treating 700 drug-sensitive TB patients with directly-observed therapy
- CDC reported one MDRTB patient infected 9 people and caused $1 million worth of hospitalizations

30

The New York City experience demonstrated that a total community response was required to effectively control tuberculosis:

- Medical and public health
- Media
- Correctional institutions
- Hospitals
- Shelters for homeless
- Drug abuse centers
- HIV treatment facilities
- Voluntary organizations
- City, state and federal government working together

31

Greatest Priority for the Reduction of TB in New York and Sverdlovsk are:

- Early and effective detection
- Lab diagnosis & drug susceptibility
- Prompt and completion of treatment for cure

- These principals have been the core of training and education by Drs. Iseman and Heifets with the TB leadership in Sverdlovsk

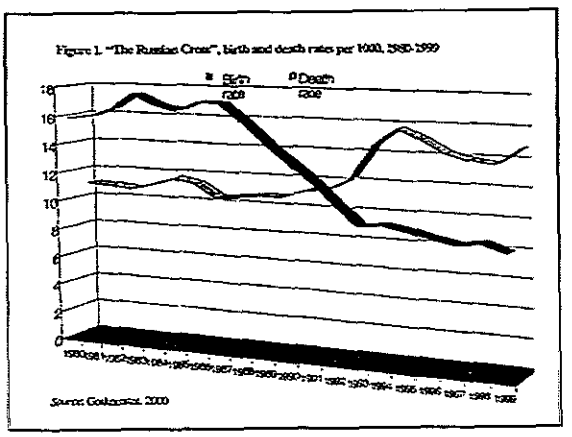
32

Eurasian Medical Education Program

"The Russian Cross"

Harvey I. Sloane, MD
Director, Public Health

1



Source: Goskomstat, 2000

The economic, security and health challenges to the Russian Federation

President Putin – July 2002
1st speech to the people of Russia:

"The most acute problem facing Russia is its declining population*. Unless this is reversed, the very survival of the nation will be endangered."

* The decline of the Russian population is 750,000 people/year

3

The economic, security and health challenges to the Russian Federation, cont.

If the epidemic of early disease and death from cardiovascular disease is compounded by TB and HIV disease and deaths, Russia's future will be compromised. The largest impact is on males in their most productive years (18-50).

4

Effect on Security

- It is estimated that 1/3 of prospective conscripts to the Russian military service are deemed unfit due to:
  - HIV infection
  - IVD
  - Hepatitis

5

Potential Economic Effects

- Declining GDP
- Declining investment
- Decrease in effective, i.e., quality-adjusted, labor supply

Source: Ruehl et al., 2002

6

Prevention of Population Decline

- Public awareness
- Personal responsibility (safe sex)
- Early detection
- Prompt treatment and monitoring
- Commitment of Russian government and Russian families to prevent disease

Eurasian Medical Education Program

Tuberculosis in Russian Prisons

Harvey I. Sloane, MD
Director, Public Health

1

Tuberculosis in Russian Prisons

1. 1/3 of all TB in Russia is in the prisons, 50 times higher than in the general population
2. High MDRTB – 25% of patients with TB in prisons have MDRTB
   - "Nowhere in the world has the epidemic of drug-resistant TB been documented of this magnitude."
   - This is largely because first-line drugs were often unavailable in 1999-2000

2

Sverdlovsk Prison

Visit to Nizhniy Tagil – Prison 51 TB hospital
January 2001

- Men's TB ward – 30 men triple bunked in 32 sq. meter room (1.1 sq. meter/prisoner)
  - No ventilation in crowded room
  - Men appeared extremely thin and under-fed
  - Men treated with 1st line drugs – no visit to MDRTB patients – 2nd line drugs

3

Sverdlovsk Prison, cont.

Visit to Nizhniy Tagil – Prison 51 TB hospital
January 2001

- Staff had limited lab resources and mechanisms to prevent spread of TB infection
  - 27 members of staff contracted TB and 2 died
- Limited follow-up in Oblast of released TB-infected prisoners

4

Tuberculosis in Russian Prisons, cont.

3. Because of amnesty and early release of large numbers of prisoners, an estimated 10% who have tuberculosis are not always followed up in the civilian sector
4. Therefore, to significantly impact civilian TB in Sverdlovsk, prison TB must be adequately addressed

5

Recommendations from TB Prison Conference in St. Petersburg, 2002

TB control in prison and civil society integrated

- At entry – TB registry
- If prisoner is TB infected, then civilian follow-up on contacts
- Release – referral to civilian sector

6

Prison TB Control

A. Effective screening at point of entry into prison
B. Need for lab diagnosis and drug-sensitivity
C. Prompt completion of therapy
D. Gradual increase in availability of 2nd line drugs for MDRTB
E. Capacity to isolate contagious patients

7

Prison Improvement

A. Reduce crowding
B. Improve lighting, ventilation, UV light and fans to reduce spread of TB
C. Better nutrition for TB patients
D. Reduce time before trial in Sizo

8

Continuity of Care Between Prison and Civil Society

- Access to TB registry to see if newly arrested person has TB and has not completed treatment
- Before release, communication between prison and civilian health officials in Orel

9

All prisoners should be tested for HIV, and, if positive, counseled in prevention of infection of others (condoms)

TB Among Prisoners in Baltic States

- Progress since meeting in 2000
  - The impact of the reforms in the penal code in the Russian Federation
  - The number of inmates reduced, especially in the pre-trial detention centers
- Progress due to WHO pilot projects in 26 Oblasts
  - Standardization of treatment regimen for first-line drugs
  - Higher budget allocation for prisoners
  - Better collaboration with the civilian public health service
  - Improvement of living conditions

11

TB Among Prisoners in Baltic States, continued

- Remaining challenges:
  - Diagnostic capabilities and screening routines (especially bacteriology)
  - Infra-structures of prisons must be further improved (ventilation, isolation)
  - Cure rates are generally low (65% and less are reported)
  - Standardization of first-line treatment regimen (incompatibility of regimens enhance the development of drug resistance)

12

TB Among Prisoners in Baltic States, continued

- Remaining challenges, continued:
  - Reporting and surveillance of tuberculosis from prisons are inaccurate
  - HIV in prisons is high for intravenous drug users
  - MDR TB in prisons continues to cause concern
  - Collaboration with civilian public health service (about half of the released prisoners with TB are lost to follow-up)

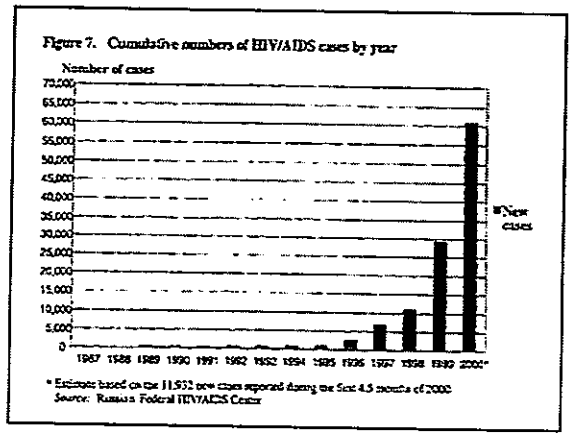
13

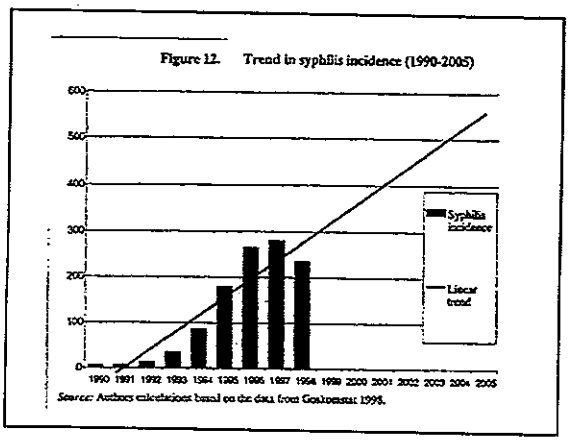
Eurasian Medical Education Program

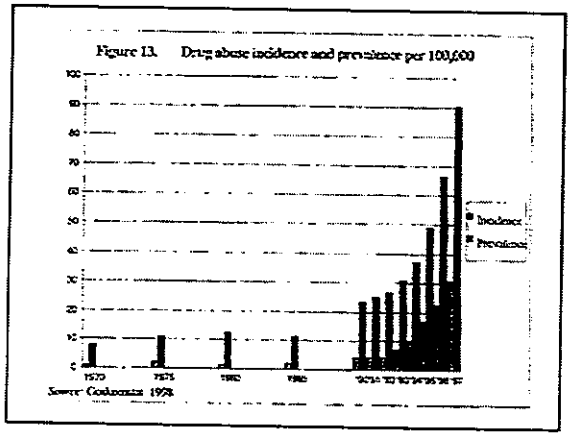
HIV/AIDS

Harvey I. Sloane, MD
Director, Public Health

1







Russia has a unique combination of:

- Strong legacy of health services in the socialist model
- Long-established institutions
- Membership of G8
- Fast-growing epidemic of HIV/AIDS
- Large burden of TB
- So far, a weak response to the epidemics

5

HIV/AIDS in Russia: Big & Growing

214,090 registered HIV +ve

(Source: Russian Federal AIDS Center, 2002)

Still a relatively small % of population, but

- Rapid spread among high-risk groups, particularly high-risk youths
- Evidence of spread into bridge populations
- Increasing heterosexual spread (6% in 2000, 15% in 2001)
- Likely spread into general population

6

Major factors fueling further spread

- Behaviors
  - IDUs sharing needles/syringes
  - Unsafe sex…
- High prevalence of STIs

…and, indirectly…

- *Very weak prevention efforts*
- *Increased vulnerability in the post-socialist era*

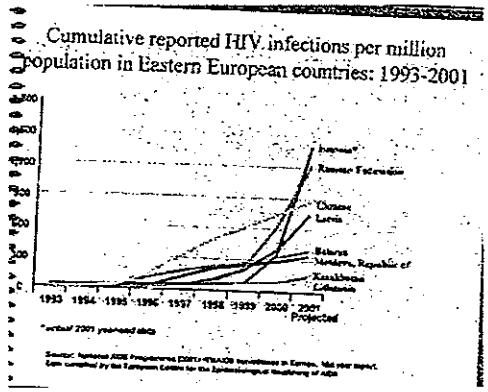
7

Potential Economic Effects

- Declining GDP
- Declining investment
- Decrease in effective, i.e., quality-adjusted, labor supply

Source: Rozhi *et al.*, 2002

8



How has it spread?

(Cumulative, as of September 2002)

Routes	%
Injecting drug users:	53.9
Unknown	40.9
Mother-to-Child	1.4
Heterosexual	3.2
Men having sex with men	0.4
Nosocomial	0.1

Source: Russian Federal AIDS Center, 2002

10

Promote a more positive environment for AIDS control

Encourage/broker high-level commitment

- Between governments
- Through professional associations
- Through international organizations

Promote reforms of the judicial system

- Crucial for prevention among IDUs
- Reduce effect of prisons as epidemiological pumps
- Link Ministry of Justice with the Ministry of Health

11

Doing what counts: The centrality of science

Crucial, for maximum impact on epidemic:

1. Interrupt transmission among high-risk core transmitters
2. Prevent spread from high-risk core transmitters to bridge populations

Desirable, but with less epidemiological impact:

3. Generalized information and advocacy by itself

Ineffective:

Moralizing & calls for total abstinence: wishful thinking

12

200

The central role of science:

four key elements for tackling HIV/AIDS

- Surveillance: well-trained investigators
- Superior laboratories and staff
- Effective communications technology
- Public trust…policy & advice based on evidence

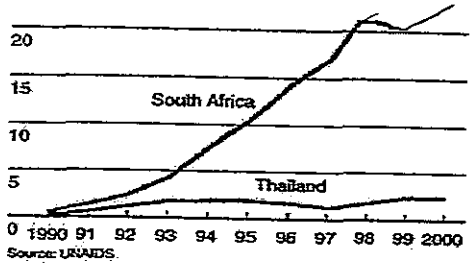
13

Ensuring adequate financing

- Estimates of incremental resource requirements
- Diagnostic equipment and supplies – all levels
- Condoms
- Laboratory infrastructure for HAART

14

HIV Control in 2 Countries



- Thailand has had a massive HIV/AIDS public awareness and condom distribution program

15

The next wave (second wave) of HIV/AIDS after sub-Sahara Africa will be China, Russia, India, Ethiopia and Nigeria. The estimate number of infected people in those countries by 2011 (50-75 million) will surpass the estimate of the the African sub-Sahara region (30-45 million)*

*Report by National Intelligence Council, US Government

16

Eurasian Medical Education Program

Public Health in the United States

Harvey I. Sloane, MD
Director, Public Health

1

Public Health - Definition

- Public health is a series of activities to promote health, to prevent disease and injury, to prevent premature death, to insure positive well-being, which is population-based. It is NOT diagnosis, treatment and rehabilitation of individuals from disease – that is medical care.
- The U.S. only commits 3% of the $1.2 trillion health budget to public health.

2

The 20th Century

- **Life Expectancy** – (47 to 77) 30 years of life added. High-tech medicine has helped, but public health improvement accounts for 25 to 30 years.
  1. Immunization – smallpox/polio to be eradicated
  2. Infection Control – water good, sewage treatment, antibiotics, TB 20,000 lives 1953 – today 2,000

3

The 20th Century

3. Heart Disease – 50% death rate reduction from 1965 strokes – 60% decline
   *NEJM – Monograph by Eugene Braunwald, MD
   - Better medical and emergency treatment
   - Diet weight control, high blood pressure management
   - Smoking reduction from 55% to 25% (male)
4. Better fortified and safer foods – goiter, pellagra and rickets no longer endemic
   *Food Safety – Food and Drug Administration

4

The 20th Century

5. Workplace safety – (1900-25) 356 mine disasters (5 or more killed) – (1975-2000) 14 mine disasters
   - Occupational illness declined (silicosis decline)
6. Motor vehicle safety – deaths 31/100,000 (1937) to 16/100,000 (today)
   - Seatbelts, safer cars and roads, DWI laws
7. Tobacco control – 55% (1950) – 25% (2000) in males
   - Surgeon General report in 1964 – tax increases – litigation and political advocacy

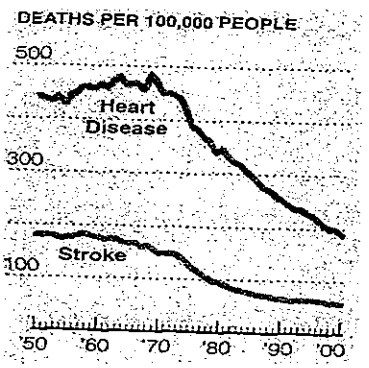
5

The 20th Century

8. Childbirth safety – 1913 leading cause of death for women in reproductive years (after TB)
   - Infant mortality reduction 90%
9. Family planning – 3.3 births/woman in 1917 to 2.1 births/woman today
   - Liberated women – allowed child spacing
10. Flouridation – since 1945 – today almost cavity-free generation

"What an incredible difference the 100 years have made."

6



Source: National Institutes of Health

7

The 20th Century

- **Challenges for the future**

1. Universal health insurance with a comprehensive primary care system
2. Closing the health gap between rich and poor – whites and minorities
3. Containing emerging infections
4. Continued assault on heart disease

8

The 20th Century

- **Challenges for the future, continued**

5. Raising our children out of poverty and tending to their development and emotional needs
6. Improving lifestyles – weight, alcohol and tobacco consumption, exercise, sexual behavior, illicit use of drugs and firearms
7. Improved health literacy

9

Emerging Infectious Diseases (EID)

- Infectious disease that has appeared in a population within the last 2-3 decades, has expanded its range, or threatens to increase in the near future.

EID (con't)

- "New" infectious diseases:
  Due to previously unknown agents or existing organisms undergoing genetic changes: over 30 new disease agents identified in the last 25 years. (e.g. HIV/AIDS, Legionnaire's disease, lyme disease, bovine spongiform encephalopathy (BSE) or "mad cow disease","CJD"

EID (con't)

- "Re-emerging" infectious diseases:
  Caused by known agents, once under control, but now resistant to common antimicrobial drugs or appearing in new geographic areas (e.g. Tuberculosis, malaria, gonorrhea, cholera [in Central and South America])

Emerging Infectious Diseases Factors

- Societal changes-population growth and migration
- Changes in health care-widespread use of antibiotics
- Increase in immunosuppressed patients
- Globalization of food supply and changes in food production (use of antibiotics in animal feeds)

EID Factors (con't)

- Human behavior-widespread, frequent travel
- Environmental changes: flood, drought, famine
- Decay of Public Health Infrastructure
- Microbial adaptation and change

Emerging Infectious Diseases "New"

- HIV/AIDS
- Legionnaire's
- "Mad Cow" (BSE)
- Hantavirus Pulmonary Syndrome
- Ebola virus
- West Nile Encephalitis (NYC)
- Cryptosporidiosis
- Cyclospora
- E. coli 0157:H7
- Influenza (Hong Kong 1997)
- Staph. aureus (vancomycin-resistant)
- Toxic-shock Syndrome
- Nipah virus (Malaysia)

Why some infectious disease are making deadly comebacks

- Changing lifestyles
  - Changes in food processing.. and handling
    - E. Coli O157:H7
    - Hepatitis A
    - Listeriosis
    - Salmonellosis
  - Increased use of child-care facilities
    - Cryptosporidiosis
    - Giardiasis
    - Hepatitis A
    - Meningitis
    - Shigellosis

Why some infectious disease are making deadly comebacks

Changing lifestyles (con't)

- Substance abuse and unsafe sexual practices
  - Chlamydia
  - Hepatits B
  - HIV infection
  - All infectious Diseases
- Increased air travel

Why some infectious disease are making deadly comebacks (con't)

Growing global population and movement

- Changes in land use
- Increased urbanization in the tropics
  - Hantavirus pulmonary syndrome
  - Lyme disease
  - Rabies
  - Dengue hemorrhagic fever
  - Yellow fever

Why some infectious disease are making deadly comebacks (con't)

Changing public policies

- Breakdowns in public health prevention programs
  - Cryptosporidiosis
  - Dengue hemorrhagic fever
  - Measles
  - Rabies
  - Tuberculosis

Emerging Resistance to Antibiotics

- Gram Positive Cocci:
  - Streptococcus pneumoniae (pneumococcus) Until relatively recently most pneumococci were very susceptible to penicillin with a minimum inhibitory concentration (MIC) of <0.06 mcg/ml
  - 1967: 1st clinical strain of penicillin-resistant pneumococcus (in patient with hypogammaglobulinemia)
  - 1977: resistant strain from patient with meningitis in South Africa

Emerging resistance to Antibiotics (con't)

- 1980: increasing prevalence of resistant strains (Australia, New Guinea, Hungary)
- 1996-97: in U.S. 33% of strains penicillin-resistant (13% with MIC >1 mcg/ml)

Antimicrobial resistance of *S. pneumoniae* isolates* from 201 US medical centers

Antibiotic	MIC_{90}	%Intermediate	%Resistant
Trovafloxacin	0.19	0.1	0.1
Levofloxacin	1.5	0.3	0.2
Penicillin	1.5	21.2	12.8
Ceftriaxone	1.0	11.6	4.5
Erythromycin	8.0	2.6	20.4
Vancomycin	1.5	NA	NA

Penicillin Resistance

- Beta-lactam antibiotics (penicillins, cephalosporins, etc.)
- Bind to specific bacterial enzymes (penicillin-binding proteins-PBP's) interfering with cell wall synthesis
- Genetic mutations lead to decreased affinity of penicillin for PBP's
- Penicillin resistant pneumococci also show increased resistance to non beta-lactam antibiotics (including macrolides, tetracycline, and trimethoprim-sufamethoxazole)

Gram Negative Bacteria

- Resistance to beta-lactam antibiotics through production of beta-lactamases, which inactivate susceptible antibiotics

Beta-lactamases
- penicillinases, cephalosporinases, etc
- broad-spectrum beta-lactamases (TEM-1,TEM-2, SHV-1) (inhibited by clavulanate, and other beta-lactamase inhibitors)
- extended-spectrum beta-lactamases (ESBL)

Table 1. ESBL-Producing Enterobacteriaceae

- Klebsiella pneumoniae
- Escherichia coli
- Citrobacter
- Enterobacter
- Other Klebsiella species
- Morganella morganii
- Proteus
- Salmonella
- Serratia marcescens

Table 2. ESBL-Producing Enterobacteriaceae May Be Resistant To:

- Penicillins
- Cephalosporins
- Azetreonam
- Inhibitor/drug combinations
- Aminoglycosides
- Trimethoprim
- Sulfonamides
- Chloramphenicol

Table 3. Treatment Options for ESBL-Producing Gram-Negative Bacilli

Intervention	Comment
– Carbapenems	– A drug of choice
– B-lactam/B-lactamase inhibitor combination	– May be effective (must be given in relatively high doses)
– Fluoroquinolones, aminoglycosides, trimethoprim/ sulfamethoxazole	– May be useful if organism is susceptible

EID (con't)

- Bioterrorism/biological warfare:
  - Anthrax
  - Smallpox
  - Plague
  - Tularemia
- References:
  - "Anthrax as a Biological Weapon-Medical and Public Health Management". JAMA. 1999;281:1735-1745.
  - "Smallpox as a Biological Weapon". JAMA. 1999;281:2127-2137.
  - "Plague as a Biological Weapon". JAMA. 2000;283:2281-2290.

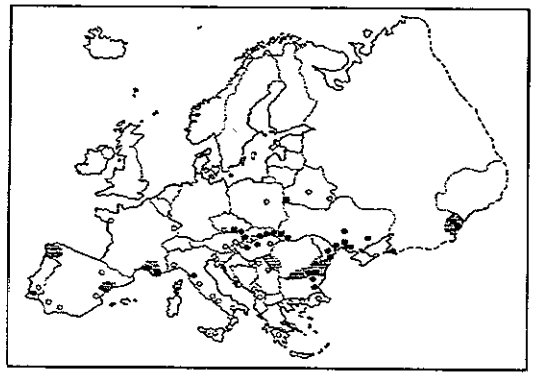
West Nile Virus Fever

- 1937:WNV first isolated from blood of febrile woman in Uganda
- 1950's:Found in patients, birds, mosquitoes in Egypt. Recognized as most widespread of the flaviviruses in Africa and Eurasia

No large outbreak of WNV fever in Europe until:

- 1996: More than 500 clinical cases in Romania (Bucharest region) with high rates of neurologic disease and death (up to 10%)
- 1999 July-September: Widespread outbreak of meningoencephalitis in Southern Russia (Volgograd, Astrakhan): 1,000 cases, 40 deaths
- 1999 August: First known outbreak in the Western Hemisphere: 62 cases, 7 deaths in New York City area

European Distribution of West Nile Virus



West Nile Fever-Clinical Features

- Febrile, influenza-like illness with abrupt onset, incubation period 3-6 days (up to 15 days in encephalitis cases)
- Moderate to high fever (3-5 days, rarely biphasic)
- Frontal headache, sore throat, myalgia, arthralgia, conjunctivitis
- Maculopapular or roseolar rash (1/2 cases)
- Lymphadenopathy

West Nile Fever-Clinical Features (Continuation)

- Acute "aseptic" meningitis or encephalitis (2-15%) with neck stiffness, vomiting, confusion, somnolence, tremor, convulsions, coma.
- Hepatitis, pancreatitis, myocarditis may occur.

West Nile Fever-Clinical Features (Continuation)

- Recovery usually complete (2-10% fatal, most over age 50 yrs)
- More rapid recovery in children
- May have long-term myalgias and weakness
- No permanent sequellae noted

WNV Fever-Treatment

- Supportive; no specific treatment
- No human vaccine but potential veterinary vaccine (live attenuated virus) developed in Israel
- Protective immune response in geese and mice
- Attenuated vaccine strains have completely lost neuroinvasive capability

WNV-New York

- How did WN virus get to New York?
  virus sequence studies showed close similarity between New York strain and an isolate from a dead goose in Israel (1998)
- Possible mechanisms of transmission:
  - viremic human
  - viremic bird
  - stowaway mosquito
  - international introduction (bioterrorism)

WNV Encephalitis-Russia, 1999

August-September 1999: Outbreak in Russia (Volgograd Region)

- 826 patients admitted with acute "aseptic" meningoencephalitis, meningitis, or fever
- Of 84 cases of meningoencephalitis, 40 fatal, 14 brain specimens WNV positive by reverse transcriptase PCR

The Future-Europe

- "The mechanism of West Nile virus persistence in disease-endemic foci of temperate Europe presents a challenge for further research"
- "The virus could persist in hibernating Culex spp; transovarially infected Culex spp; or chronically infected vertebrate hosts..."

The Future-Europe (Continuation)

- "Alternatively the virus may be reintroduced by chronically infected migratory birds from tropical foci"
- "If the reintroduction scheme is correct, a greatly increased activity of West Nile virus in Africa should be followed by an epidemic occurrence of West Nile fever in Europe in the next few years"

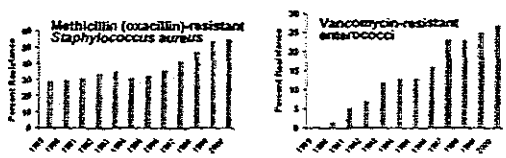
(Hubalek, Halouzka) in Emerging Infectious Diseases, 5, 643, 1999

12 Steps To Prevent Antimicrobial Resistance

- Targeted intervention programs for clinicians caring for high risk patients
  - *hospitalized adults*
  - *hospitalized children*
  - *geriatric patients*
  - *emergency patients*
  - *obstetrical patients*
  - *critical care patients*
  - *dialysis patients*
  - *surgical patients*
- Goal: Improve clinician practices & prevent antimicrobial resistance
- Partnership with professional societies; evidence base published in peer-reviewed specialty journals
- Educational tools – web-based / didactic learning modules, pocket cards, slide presentations, etc.

CDC

Antimicrobial Resistance among Pathogens Causing Hospital-Onset Infections



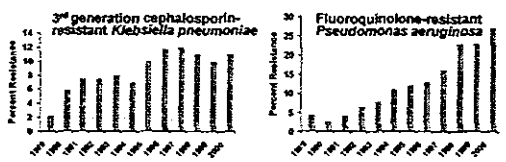
Non-Intensive Care Unit Patients

Intensive Care Unit Patients

Source: National Nosocomial Infections Surveillance (NNIS) System

CDC

Antimicrobial Resistance among Pathogens Causing Hospital-Onset Infections



Non-Intensive Care Unit Patients

Intensive Care Unit Patients

Source: National Nosocomial Infections Surveillance (NNIS) System

CDC

12 Steps to Prevent Antimicrobial Resistance: Hospitalized Adults

Prevent Infection

1. Vaccinate
2. Get the catheters out

Diagnose and Treat Infection Effectively

3. Target the pathogen
4. Access the experts

Use Antimicrobials Wisely

5. Practice antimicrobial control
6. Use local data
7. Treat infection, not contamination
8. Treat infection, not colonization
9. Know when to say "no" to vanco
10. Stop treatment when infection is cured or unlikely

Prevent Transmission

11. Isolate the pathogen
12. Break the chain of contagion

CDC

Prevent Infection

Step 1: Vaccinate

Fact:

Pre-discharge influenza and pneumococcal vaccination of at-risk hospital patients AND influenza vaccination of healthcare personnel will prevent infections.

CDC

Prevent Infection

Step 2: Get the catheters out

Fact: Catheters and other invasive devices are the # 1 exogenous cause of hospital-onset infections.

Actions:

- ✓use catheters only when essential
- ✓use the correct catheter
- ✓use proper insertion & catheter-care protocols
- ✓remove catheters when not essential

CDC

Diagnose & Treat Infection Effectively
Step 3: Target the pathogen

Fact: Appropriate antimicrobial therapy saves lives.

Actions:

- ✓ culture the patient
- ✓ target empiric therapy to likely pathogens and local antibiogram
- ✓ target definitive therapy to known pathogens and antimicrobial susceptibility test results

CDC

Methods to Improve Antimicrobial Use

- Passive prescriber education
- Standardized antimicrobial order forms
- Formulary restrictions
- Prior approval to start/continue
- Pharmacy substitution or switch
- Multidisciplinary drug utilization evaluation (DUE)
- Interactive prescriber education
- Provider/unit performance feedback
- Computerized decision support/on-line ordering

> Link to: *SHEA / IDSA: Guidelines for the Prevention of Antimicrobial Resistance in Hospitals*

CDC

Prevent Transmission
Step 12: Break the chain of contagion

Fact: Healthcare personnel can spread antimicrobial-resistant pathogens from patient to patient.

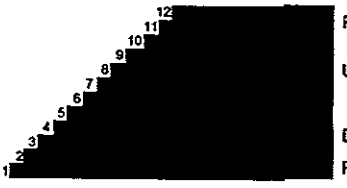
Actions:

- ✓ stay home when you are sick
- ✓ contain your contagion
- ✓ keep your hands clean
- ✓ set an example!

CDC

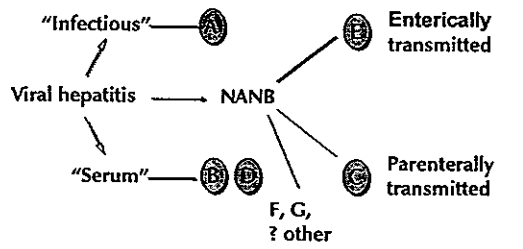
12 Steps to Prevent Antimicrobial Resistance: Hospitalized Adults

Clinicians hold the solution…
Take steps NOW to prevent antimicrobial resistance!



CDC

Viral Hepatitis - Historical Perspective



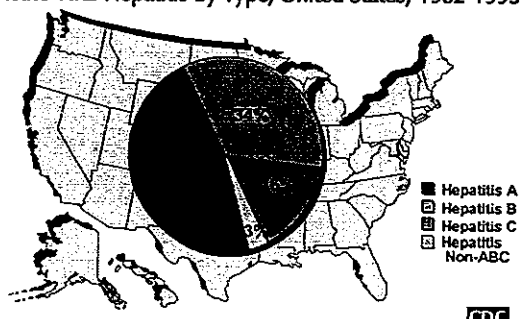
CDC

Viral Hepatitis - Overview

	Type of Hepatitis				
	A	B	C	D	E
Source of virus	feces	blood/ blood-derived body fluids	blood/ blood-derived body fluids	blood/ blood-derived body fluids	feces
Route of transmission	fecal-oral	percutaneous permucosal	percutaneous permucosal	percutaneous permucosal	fecal-oral
Chronic infection	no	yes	yes	yes	no
Prevention	pre/post-exposure immunization	pre/post-exposure immunization	blood donor screening; risk behavior modification	pre/post-exposure immunization; risk behavior modification	ensure safe drinking water

CDC

Acute Viral Hepatitis by Type, United States, 1982-1993



Source: CDC Sentinel Counties Study on Viral Hepatitis

CDC

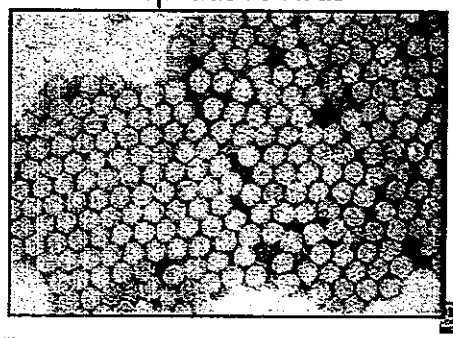
Estimates of Acute and Chronic Disease Burden for Viral Hepatitis, United States

	HAV	HBV	HCV	HDV
Acute infections (x 1000)/year*	125-200	140-320	35-180	6-13
Fulminant deaths/year	100	150	?	35
Chronic infections	0	1-1.25 million	3.5 million	70,000
Chronic liver disease deaths/year	0	5,000	8-10,000	1,000

* Range based on estimated annual incidence, 1984-1994.

CDC

Hepatitis A Virus



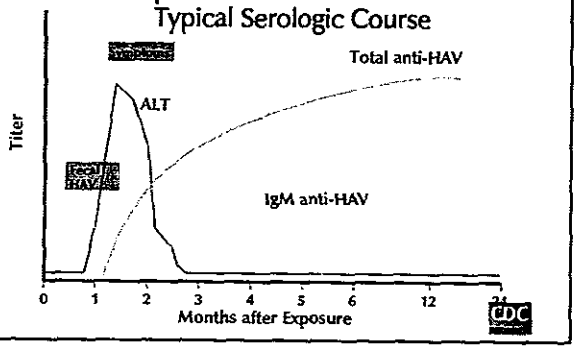
CDC

Hepatitis A - Clinical Features

- Incubation period: Average 30 days; Range 15-50 days
- Jaundice by age group: <6 yrs, <10%; 6-14 yrs, 40%-50%; >14 yrs, 70%-80%
- Complications: Fulminant hepatitis; Cholestatic hepatitis; Relapsing hepatitis
- Chronic sequelae: None

CDC

Hepatitis A Virus Infection
Typical Serologic Course



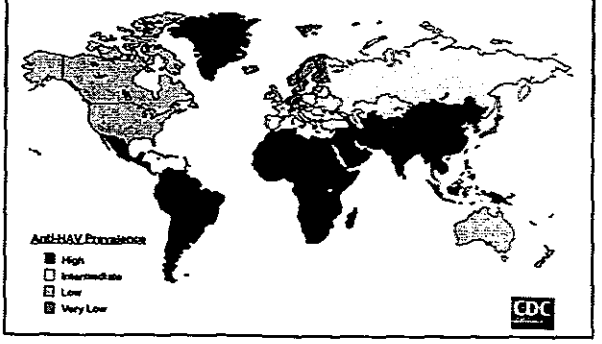
Hepatitis A Virus Transmission

- Close personal contact
  (e.g., household contact, sex contact, child day care centers)
- Contaminated food, water
  (e.g., infected food handlers, raw shellfish)
- Blood exposure (rare)
  (e.g., injecting drug use, transfusion)

Global Patterns of Hepatitis A Virus Transmission

Endemicity	Disease Rate	Peak Age of Infection	Transmission Patterns
High	Low to High	Early childhood	Person to person; outbreaks uncommon
Moderate	High	Late childhood/ young adults	Person to person; food and waterborne outbreaks
Low	Low	Young adults	Person to person; food and waterborne outbreaks
Very low	Very low	Adults	Travelers; outbreaks uncommon

Geographic Distribution of HAV Infection



Hepatitis A Vaccine Efficacy Studies

Vaccine	Site/Age Group	N	Vaccine Efficacy (95% CI)
HAVRIX® (SKB) 2 doses 360 EL.U.	Thailand 1-16 yrs	38,157	94% (79%-99%)
VAQTA™ (Merck) 1 dose 25 units	New York 2-16 yrs	1,037	100% (85%-100%)

JAMA 1994;271:1363-4
N Engl J Med 1992;327:453-7

ACIP Recommendations - Hepatitis A Vaccine Preexposure Vaccination

- Persons at increased risk for infection
  - travelers to intermediate and high HAV-endemic countries
  - homosexual and bisexual men
  - drug users
  - persons with chronic liver disease
- Communities with high rates of hepatitis A (e.g., Alaska Natives, American Indians)
  - routine childhood vaccination

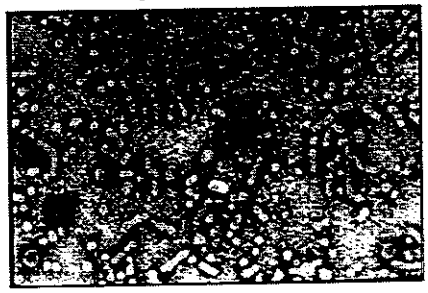
Hepatitis A Prevention - Immune Globulin

- Preexposure
  - travelers to intermediate and high HAV-endemic regions
- Postexposure (within 14 days)

  Routine
  - household and other intimate contacts

  Selected situations
  - institutions (e.g., day care centers)
  - common source exposure (e.g., food prepared by infected food handler)

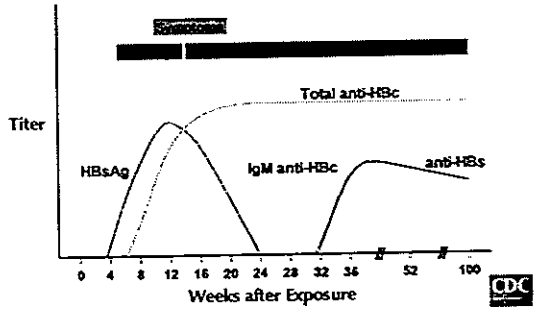
Hepatitis B Virus



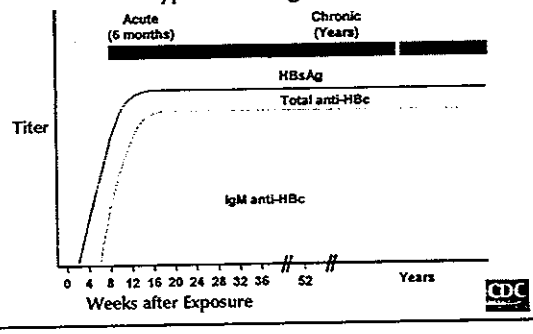
Hepatitis B - Clinical Features

• Incubation period:	Average 60-90 days Range 45-180 days
• Clinical illness (jaundice):	<5 yrs, <10% ≥5 yrs, 30%-50%
• Acute case-fatality rate:	0.5%-1%
• Chronic infection:	<5 yrs, 30%-90% ≥5 yrs, 2%-10%
• Premature mortality from chronic liver disease:	15%-25%

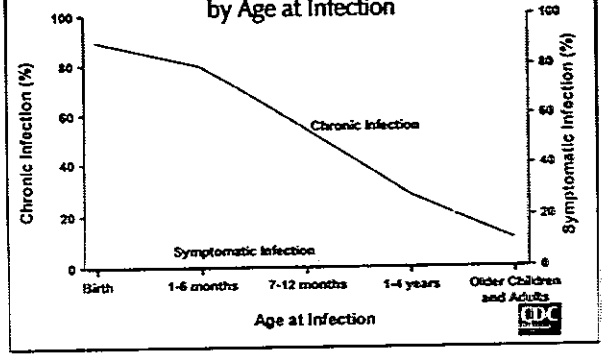
Acute Hepatitis B Virus Infection with Recovery
Typical Serologic Course



Progression to Chronic Hepatitis B Virus Infection
Typical Serologic Course



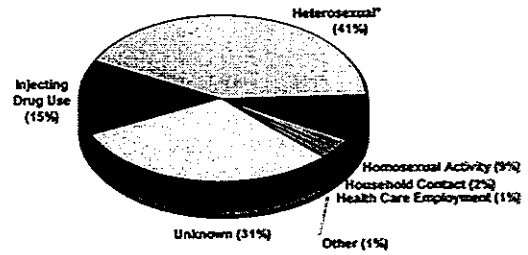
Outcome of Hepatitis B Virus Infection by Age at Infection



Geographic Distribution of Chronic HBV Infection

CDC

Risk Factors for Acute Hepatitis B United States, 1992-1993



* Includes sexual contact with acute cases, carriers, and multiple partners.
Source: CDC Sentinel Counties Study of Viral Hepatitis

CDC

Elimination of Hepatitis B Virus Transmission United States

Strategy

- Prevent perinatal HBV transmission
- Routine vaccination of all infants
- Vaccination of children in high-risk groups
- Vaccination of adolescents
  - all unvaccinated children at 11-12 years of age
  - "high-risk" adolescents at all ages
- Vaccination of adults in high-risk groups

CDC

Features of Hepatitis C Virus Infection

Incubation period	**Average 6-7 weeks Range 2-26 weeks**
Acute illness (jaundice)	**Mild (≤20%)**
Case fatality rate	**Low**
Chronic infection	**75%-85%**
Chronic hepatitis	**70% (most asx)**
Cirrhosis	**10%-20%**
Mortality from CLD	**1%-5%**

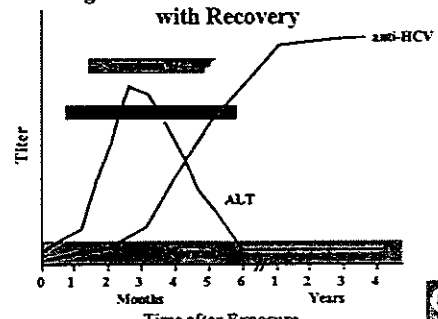
CDC

Chronic Hepatitis C Factors Promoting Progression or Severity

- Increased alcohol intake
- Age > 40 years at time of infection
- HIV co-infection
- ?Other
  - Male gender
  - Other co-infections (e.g., HBV)

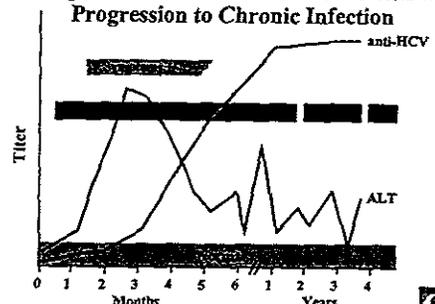
CDC

Serologic Pattern of Acute HCV Infection with Recovery

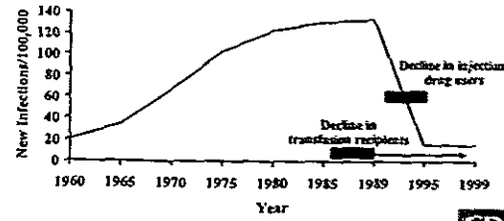


CDC

Serologic Pattern of Acute HCV Infection with Progression to Chronic Infection



Estimated Incidence of Acute HCV Infection United States, 1960-1999



Source: Hepatology 2000;31:777-82; Hepatology 1997;26:62S-65S

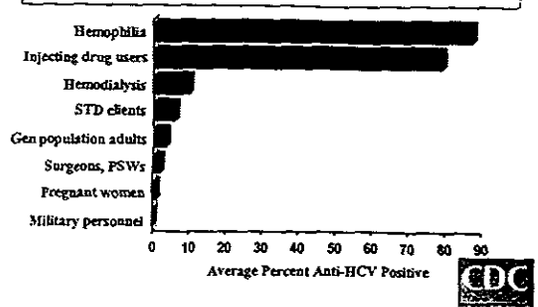
Transmission of HCV

- Percutaneous
  - Injecting drug use
  - Clotting factors before viral inactivation
  - Transfusion, transplant from infected donor
  - Therapeutic (contaminated equipment, unsafe injection practices)
  - Occupational (needlestick)
- Permucosal
  - Perinatal
  - Sexual

Nosocomial Transmission of HCV

- Recognized primarily in context of outbreaks
- Contaminated equipment
  - hemodialysis*
  - endoscopy
- Unsafe injection practices
  - plasmapheresis,* phlebotomy
  - multiple dose medication vials
  - therapeutic injections

HCV Prevalence by Selected Groups United States



HCV Testing Routinely Recommended

Based on increased risk for infection

- Ever injected illegal drugs
- Received clotting factors made before 1987
- Received blood/organs before July 1992
- Ever on chronic hemodialysis
- Evidence of liver disease

Based on need for exposure management

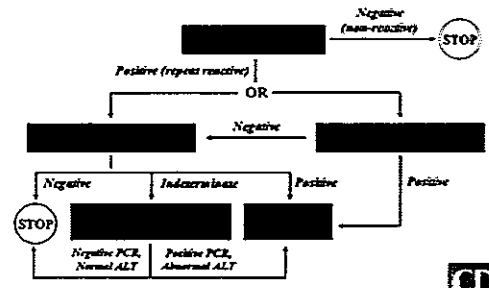
- Healthcare, emergency, public safety workers after needle stick/mucosal exposures to HCV-positive blood
- Children born to HCV-positive women

Postexposure Management for HCV

- IG, antivirals not recommended for prophylaxis
- Follow-up after needlesticks, sharps, or mucosal exposures to HCV-positive blood
  - Test source for anti-HCV
  - Test worker if source anti-HCV positive
    - Anti-HCV and ALT at baseline and 4-6 months later
    - For earlier diagnosis, HCV RNA by PCR at 4-6 weeks
  - Confirm all anti-HCV results with RIBA
- Refer infected worker to specialist for medical evaluation and management

CDC

HCV Infection Testing Algorithm for Diagnosis of Asymptomatic Persons



Source: MMWR 1998;47 (No. RR 19)

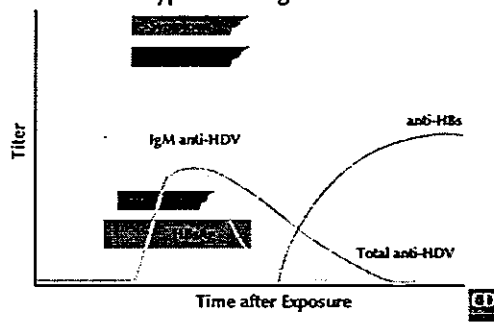
CDC

Medical Evaluation and Management for Chronic HCV Infection

- Assess for biochemical evidence of CLD
- Assess for severity of disease and possible treatment, according to current practice guidelines
  - 30-40% sustained response to antiviral combination therapy (interferon alpha, ribavirin)
  - Vaccinate against hepatitis A
- Counsel to reduce further harm to liver
  - Limit or abstain from alcohol

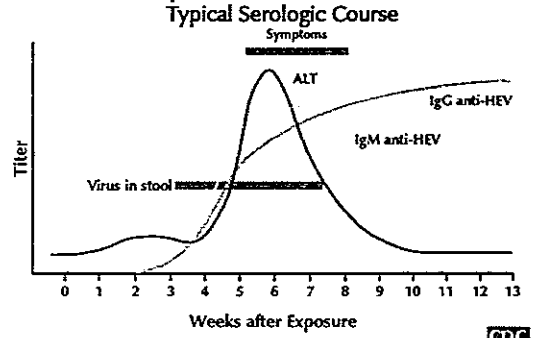
CDC

HBV - HDV Coinfection
Typical Serologic Course



CDC

Hepatitis E Virus Infection
Typical Serologic Course



CDC

EURASIAN MEDICAL EDUCATION PROGRAM

TRIP REPORT

Kazan
April 20-25, 2003

In Partnership with:
Kazan State Medical Academy
Ministry of Health, Republic of Tartarstan

Visiting Professors

Sara E. Walker, MD, MACP
Professor of Medicine, University of Missouri
Immediate Past President, American College of Physicians

Henry M. Greenberg, MD, FACP
Associate Professor of Clinical Medicine, Columbia University
Director, Coronary Care Unit, St. Luke's-Roosevelt Medical Center, NY

Eurasian Medical Education Program

Richard G. Farmer, MD, MS, MACP
Medical Director, Eurasian Medical Education Program
Clinical Professor of Medicine, Georgetown University, Washington, DC

Trip Report

This was the 36th program in Russia for the Eurasian Medical Education Program (EMEP), conducted over a 5-year period. EMEP has now directly encountered more than 5,000 Russian physicians in lectures and currently has five data collection programs continuing in polyclinics to assess effectiveness of the programs in benefiting patient care.

This was the 12th EMEP program in Kazan since June 1998, and all programs have been co-sponsored by the Kazan State Medical Academy, and the Ministry of Health, Republic of Tartarstan. All programs are developed among these three partners and this one was chosen to emphasize public health issues. The American co-sponsor is the American College of Physicians (ACP), and it was a great privilege to have the current ACP president as a visiting professor for this occasion. This program was a Republican Conference and physicians were allowed time from work to attend by a decree – prikaz – issued by the Minister of Health.

Sunday, April 20, 2003

Departure from US April 19, arrival in Kazan April 20.

Monday, April 21, 2003

Republican Conference: "Prevention of Chronic Diseases as the Major Public Health Problem."

Highlights included two lectures by Dr. Henry Greenberg – one on hyperlipidemia as a public health problem and one on hypertension. There has not been as much emphasis on health issues relating to elevated lipids as there should be, and Dr. Greenberg reviewed rational and low-cost treatment.

EMEP has emphasized hypertension as a major health problem previously, but Dr. Greenberg reported on an important trial that showed that older, less expensive drugs were very valuable.

Dr. Galyavich reported on the importance of cardiovascular disease in Tartarstan and that it affects 20% of the entire population; 40% of adults have hypertension. He also showed data from Polyclinic #11 (where EMEP has a data program) showing birth and death rates: in 1990 the birth rate was 15.5

per 1,000 population and death rate 10.3. In 1994, the birth rate was 10.1 and death rate 14.6. In 2002, the birth rate was 9.5 and death 12.3. He also discussed the positive benefit that EMEP has had through lectures and direct programs in Polyclinics #11 and #18.

Dr. Walker discussed osteoarthritis as a significant cause of disability and discussed treatment, including lifestyle modification.

The EMEP diabetes program, involving the entire Republic of Tartarstan, was discussed by Professor Husainov, professor, and Dr. Zyangirova, Chief of Endocrinology for Kazan and Director of the EMEP-sponsored diabetes program. They demonstrated significant improvement in patient compliance and decrease in hospitalization, and attributed this to EMEP.

Dr. Richard Farmer described the hospice system in the United States, designed to benefit patients with limited (less than six months expected) life expectancy. This program has been in existence for thirty years and is beneficial to patients and families, but also provides a large saving of healthcare expenditures by avoiding expensive hospitalization for patients who are terminally ill. There was considerable interest in the program; there is only one hospice in Russia, in Moscow, and there was interest in developing one in Kazan.

Meeting with Minister of Health, Dr. Kamil Zyatdinov. This was a formal meeting, at his request, to discuss his support for EMEP, the current program and future plans. He would like to have programs throughout Tartarstan. Also attending was Professor Ildus Nizamov, Vice-Rector of the Academy of Education and Director of the Department of Public Health, who helped organize the current program.

Tuesday, April 22, 2003

Continuation of the conference on chronic disease and the major public health problem in Tartarstan. Professor Nizamov presented a highly organized, extremely interesting report on public health in Russia and Tartarstan in particular. He noted that the birth and death rates crossed in 1992, and deaths have exceeded births since, although there was some improvement in 2002. Infant mortality has decreased and male life expectancy is now up to 60.0 years (from a low of 57.0). However, death rates

are four to five times higher among men of working age than women. There is a net population loss of about 750,000 per year. The number of abortions have decreased, but still are 2-3 per woman (down from 5-7).

Dr. Farmer then presented a report of the activities of EMEP over the past five years, with illustrations, and described programs in Tartarstan.

Dr. Farmer described public health in the United States as consisting of: 1) public surveillance – water, food, environment; 2) public education – smoking, seat belts, alcoholism, diet and exercise – and the health benefits derived, and; 3) dealing with specific infections – AIDS, hepatitis, E. coli, Legionnaire's disease and SARS (a table published the previous Thursday was shown – translated into Russian!). Data showing dramatic health improvement over the past twenty-five years were presented.

Dr. Farmer then described the system of medical education in the United States and the emphasis on primary care, disease and complication prevention, and chronic disease management.

The highlight of the second day was a formal presentation by Professor Walker, ACP Immediate Past President, in honor of Rector Mikhailov, in recognition of his support of EMEP for five years. Her subject was the public health importance of osteoporosis, and the prevention and management of it. A plaque was presented to Rector Mikhailov in recognition of his contribution; it was inscribed in his honor.

The closing ceremony consisted of tributes to the eight physicians who had been essential to the success of EMEP for the past five years. Each was presented with a certificate signed by EMEP participants: Drs. Burger, Sloane, Ms. Wirth, Drs. Greenberg and Farmer. They were presented to:

Mars K. Mikhailov, MD, PhD, D Sci

Rector and Professor, Kazan State Medical Academy

Ildus Nizamov, MD, PhD, D Sci

Professor and Deputy Rector (Education), Kazan State Medical Academy

Anatoli Tsibulkin, MD, PhD, D Sci

Professor and Deputy Rector (Science), Kazan State Medical Academy

Kamil Zyatdinov, MD, PhD, D Sci

Minister of Health, Republic of Tartarstan

Nyaz Galiullin, MD, PhD

First Deputy Minister of Health, Republic of Tartarstan

Albert Galyavich, MD, PhD, D Sci

Chief Cardiologist, Republic of Tartarstan

Professor, Kazan State Medical University

Svetlana Zyangirova , MD

Head, Endocrinology Center, City of Kazan

Ruben Burnashov, MD, PhD

Advisor on Health to the Prime-Minister, Republic of Tartarstan

Attendance: April 21 – 220 physicians

April 22 – 121 physicians

Evaluation forms were distributed – of those responding, 91% described the "general quality" of the program to be "excellent" and 99% considered the speakers to be "well-prepared"!

Following the program we visited Raifa Monastery and were guests at a dinner given by the Minister of Health.

Wednesday, April 23, 2003

Visit and workshop at Polyclinic #11, hosted by Professor Galyavich, who supervises the hypertension data collection program. The polyclinic serves a population of 70,000 and there are 28 primary care physicians (each manages about 2,000 patients). Data has been collected for more than a year and there are about 300 patients in the program being treated and followed for hypertension. The two most significant problems are the cost of medicine and the number of patients (men) who smoke. This data collection program involves only primary care physicians and is supervised by Professor Galyavich; there was considerable enthusiasm for the program.

Visit and lecture at Polyclinic #18. This polyclinic is a large one, with 115 physicians,; it is associated with another polyclinic and serves a population of 136,000. Each primary care physician is responsible for 1,750 patients. The director is in charge of the hypertension data collection program, under Professor Galyavich's supervision. A complete report was presented during our visit in October 2002, and they will update it in June 2003. It is a very active polyclinic and they have weekly conferences. We were able to speak to an audience of 25 physicians; each of us spoke as follows:

Dr. Greenberg – hypertension

Dr. Walker – osteoporosis

Dr. Farmer – gastritis and ulcer

There were many questions. (Two years ago Dr. Greenberg and I were the first American physicians to visit the polyclinic – they were quite familiar with us now and the discussion was lively.)

Thursday, April 24, 2003

Visit to the Endocrinology Center and discussion with Dr. Zyangirova and her colleagues. She has directed data collection in diabetes for about three years and has demonstrated significant clinical improvements, which she attributes to the EMEP series of lectures before data were collected. The prevalence of diabetes has increased (116 per 10,000 in 1985 and 212 in 2002), but obesity is not the problem it is in the United States. In their registry are 17,166 Type 2 diabetics, 1,177 Type 1 adults and 196 Type 1 in children. Complications of chronic diabetes continue to be a big problem, but acute complications (diabetic coma) are rare, less than 1%.

They are collecting data on representative cohorts of patients – about 400 – and a complete report was presented during our visit in October 2000; the update will be reported in June 2003. Dr. Zyangirova designed the computer data model and meticulous data collection has been carried out for 3 years.

A formal meeting with Rector Mikhailov was the setting for discussion of the accomplishments of the EMEP in Kazan for the past five years.

Friday, April 25, 2003

Departure from Kazan.

Summary Comments

In many ways, this was the most satisfactory visit in the entire EMEP activity. EMEP is thoroughly integrated into the activities of the Kazan State Medical Academy and the Ministry of Health, is respected, and functions collegially. Each program is planned collaboratively and with subjects requested by our Russian colleagues. As Medical Director, I then recruit ACP physicians who are good teachers and experts in the subject.

During the five years, the ACP has contributed about $250,000 in in-kind contributions by speakers, using the usual fee or honorarium for such lectures; all are contributed voluntarily. The ACP, the largest medical specialty organization in the United States, with 115,000 physician members, is likewise proud of its involvement in EMEP. I made a presentation at the Annual Meeting on April 2, 2003, which was very favorably received.

Much of the success of EMEP in Kazan is due to the efforts and reputation of Dr. Lilia Ziganshina, the EMEP Coordinator. She is highly respected academically and for her organizational skill, and she has "opened doors" for EMEP!

The Eurasian Medical Education Program began with lectures to groups of physicians, as continuing medical education programs. After the initial series of three programs, data collection was begun in both diabetes and hypertension to measure effectiveness of the programs. We then visited polyclinics and dealt directly with primary care physicians in day-to-day management issues of patient care for common and chronic diseases. As noted, evaluation forms were developed and utilized to determine audience response to lectures.

Handouts, translated into Russian, as "take home" information, have been given to the audience members since the inception of EMEP.

Five different journals were purchased by the Eurasian Medical Education Program for the Academy library each year. It has been estimated that about 4,000 Russian physicians have read these journals.

Slides were prepared for each lecture, translated into Russian, and given to the academic physicians who do the continuing medical education lectures. It is estimated that about 2,500 additional physicians per year are thus exposed to EMEP information. For example, it was estimated that 90% of diabetes doctors in the entire Republic of Tartarstan had been exposed to EMEP lectures given by Dr. Gerald Bernstein, President of the American Diabetes Association.

In summary, EMEP has been built on collaboration, participation and trust. It is a program that has proven results, directly benefiting Russian patients with management of their most important and serious diseases, and in the opinion of this participant, deserves continued and expanded support.

Richard G. Farmer, MD, MS, MACP
Medical Director, EMEP
May 12, 2003

to the prikaz of the MOH Republic of Tatarstan
№_____
«____»_____2002 г.

PROGRAMME

of the Republican Conference

Prevention of Chronic Diseases as the Major Public Health Problem (Cardiology, Rheumatology, Pharmacology and Managerial Aspects)

The site of the conference: Kazan, Mushtari Street, 11 (conference hall of the KSMA)
Conference starts at 10.00 a.m..
Registration of participants - 9.00 a.m..

21 APRIL (MONDAY)

10.00 – 11.00
Hyperlipideamia: Public Health Problem and Clinical Perspectives
Henry M. Greenberg
Директор Центра коронарной помощи,
Клиника Св. Люк-Рузвельта, Нью-Йорк, США
Профессор медицины, Колумбийский Университет, США

11.00 – 12.00
Hypertension as a Public Health Problem
Henry M. Greenberg
Директор Центра коронарной помощи,
Клиника Св. Люк-Рузвельта, Нью-Йорк, США
Профессор медицины, Колумбийский Университет, США

12.00 – 12.30
Prevention of Cardiovascular Complications in Patients with Hypertension (Results of New Trials)
Albert S.Galyavich
Главный кардиолог МЗ РТ, зав.каф. факультетской терапии КГМУ, профессор

12.30 – 13.10
Inflammatory Diseases of the GI Tract: Prevention of Complications
Richard G. Farmer
Медицинский директор Евразийской Медицинской Образовательной Программы
Профессор медицины,
Медицинского Центра университета Георгтауна,
Вашингтон, DC, США

13.10 – 13.55
Break for lunch

14.00 - 15.00
Osteoarthritis as the Cause of Disability. The Use of NSAIDs – Risks and Benefits
Sara E. Walker
Президент Американского колледжа врачей,
Профессор медицины,
Университет Миссури, Колумбия, США

15.00 – 15.30
Prevention of Diabetes Mellitus' Complications in Children and Adults
Svetlana T. Zyangirova
Главный эндокринолог управления здравоохранения г. Казани, главный врач Казанского городского эндокринологического диспансера

15.30 – 16.00
Hospice Experience – Public Health Problems and Social Work
Janice M. Farmer, социальный работник, Вашингтон, США

22 APRIL (TUESDAY)

10.00 – 10.30
Public Health and the Most Essential Problems of the Health Care Reforms in the Republic of Tatarstan
Ildus G. Nizamov
Проректор КГМА по учебной работе, зав. кафедрой общественного здоровья, управления и экономики здравоохранения, профессор

10.30 – 11.00
5-Year Experience of the Eurasian Medical Education Program in the Republic of Tatarstan – Results and Perspectives
The leadership the EMEP, the Ministry of Health and of the KSMA

11.00 – 11.40
Health of the Population of the USA and the Health Care System of the USA. Public Health and Chronic Disease Prevention
Richard G. Farmer
Медицинский директор Евразийской Медицинской Образовательной Программы
Профессор медицины,
Медицинского Центра университета Георгтауна,
Вашингтон, DC, США

11.40 – 12.25
Medical Education in the USA: Importance of Prevention and Public Health
Richard G. Farmer
Медицинский директор Евразийской Медицинской Образовательной Программы
Профессор медицины,
Медицинского Центра университета Георгтауна,
Вашингтон, DC, США

12.25 – 13.30
Honorary lecture for the Rector of the Kazan State Medical Academy, Professor Mars K. Mikhailov
Osteoporosis: Public Health Problem - Radio-Diagnostics, Risk Factors and Management
Sara E. Walker
Президент Американского колледжа врачей,
Профессор медицины,
Университет Миссури, Колумбия, США

Closing Ceremony
Sara E. Walker
Президент Американского колледжа врачей,
Профессор медицины,
Университет Миссури, Колумбия, США
Richard G. Farmer
Медицинский директор Евразийской Медицинской Образовательной Программы
Профессор медицины, отделение гастроэнтерологии
Медицинского Центра университета Георгтауна,
Вашингтон, DC, США
Henry M. Greenberg
Директор Центра коронарной помощи,
Клиника Св. Люк-Рузвельта, Нью-Йорк, США
Профессор медицины, Колумбийский Университет, США

Hyperlipidemia: A Public Health and Clinical Perspective

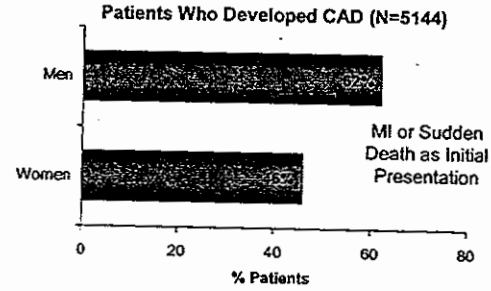
Henry Greenberg, MD, FACP
Eurasian Medical Education Program
Kazan, Tatarstan
April 2003

Impact of Atherosclerosis and CHD*

- CHD: 1 out of every 5 deaths per year
- 1.1 million myocardial infarctions annually
- Coronary bypass surgery: 553,000
- Percutaneous coronary interventions: 926,000
- $101 billion direct and indirect costs

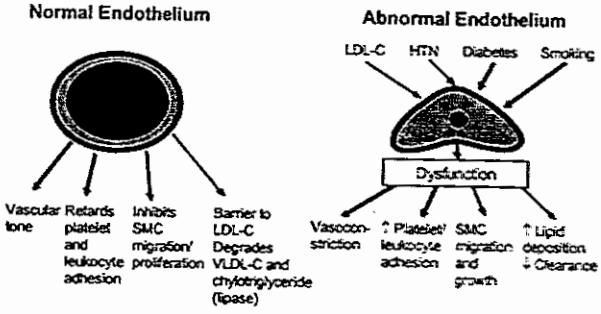
* 1998.
American Heart Association. *2001 Heart and Stroke Statistical Update*. 2000.

Initial Presentation of CAD May Be MI or Sudden Death: Framingham Heart Study



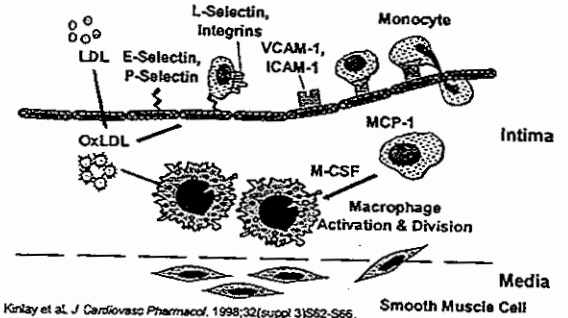
Murabito et al. *Circulation*. 1993;88:2548-2555.

Effect of Risk Factors on Endothelial Dysfunction



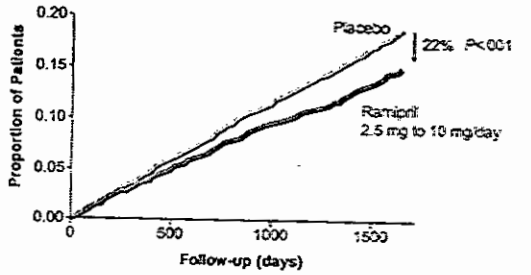
Adapted from Omoigui and Dzau. *J Vasc Med Biol*. 1991;3:382-391.

Atherosclerosis: Lesion Initiation



Kinlay et al. *J Cardiovasc Pharmacol*. 1998;32(suppl 3):S62-S66.
Newby et al. *J Cardiovasc Res*. 1999;345-360.

HOPE Study: Composite Outcome of MI, Stroke, or Death From Cardiovascular Causes



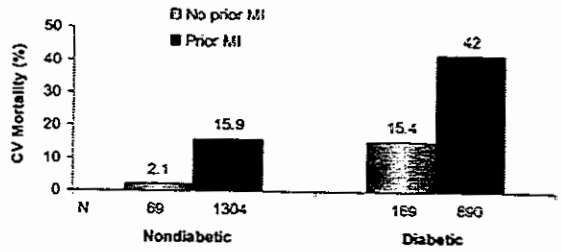
The Heart Outcomes Prevention Evaluation Study Investigators. *N Engl J Med*. 2000;342:145-153.

The Diabetes Epidemic

- An estimated 15.7 million Americans have diabetes
  - 10.3 million have physician-diagnosed diabetes
  - An estimated 5.5 million have undiagnosed diabetes
  - 90% have type 2 diabetes
- 798,000 new cases diagnosed/year
- Number of people with diabetes projected to increase 42% in developed countries and 170% in developing countries by 2025
- Two thirds of people with diabetes die of CVD

CDC National Diabetes Fact Sheet. American Heart Association. *2001 Heart and Stroke Statistical Update*. 2000. American Diabetes Association. *Diabetes Care*. 2000;23:381-389.

Survival in Patients With Diabetes Is Similar to Survival Post-MI



Haffner et al. *N Engl J Med*. 1998;339:229-234.

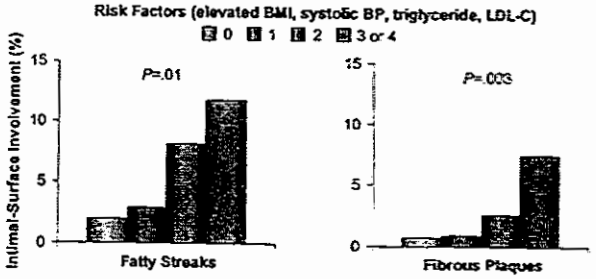
ATP III: The Metabolic Syndrome

Diagnosis Is Established When ≥3 of These Risk Factors Are Present

Risk Factor	Defining Level
Abdominal obesity (Waist circumference)	
Men	>102 cm (>40 in)
Women	>88 cm (>35 in)
TGs	≥150 mg/dL
HDL-cholesterol	
Men	<40 mg/dL
Women	<50 mg/dL
Blood pressure	≥130/≥85 mm Hg
Fasting glucose	≥110 mg/dL

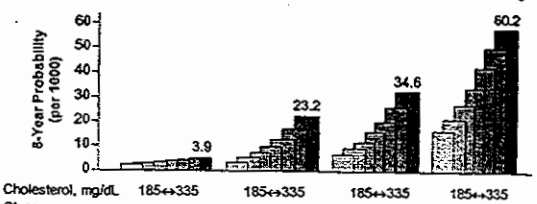
Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *JAMA*. 2001;285:2486-2497.

Number of Risk Factors in Young Adults Correlates With Coronary Atherosclerosis: Bogalusa Heart Study



BMI = body mass index.
Berenson et al. *N Engl J Med*. 1998;338:1650-1656.

Risk of CHD by CV Risk Profile and Cholesterol: Framingham Heart Study



Cholesterol, mg/dL	185↔335	185↔335	185↔335	185↔335
Glucose intolerance	0	+	+	+
Systolic BP, mm Hg	105	195	195	195
Cigarettes	0	0	+	+
LVH on ECG	0	0	0	+

Kannel. *J Am Coll Cardiol*. 1990;15:206-211.

ATP III: LDL Cholesterol Goals and Cutpoints for Lifestyle Changes and Drug Therapy

Risk Category	LDL Goal (mg/dL)	LDL Level at Which to Initiate Therapeutic Lifestyle Changes (mg/dL)	LDL Level at Which to Consider Drug Therapy (mg/dL)
CHD or CHD Risk Equivalents (10-year risk >20%)	<100	≥100	≥130 (100-129: drug optional)
2+ Risk Factors (10-year risk ≤20%)	<130	≥130	10-year risk 10%-20%: ≥130
			10-year risk <10%: ≥160
0-1 Risk Factor	<160	≥160	≥190 (160-189: LDL-lowering drug optional)

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *JAMA*. 2001;285:2486-2497.

New Adult Treatment Panel III Cholesterol Guidelines: Summary Features

- Diabetes = CHD risk equivalent
- Framingham projections of 10-year absolute CHD risk
- Multiple metabolic risk factors treated with intensified lifestyle changes
- Optimal LDL cholesterol <100 mg/dL
- Categorical low HDL cholesterol <40 mg/dL
- Lower triglyceride cutpoints
- Treatment beyond LDL lowering for persons with TGs ≥200 mg/dL

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *JAMA*. 2001;285:2486-2497.

Adult Treatment Panel III: Major Risk Factors (Exclusive of LDL Cholesterol) That Modify LDL Goals

- Cigarette smoking
- Hypertension (BP ≥140/90 mm Hg or on antihypertensive medication)
- Low HDL cholesterol (<40 mg/dL)*
- Family history of premature CHD
  - CHD in male first degree relative <55 years
  - CHD in female first degree relative <65 years
- Age (men ≥45 years; women ≥55 years)

*HDL cholesterol ≥60 mg/dL counts as a "negative" risk factor; its presence removes one risk factor from the total count.

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *JAMA*. 2001;285:2486-2497.

Adult Treatment Panel III: Risk Assessment

Count Major Risk Factors

- For patients with multiple (2+) risk factors
  - Perform 10-year risk assessment
- For patients with 0 to 1 risk factor
  - 10-year risk assessment not required
  - Most patients have 10-year risk <10%

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *JAMA*. 2001;285:2486-2497.

Adult Treatment Panel III: CHD Risk Equivalents

- Other clinical forms of atherosclerotic disease (peripheral arterial disease, abdominal aortic aneurysm, and symptomatic carotid artery disease)
- Diabetes
- Multiple risk factors that confer a 10-year risk for CHD >20%

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. *JAMA*. 2001;285:2486-2497.

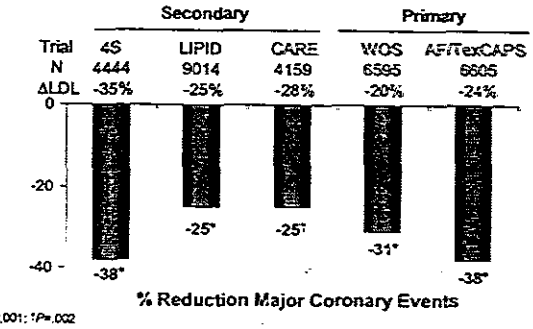
Almonds lower LDL

Reductions in LDL Cholesterol and LDL:HDL Ratio with Half-Dose and Full-Dose Almonds

Reduction area	Half-dose almonds	p value	Full-dose almonds	p value
LDL cholesterol	4.4 ± 1.7%	0.018	9.4 ± 1.9%	<0.001
LDL:HDL	7.8 ± 2.2%	0.001	12.0 ± 2.1%	<0.001

Jenkins DJA et al. *Circulation* [DOI:10.1161/01.CIR.0000028421.91733.20]. 2002.

Overview of Statin Trials

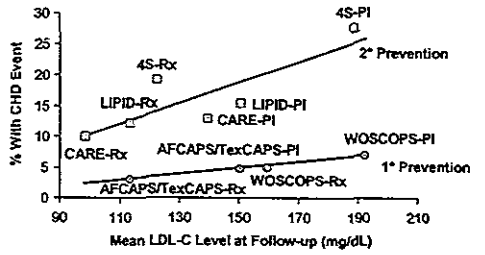


% Reduction Major Coronary Events

*P<.001; †P=.002

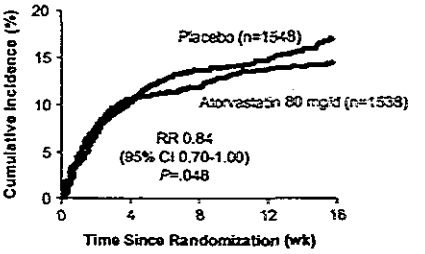
LaRosa et al. *JAMA*. 1999;282:2340-2346.

Relationship Between CHD Events and LDL Cholesterol in Recent Statin Trials



PI=placebo; Rx=treatment.
Ballantyne. *Am J Cardiol.* 1998;82:3Q-12Q.

MIRACL: Reduction in Risk of Fatal/Nonfatal Cardiovascular Events With In-Hospital Statin Treatment in ACS



MIRACL=Myocardial Ischemia Reduction with Aggressive Cholesterol Lowering.
Schwartz et al for the MIRACL Study Investigators. JAMA. 2001;285:1711-1718.

GREACE 7/18/02

Risk Reduction (RR) with Atorvastatin Compared to Usual Care

End point	RR (CI)	p value
Total mortality	0.57 (0.39-0.78)	0.0021
Coronary mortality	0.53 (0.29-0.74)	0.0017
Coronary morbidity	0.46 (0.25-0.71)	<0.0001
Stroke	0.53 (0.30-0.82)	0.034

Athyros et al. *Curr Med Res Opin* 2002;18:220-8

CHD Prevention Trials With Statins in Diabetic Subjects: Subgroup Analyses

Study	Drug	N	HDL	Trig	LDL	CHD Risk Reduction
Primary Prevention						
AFCAPS/TexCAPS	Lovastatin	155	+6	-15	-25	-43% (NS)
Secondary Prevention						
CARE	Pravastatin	586	+4	-11	-32	-25% (*P*=.05)
4S	Simvastatin	202	+7	-11	-36	-55% (*P*=.002)
LIPID	Pravastatin	782	+8	-14	-25	-19% (NS)

Downs et al. *JAMA.* 1998;279:1615-1622; Pyörälä et al. *Diabetes Care.* 1997;20:614-620; Goldberg et al. *Circulation.* 1998;98:2513-2519; The Long-Term Intervention with Pravastatin Disease (LIPID) Study Group. *N Engl J Med.* 1998;339:1349-1357.

CHD Prevention Trials With Fibrates in Diabetic Subjects: Subgroup Analyses

Study	Drug	N	HDL	Trigs	LDL	CHD Risk Reduction
Primary Prevention						
Helsinki Heart Study	Gemfibrozil	135	+5%	-22%	-6%	-68% (NS)
SENDCAP	Bezafibrate	164	+6%	-33%	-10%	-67% (*P*=.01)
Secondary Prevention						
VA-HIT	Gemfibrozil	627	+6%	-31%	—	-24% (*P*=.05)

Koskinen et al. *Diabetes Care.* 1992;15:820-825.
Rubins et al. *N Engl J Med.* 1999;341:410-418; Elkeles et al. *Diabetes Care.* 1998;21:641-648.

American Diabetes Association Order of Priorities: Adult Diabetes Mellitus Dyslipidemia

1) LDL lowering
2) HDL raising
3) Triglyceride lowering
4) Combined (mixed) hyperlipidemia

American Diabetes Association. *Diabetes Care.* 2000;23(suppl 1):S57-S60.

Rosuvastatin vs Atorvastatin

Changes in Lipid Fractions After 52 Weeks of Therapy

Agent	LDL-C	HDL-C	Triglycerides
Atorvastatin 10 mg	-44%	-1%	-19%
Rosuvastatin 5 mg	-47%*	+2%	-20%
Rosuvastatin 10 mg	-53%**	+4%*	-21%

*p<0.05 **p<0.001

Olsson et al. Presented at the XXIII Congress of the European Society of Cardiology. Sep 3, 2001

Ezetimibe plus statins 5/17/02

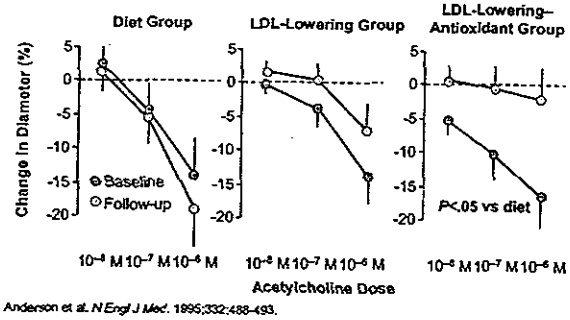
Percentage changes in certain lipid-related variables from baseline to endpoint

Variable	Statin 80 mg (n=17)*	Ezetimibe plus statin 10/80 mg (n=33)*	p value
Direct LDL-C	-6.7	-20.7	0.007
Calculated LDL-C	-6.6	-21.4	<0.001
Total cholesterol	-5.3	-15.7	<0.01
Apolipoprotein B median % change	-4.1	-16.0	0.06
HDL-C	4.4	-2.8	0.09
Triglycerides	-5.8	-10.8	0.54
Lipoprotein (a)	21.6	7.0	0.40

* Not every patient had end-of-treatment assessment for every variable; the number of patients within groups ranged from 16 to 17 (statin-BP) and 29 to 33 (ezetimibe plus statin-42/80)

Gagné C et al. Circulation 2002; 105: 10.1161/01.CIR.0000018744.58460.62

Improvement in Endothelial Dysfunction After Lipid Lowering and Antioxidant Therapy



Anderson et al. *N Engl J Med*. 1995;332:488-493.

Statin & CAC

Measure of Coronary Artery Calcification, cholesterol, and triglycerides over 2-year period

Measure	Baseline	12 months, untreated	12 months, cerivastatin	P value
Mean volume CAC (mm3)	155	201	203	0.01*
LDL (mg/dL)	--	164±30	107±21	<0.0001
HDL (mg/dL)	--	51±12	52±12	0.3
Triglycerides (mg/dL)	--	184±106	152±68	0.004
Total cholesterol	--	244±32	189±28	<0.0001

*p value reflects comparison of CAC increase between baseline and 12 mo vs increase between untreated and treated period

Achenbach S et al. *Circulation* 2002.

Possible Antiatherogenic Actions of Statins

- ↓ Cholesterol esterification, LDL oxidation, macrophage uptake of oxLDL
- ↓ SMC proliferation and/or migration
- ↓ Monocyte-endothelial cell adhesion
- ↓ Expression of adhesion molecules
- ↓ Tissue factor expression
- ↑ Endothelial NOS III
- ↓ $^{\cdot}O_2^-$ production
- ↓ Vascular A-II levels

Anti-inflammatory effects (↓ CRP)

Blumenthal. *Am Heart J*. 2000;139:577-583; Vaughan et al. *J Am Coll Cardiol*. 2000;35:1-10.

Non-coronary benefits of statins

- Reduces CRP
- Improves endothelial function
- May reduces Alzheimer's disease
- May slow progression of osteoporosis
- May reduce incidence of colon cancer
- May retard progression of multiple sclerosis, rheumatoid arthritis, and diabetes
- May impede aortic valve calcification

Risk Factor-Adjusted Relative Risk of First Cardiovascular Event by Increasing Quintile of CRP and LDL

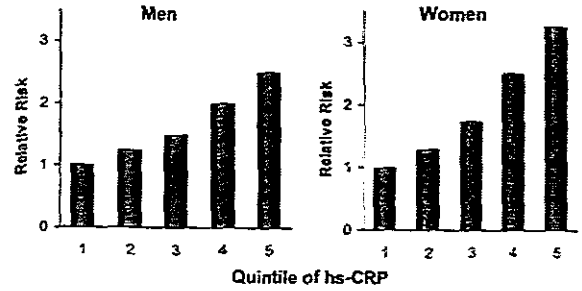
Quintiles

Measurement	1st	2nd	3rd	4th	5th
CRP	1.0	1.4	1.6	2.0	2.3*
LDL	1.0	0.9	1.1	1.3	1.5*

*p<0.001

Ridker PM et al. *N Engl J Med* 2002; 347:1557-1565.

Risk of MI Associated With Increasing Quintiles of CRP



Ridker et al. *Circulation*. 2001;103:1813-1818.

Effect of Statins on CRP

Trial (N)	Treatment/ Duration	Effect on CRP	P
CARE (472)	Pravastatin/5 y	↓ 17.4%	.004
Ridker et al (785)	Cerivastatin/8 wk	↓ 13.3%	<.001
AFCAPS/TexCAPS (5742)	Lovastatin/1 y	↓ 14.8%	<.001

Ridker et al. *Circulation*. 1999;100:230-235; Ridker et al. *Circulation*. 2001;103:1191-1193; Ridker et al. *N Engl J Med*. 2001;344:1959-1965.

MIRAGE 4/18/02

Risk of Alzheimer's Disease by Use of Statins or Other Cholesterol-Lowering Medications

Therapy	Odds ratio	95% CI
Statins	0.27	0.14-0.33
Nonstatin cholesterol-lowering medications	0.73	0.30-1.8

Jick et al. *Lancet* 2002;356(9242):1627-31

Statins and DVT risk

Rate and Adjusted Hazard Ratio (HR) for DVT in Female Cohort

Drug	RR of total mortality (Q4 set as reference)	HR (95% CI)
Thyroid replacement (n=22 118)	11.9	1.0 (referent)
Non-statin lipid lowering agent (n=5155)	9.5	0.84 (0.63-1.12)
Statin (n=33 070)	7.6	0.68 (0.59-0.79)
Estrogen (n=29 165)	12.6	1.16 (1.01-1.33)

Ray et al. *Arch Intern Med* 2001; 161: 1405-10.

Statin therapy in elderly 7/23/02

Percentage of Patients Adherent to Statin Therapy

Time since start of first prescription	Adherence (%)
3 months	60
6 months	43
60 months	26
120 months	32

Benner et al. JAMA 2002; 288:455-61

Summary

- Atherosclerosis begins early in life and has a long preclinical latency with arterial wall involvement and remodeling
- Endothelial dysfunction occurs as a result of exposure to risk factors such as elevated LDL cholesterol, increased systolic BP, and diabetes
- The effect of risk factors is multiplicative not just additive
- Cardiovascular risk and the risk of renal decline are closely linked

Summary

- Aggressive treatment of at-risk patients should be pursued, following the latest guideline recommendations
- Lipid lowering reduces clinical events and appears to stabilize plaque
- ACE inhibitors and CCBs reduce clinical events and may have antiatherosclerotic actions

Hypertension: A Public Health Perspective

A Focus on ALLHAT

Henry Greenberg, MD, FACP
Eurasian Medical Education Program
St.Luke's Roosevelt Hospital
Columbia University
Kazan, April 2003

Hypertension Is a Major Treatable Risk Factor for Cardiovascular Disease

- Powerful independent risk factor for CHD, stroke, PAD, and heart failure
- Relationship with risk is continuous and graded
- Benefits of blood pressure reduction with pharmacologic or other treatment are incremental and continuous

CHD = Coronary heart disease.
PAD = Peripheral arterial disease.
Neaton JD, et al. In: Laragh JH, Brenner BM, eds. *Hypertension: Pathophysiology, Diagnosis, and Management*. 2nd ed. New York, NY: Raven Press; 1995:127-144.
Morabito JM, et al. *Am Heart J*. 2002;143:961-965.
Lloyd-Jones DM. *Curr Cardiol Rep*. 2001;3:184-190.

2

CVD and Hypertension: US Morbidity and Mortality

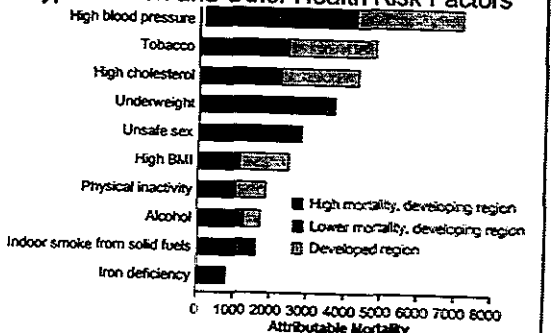
50 million Americans have high BP

- The age-adjusted prevalence of high BP in the US population is
  - 26.4% for men21.5% for women
- In persons <55 years, high BP occurs in higher percentage of men than women; in >55 years, in higher percentage of women than men
- Increased prevalence of high BP in elderly
  - 77% in women ≥75 years, 64% in men ≥75 years
- From 1989 to 1999, age-adjusted death rate from hypertension increased 21%; actual number of deaths rose 46%

American Heart Association. *2000 Heart and Stroke Statistical Update*. 1999; American Heart Association. *2002 Heart and Stroke Statistical Update*. 2001; American Heart Association. *Biostatistical Fact Sheet–Populations*. 2002.

3

Global Mortality 2000: Impact of Hypertension and Other Health Risk Factors



Ezzati et al. *Lancet*. 2002;360:1347-1360.

4

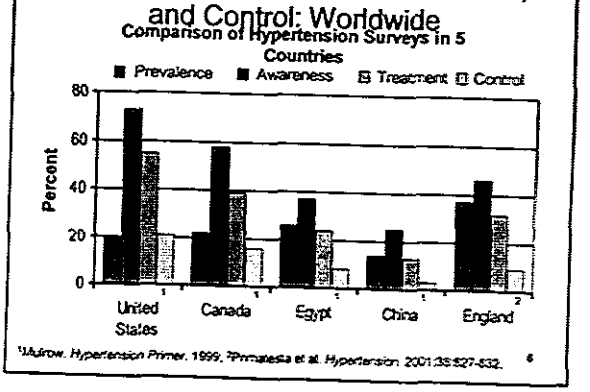
CVD and Hypertension: Worldwide Morbidity and Mortality

- Cardiovascular disease accounted for 16.6 million deaths in 2000
  - 7.3 million ischemic heart disease deaths
  - 5.4 million stroke deaths
- High blood pressure is associated with an estimated 7.1 million deaths
  - 13% of total deaths worldwide
  - 50% of CVD burden associated with suboptimal blood pressure
  - 61% of CVD burden associated with the combination of suboptimal blood pressure and suboptimal cholesterol levels
- Estimated 690 million persons have hypertension; most remain untreated or uncontrolled

Mensah. *Cardiol Clin*. 2002;20:181-185; Hoffman & Hoffman Public Relations for the World Health Organization. Available online at www.HoffmanPR.com. Accessed December 2, 2002; World Health Organization. *World Health Report 2002*. Geneva, Switzerland.

5

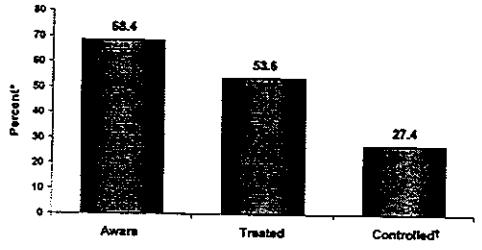
Hypertension Awareness, Treatment, and Control: Worldwide



[1]Mulrow. *Hypertension Primer*. 1999; [2]Primatesta et al. *Hypertension*. 2001;38:827-832.

6

Unmet Medical Need in US Adults With Hypertension

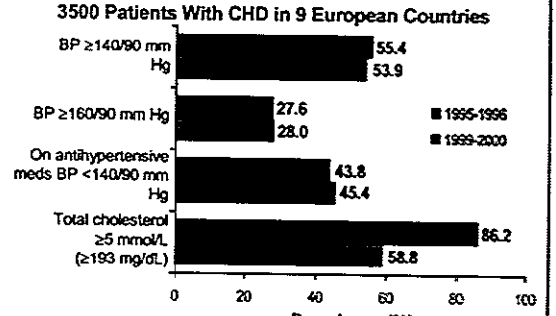


NHANES III (Phase 2) 1991-1994 (JNC VI) Kaplan NM. *Arch Intern Med.* 1997;157:2413-2416.
Estimated 50 million adults with hypertension in the United States.
* Percent = Proportions based on persons with hypertension in the survey.
† BP <140/90 mm Hg.

7

State of BP Control in Europe: EUROASPIRE

3500 Patients With CHD in 9 European Countries



EUROASPIRE I and II Group. *Lancet.* 2001;357:995-1001.

8

"Hypertension is the most important disease in the world"

Henry Greenberg, MD 2003

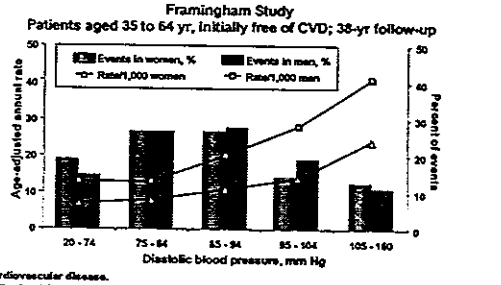
9

Why hypertension dominates

- It is the most prevalent vascular disease
- It is the major clinical marker of coronary disease
- It can be identified at little or no cost, any place, by anyone (with minimal training)
- It permits access to a patient's family for more detailed screening
- It can be treated!

10

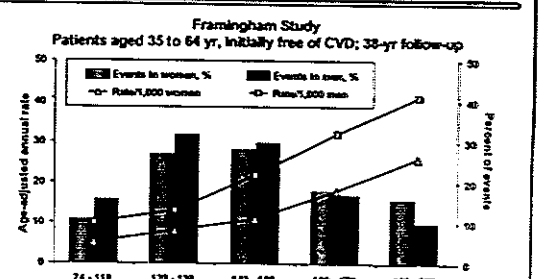
Risk for Cardiovascular Events by Diastolic Blood Pressure



CVD = Cardiovascular disease.
Kannel WB. *Am J Cardiol.* 2000;85:251-255.

11

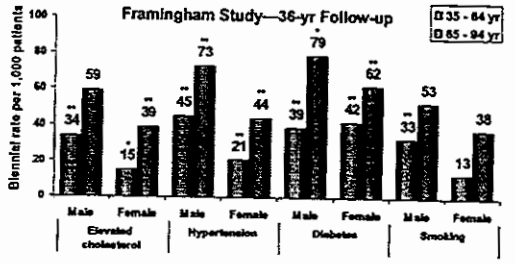
Risk for Cardiovascular Events by Systolic Blood Pressure



Kannel WB. *Am J Cardiol.* 2000;85:251-255.

12

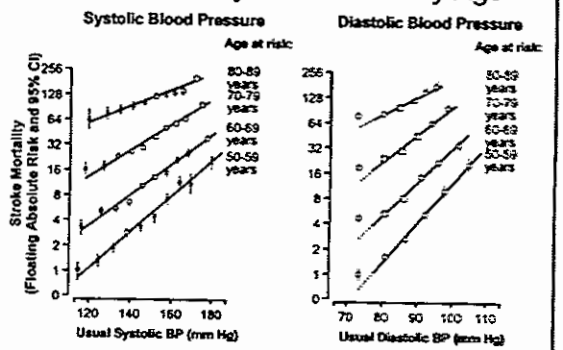
Coronary Heart Disease Risk by Major Risk Factors



*P<.01; **P<.001.
Kannel WB, MD, FACC, unpublished data, 2002.

13

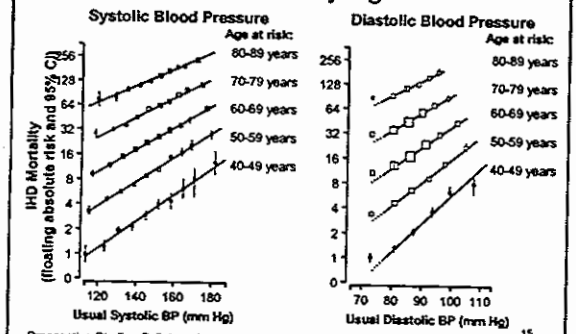
Stroke Mortality vs Usual BP by Age



Prospective Studies Collaboration. *Lancet*. 2002;360:1903-1913.

14

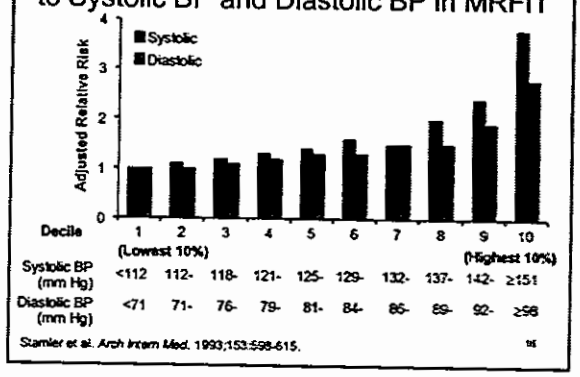
Ischemic Heart Disease Mortality vs Usual BP by Age



Prospective Studies Collaboration. *Lancet*. 2002;360:1903-1913.

15

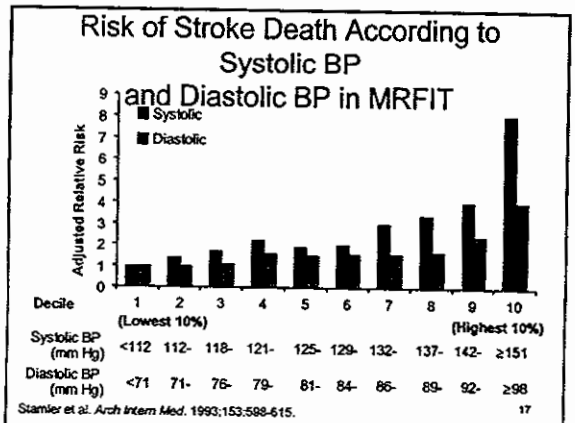
Risk of CHD Death According to Systolic BP and Diastolic BP in MRFIT



Stamler et al. *Arch Intern Med*. 1993;153:598-615.

16

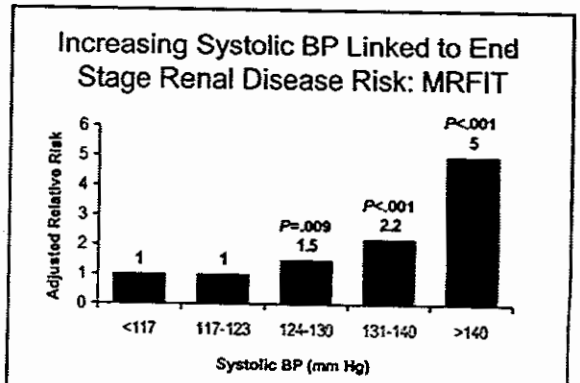
Risk of Stroke Death According to Systolic BP and Diastolic BP in MRFIT



Stamler et al. *Arch Intern Med*. 1993;153:598-615.

17

Increasing Systolic BP Linked to End Stage Renal Disease Risk: MRFIT

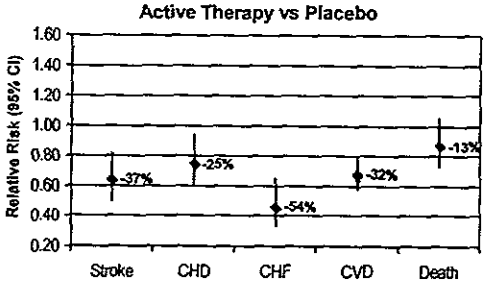


Klag et al. *N Engl J Med*. 1996;334:13-18.

18

SHEP Trial: Endpoints

Active Therapy vs Placebo

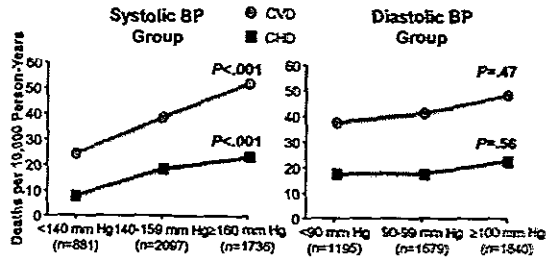


SHEP Cooperative Research Group. *JAMA*. 1991;265:3255; Kostis et al. *JAMA*. 1997;278:212-216.

19

Systolic BP, Not Diastolic BP, Predicts CVD and CHD Mortality

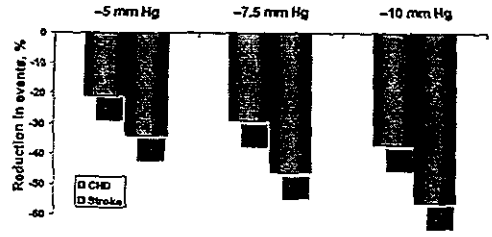
Observational Study of 4714 Middle-Aged Hypertensive Men



Benetos et al. *Arch Intern Med*. 2002;162:577-581.

20

Reducing Diastolic Blood Pressure Lowers Coronary Heart Disease and Stroke Risk*

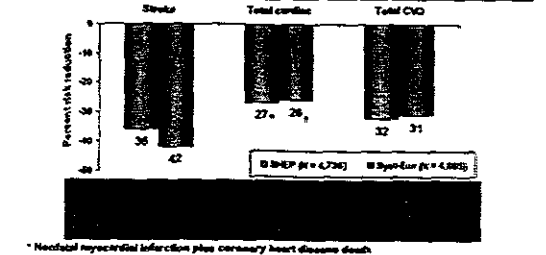


*429,000 patients for CHD, 405,500 patients for stroke, 843 strokes, 4,838 CHD events, 10-yr mean follow-up period.

MacMahon S, et al. *Lancet*. 1990;335:765-774.

21

Reduction in Systolic Blood Pressure Lowers Coronary Heart Disease and Stroke Risks



* Nonfatal myocardial infarction plus coronary heart disease death.
† Fatal and nonfatal heart failure, fatal and nonfatal myocardial infarction, and sudden death.
‡ SHEP. *JAMA*. 1991;265:3255-3264.
§ Staessen JA, et al. *Lancet*. 1997;350:757-764.
¶ Difference between active and placebo groups.

22

Advantage of Additional BP Reduction: NNT to Prevent 1 Stroke Event*

Reduction in DBP	NNT	Framingham average risk/10 yr
5 to 6 mm Hg		
Average risk	24	11%
High risk†	7	37%
7.5 mm Hg		
Average risk	20	11%
High risk†	6	37%

NNT = Number needed to treat.
* Men aged 72 to 74 yr.
† High Risk = SBP 160–170 mm Hg, CVD, diabetic, smoker.

Kannel WB, MD, FACC, unpublished data, 2002.

23

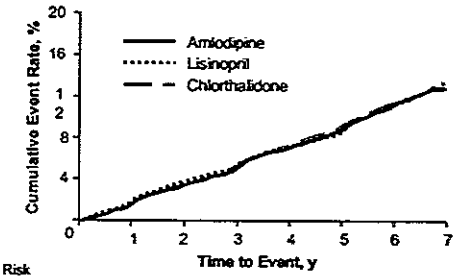
From Evidence to Practice Update in Hypertension: ALLHAT

Overview of Hypertension Trials

- Many trials have evaluated the effects of different antihypertensive regimens in specific populations, eg, patients with vascular disease, diabetes, renal disease, the elderly
- Meta-analyses have compared active treatments with placebo and with other active treatments
- ALLHAT is the largest randomized clinical trial undertaken to answer the question whether there are differences among classes of antihypertensive agents—diuretic (chlorthalidone), alpha blocker (doxazosin), ACEI (lisinopril), and CCB (amlodipine)

25

ALLHAT: Primary Outcome (CHD Death and Nonfatal MI)

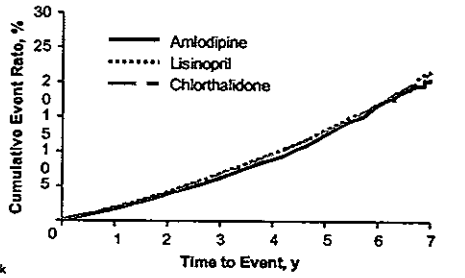


No. at Risk								
Chlorthalidone	15,255	14,477	13,820	13,102	11,362	6340	2956	209
Amlodipine	9048	8576	8218	7843	6824	3870	1878	215
Lisinopril	9054	8535	8123	7711	6662	3832	1770	195

ALLHAT Collaborative Research Group. *JAMA*. 2002;288:2981-2997.

26

ALLHAT: All-Cause Mortality

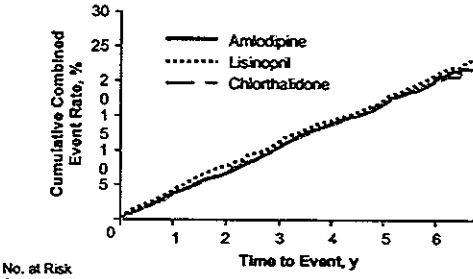


No. at Risk								
Chlorthalidone	15,255	14,933	14,564	14,077	12,480	7185	3523	428
Amlodipine	9048	8847	8654	8391	7442	4312	2101	217
Lisinopril	9054	8853	8612	8318	7382	4304	2121	144

ALLHAT Collaborative Research Group. *JAMA*. 2002;288:2981-2997.

27

ALLHAT: Combined CHD

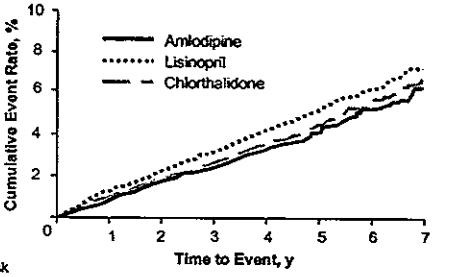


No. at Risk								
Chlorthalidone	15,255	14,211	13,320	12,415	10,587	5804	2696	187
Amlodipine	9048	8428	7940	7422	6357	3512	1672	142
Lisinopril	9054	8347	7789	7264	6207	3461	1622	170

ALLHAT Collaborative Research Group. *JAMA*. 2002;288:2981-2997.

28

ALLHAT: Stroke



No. at Risk								
Chlorthalidone	15,255	14,515	13,934	13,309	11,570	6385	3217	567
Amlodipine	9048	8617	8271	7949	6937	3845	1813	506
Lisinopril	9054	8543	8172	7784	6765	3891	1828	949

ALLHAT Collaborative Research Group. *JAMA*. 2002;288:2981-2997.

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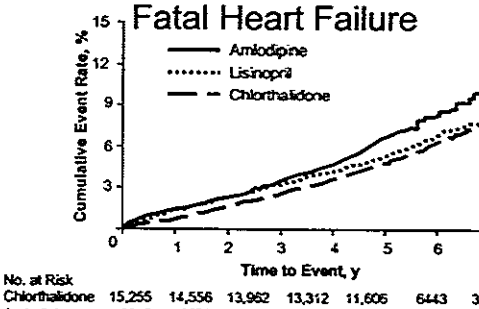
ALLHAT: Hospitalized Plus Fatal Heart Failure



No. at Risk								
Chlorthalidone	15,255	14,556	13,962	13,312	11,606	6443	3130	396
Amlodipine	9048	8579	8251	7884	6966	3833	1821	216
Lisinopril	9054	8538	8169	7780	6768	3895	1894	322

*Heart failure was not a prespecified endpoint.
ALLHAT Collaborative Research Group. *JAMA*. 2002;288:2981-2997.

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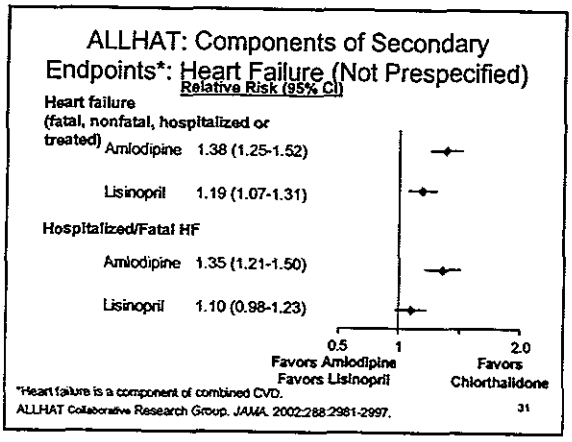
ALLHAT: Components of Secondary Endpoints*: Heart Failure (Not Prespecified)

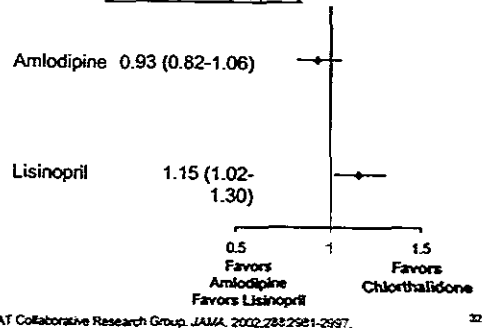


*Heart failure is a component of combined CVD.

ALLHAT Collaborative Research Group. *JAMA*. 2002;288:2981-2997.

31

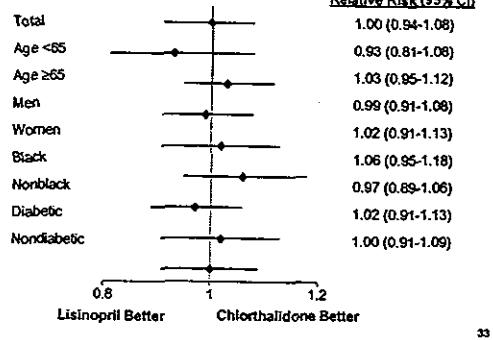
ALLHAT: Secondary Endpoints: Stroke



ALLHAT Collaborative Research Group. *JAMA*. 2002;288:2981-2997.

32

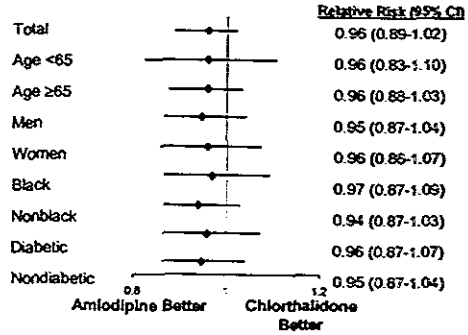
ALLHAT: Total Mortality (Lisinopril vs Chlorthalidone) Subgroups



33

ALLHAT Collaborative Research Group. *JAMA*. 2002;288:2981-2997.

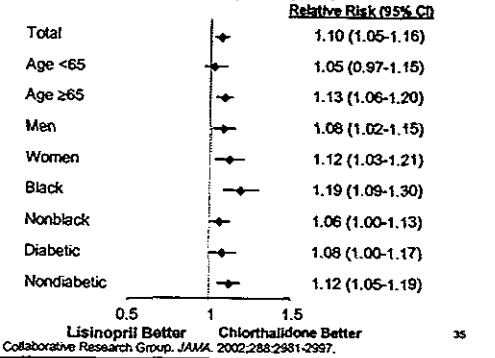
ALLHAT: Total Mortality (Amlodipine vs Chlorthalidone) Subgroups



ALLHAT Collaborative Research Group. *JAMA*. 2002;288:2981-2997.

34

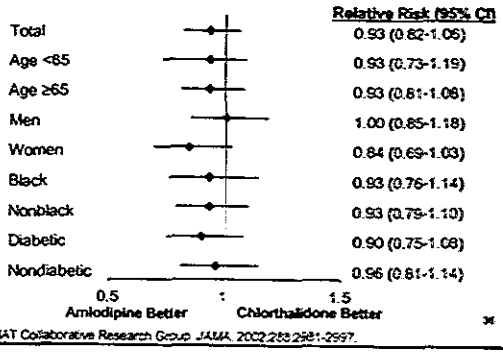
ALLHAT: Combined CVD (Lisinopril vs Chlorthalidone) Subgroups



ALLHAT Collaborative Research Group. *JAMA*. 2002;288:2981-2997.

35

ALLHAT: Stroke (Amlodipine vs Chlorthalidone) Subgroups



ALLHAT Collaborative Research Group. *JAMA*. 2002;288:2981-2997.

36

ALLHAT: Intermediate Outcomes Biochemical Changes at 4 Years: Potassium

	Chlorthalidone	Amlodipine	Lisinopril	*P* Value: Amlodipine vs Chlorthalidone	*P* Value: Lisinopril vs Chlorthalidone
Baseline					
n	14,487	8586	8573		
K, mmol/L	4.3	4.3	4.4		.001
% K <3.5 mmol/L	3.4	3.4	2.6		.001
4 Years					
n	8315	4919	4618		
K, mmol/L	4.1	4.4	4.5	<.001	<.001
% K <3.5 mmol/L	8.5	1.9	0.8	<.001	<.001

ALLHAT Collaborative Research Group. *JAMA*. 2002;288:2981-2997.

37

ALLHAT: Intermediate Outcomes Biochemical Changes at 4 Years: Fasting Glucose

	Chlorthalidone	Amlodipine	Lisinopril	*P* Value: Amlodipine vs Chlorthalidone	*P* Value: Lisinopril vs Chlorthalidone
Baseline					
n	11,273	6648	6752		
FSG, mg/dL (mmol/L)	123.5 (6.9)	123.1 (6.8)	122.9 (6.8)		
% ≥126 mg/dL (≥7 mmol/L)	28.9	29.2	29.4		
4 Years					
n	4972	2954	2731		
FSG, mg/dL (mmol/L)	126.3 (7.0)	123.7 (6.9)	121.5 (6.7)	.2	.002
% ≥126 mg/dL (≥7 mmol/L)	32.7	30.5	28.7	.11	<.001

FSG=fasting serum glucose.
ALLHAT Collaborative Research Group. *JAMA*. 2002;288:2981-2997.

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Conclusions

- Hypertension a major treatable risk factor for CVD, including CHD, stroke, PAD, and heart failure
- Incremental blood pressure reduction is meaningful from a public health perspective
- Benefits of blood pressure reduction with pharmacological treatment are incremental and continuous
- Compelling need for clinicians to use more effective BP-reducing drugs to achieve recommended treatment goals

CVD = Cardiovascular disease.

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Summary and Conclusions 1

- ALLHAT is the largest hypertension trial with great clinical relevance
- ALLHAT emphasizes the importance of controlling systolic BP
- ALLHAT demonstrates that aggressive treatment is necessary to achieve systolic BP goals
- ALLHAT shows that multiple medications often are required to get to BP goal

ALLHAT Collaborative Research Group. *JAMA*. 2002;288:2981-2997.

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Summary and Conclusions 2

- ALLHAT demonstrated that the lisinopril-based treatment was not as effective as the diuretic for reducing systolic BP
- Contrary to expectations, ALLHAT showed that results for the group taking lisinopril were not superior to the diuretic group with regard to CHD and CVD morbidity and mortality in the overall hypertensive population and in diabetics

ALLHAT Collaborative Research Group. *JAMA*. 2002;288:2981-2997.

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JNC-VII

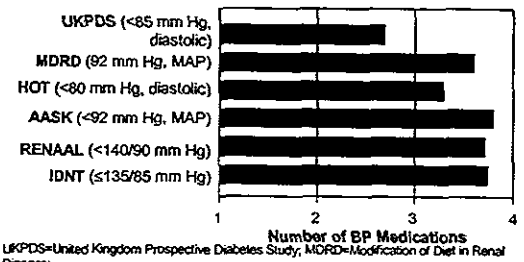
Joint National Committee on Prevention, Detection, Evaluation and Treatment of High Blood Pressure
(For release summer 2003)

Goal= <140/90, except <130/90 for diabetics and renal patients

Initial choice: Without compelling factors:
Stage I: 140-160/90/100=Thiazide diuretic, followed by any other class-ACEI,ARB,BB,CCB

Stage 2: >160/100= Thiazide diuretic plus another agent, started similtaneously

Hypertension in High Risk Patients: Number of Agents Used to Treat BP



UKPDS=United Kingdom Prospective Diabetes Study; MDRD=Modification of Diet in Renal Disease;
HOT=Hypertension Optimal Treatment; AASK=African American Study of Kidney Disease; RENAAL=Reduction of Endpoints in NIDDM with the Angiotensin II Antagonist Losartan; IDNT=Irbesartan Diabetic Nephropathy Trial; MAP=mean arterial pressure.

Bakris et al. *Am J Kidney Dis.* 2000;36:646-661; Brenner et al. *N Engl J Med.* 2001;345:861-869; Lewis et al. *N Engl J Med.* 2001;345:851-860.

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Thiazides and Related Diuretics

	Half life (hours)	Daily Oral Dose	Frequency of Dosage
Bendroflumethiazide	3-3.9	5 mg	As single dose
Chlorothiazide	1.5	125-500 mg	In 2 divided doses
Chlorthalidone*	44	12.5-50 mg	As single dose
Hydrochlorothiazide	2.5	12.5-50 mg	As single dose
Hydroflumethiazide	12-27	12.5-50 mg	As single dose
Indapamide*	10-22	1.25-5 mg	As single dose
Metolazone†	4-5	0.5-5 mg	As single dose
Polythiazide	~25	2-4 mg	As single dose
Trichlormethiazide	2-7	2-4 mg	As single dose

*Not a thiazide but a sulfonamide qualitatively similar to the thiazides; †quinazoline diuretic with properties generally similar to the thiazide diuretics.

Brater. *N Engl J Med.* 339;387-395; Jackson. In: Goodman & Gilman's *The Pharmacological Basis of Therapeutics.* 1996; Katzung, ed. *Basic & Clinical Pharmacology, Eighth Edition.* 2001; McEvoy, ed. *AHFS Drug Information.* 2002; *Physicians' Desk Reference.* 2003; Puschett. *Int Hypertension Primer. Second Edition.* 1999.

Physician Practices Treating Hypertension

- Hypertension, particularly ISH, seldom treated to recommended goal
- No increase in medication at 75% of visits despite continued BP elevation
- Drugs rarely up-titrated; reluctance to include additional drugs
- Therefore, more effective monotherapy drugs could facilitate attaining recommended treatment goals

ISH = isolated systolic hypertension.
Coppola WG, et al. *J Hum Hypertens.* 1997;11:185-191.
Barlowitz DR, et al. *N Engl J Med.* 1993;329:1957-1963.

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Barriers to Hypertension Control

Survey of PCPs of Patients With Uncontrolled HTN in Large US Health System*

- Self-reported adherence with JNC VI guidelines—14% always, 62% usually
- PCPs satisfied with BP values, despite 93% of systolic BP values being at or above 140 mm Hg
- Physicians reported 150 mm Hg was lowest systolic BP and 91 mm Hg lowest diastolic BP for recommending pharmacotherapy
- 48% of surveyed physicians believed risk of MI and stroke greater with BP of 135/95 vs 150/80 mm Hg

*Board-certified internists in Henry Ford Medical Group.
Oliveria et al. *Arch Intern Med.* 2002;162:413-420.

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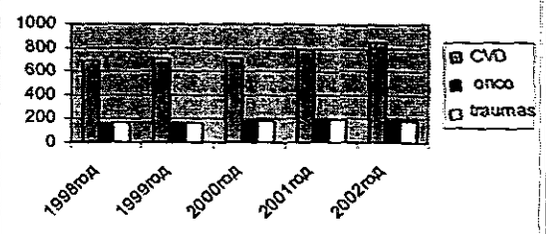
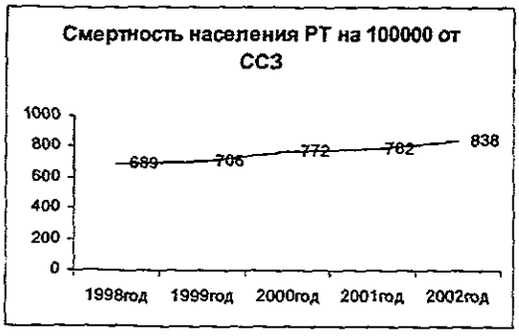
Prevention of cardiovascular complications in patients with hypertension.
Results of new research.

Chief cardiologist of the Ministry of Health of the Republic of Tatarstan and of the Department of Health of the city of Kazan
доктор медицинских наук,
Professor A.S. Galyavich, MD, PhD, D.Sci (KSMU)

Mortality rate because of major causes in population of Tatarstan

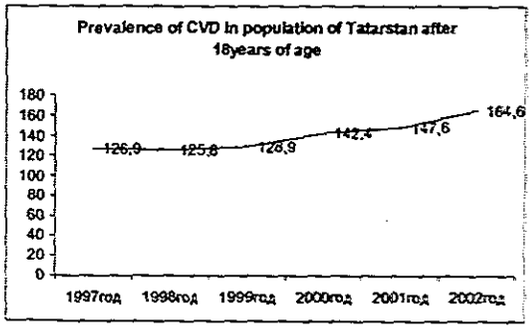


Mortality rate per 100 000 population in Republic of Tatarstan because of CVD



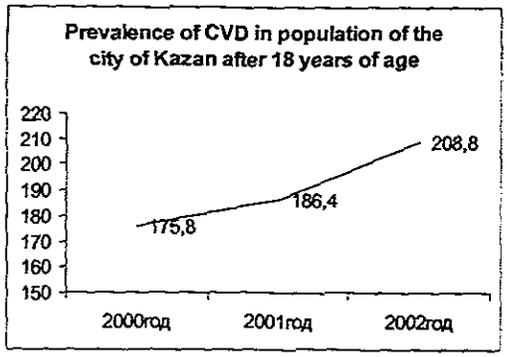
Increase by

Prevalence of CVD in population of Tatarstan after 18years of age



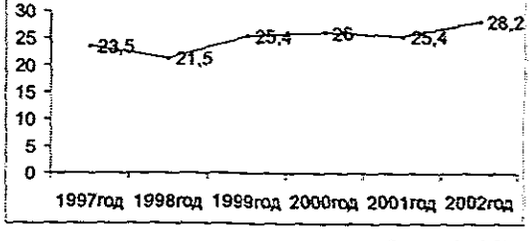
Рост на 3,5% на 10%

Prevalence of CVD in population of the city of Kazan after 18 years of age

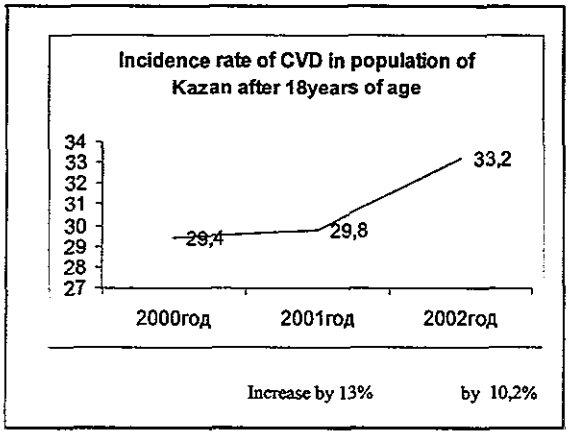


Increase by 5,7% by 10,7%

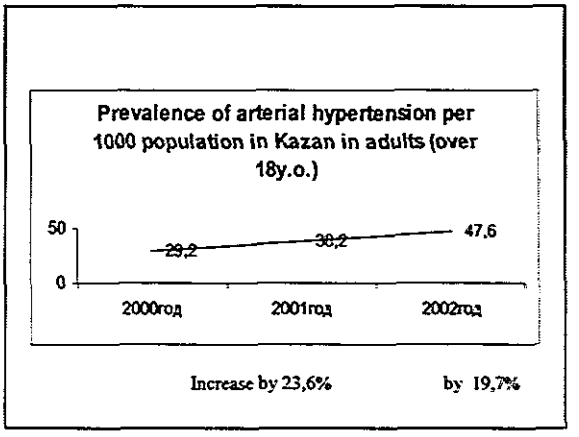
Incidence rate of CVD per 1000 population of Republic of Tatarstan after 18 years of age



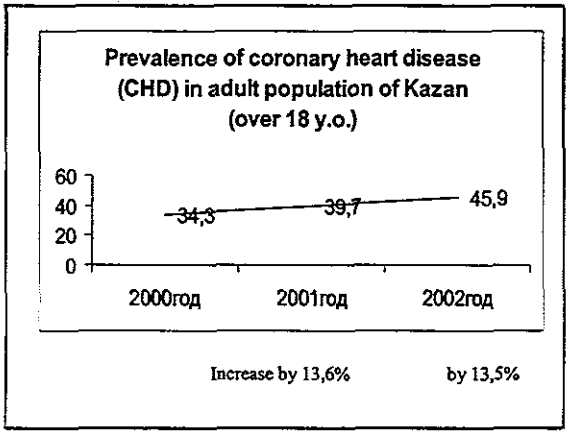
Increase by 9,9%



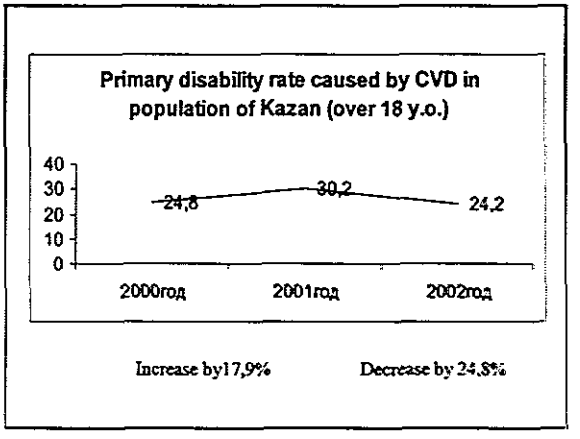
Increase by 13% by 10,2%



Increase by 23,6% by 19,7%



Increase by 13,6% by 13,5%



Increase by17,9% Decrease by 24,8%

EPOCH - epidemiologic study (CVD)

Major CVDs in European part of Russia:

1. Hypertension – 39,7%
2. Stable angina - 12,1%
3. MI - 2,3%
4. Valvular defects - 1,1%
5. History of stroke 2,5%
6. Diabetes mellitus - 2,9%
7. CHF – 2,3 % of population.

EPOCH (Arterial Hypertension AH – 39,7%)

AH I-degree - 49,1%

AH II-degree - 29,5%.

AH III-degree - 7,2%

Effectively treated patients (BP in one measurement <140/90 mm Hg) - 7,2%.

EPOCH in Tatarstan (AH – 32,4%)

City of Kazan	Country side
Prevalence of AH –29% (women – 59%)	Prevalence – 32% (women – 68%)
1 degree - 71 %	1 degree – 83%
2 degree – 22%	2 degree – 16%
3 degree – 7%	3 degree – 1%
Do not measure BP – 49%	Do not measure BP – 61%

EPOCH (drugs)

The number of preparations analysed - 10022

% of cases

ACE inhibitors - 22,6%

Beta-blockers - 9,3%

Nitrates – 9,9%

Diuretics - 7,8%

Calcium channel blockers - 5,4%

Rawolfia preparations - 10,1%

Other drugs, metabolites and sedatives, not affecting prognosis and outcomes - 24,3%.

Disease needs to be prevented at the very beginning,

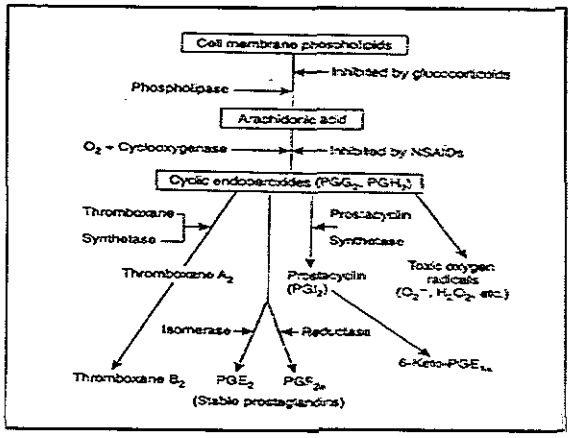
it is late to prepare a drug when disease is already here.

Publyi Ovidyi Nazon,

43y b.c. - 18 a.c.

Nonsteroidal Anti-inflammatory Drugs

Sara E. Walker MD, MACP
Professor of Medicine
University of Missouri
Columbia, Missouri



NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAIDs)

How NSAIDs work:

- Inhibit prostanoid synthesis through cyclooxygenase (COX) blockade
- Two COX isoforms: COX-1 and COX-2
- Traditional NSAIDs - inhibit both isoforms
  - Examples: ibuprofen, naprosyn
- New NSAIDs inhibit Cox-2

3

PHARMACOLOGY OF NSAIDs

- Given orally - completely absorbed
- Most are weak organic acids
- >95% bound to serum albumin
- If albumin is increased, the free serum component is increased
- Metabolized in liver, excreted in urine

4

SIDE EFFECTS OF TRADITIONAL NSAIDs (suppress COX-1 & COX-2)

- Gastric / esophageal irritation
- Peptic ulcer disease / exacerbation
- Anti-platelet activity
- Reversible hepatocellular toxicity
- Decrease in creatinine clearance
- Fluid retention
- Rhinitis, nasal polyposis, asthma
- Headaches, confusion in the elderly

5

SPECIAL PROPERTIES OF NSAIDs

- Very long half-life
  - piroxicam, oxaprozin
- Avoid in hepatic disease
  - nabumetone
- Salicylates
  - least highly protein-bound
  - zero-order kinetics

6

GASTROINTESTINAL TOXICITY OF TRADITIONAL NSAIDs

- Systemic inhibition of prostaglandin synthesis, if given by any route
- Stomach, duodenum, small/large bowel
- Dyspepsia, nausea, abdominal pain
- Esophagitis, gastritis, ulcer, perforation, hemorrhage, death
- Ulcers: >3mm in 15-31%; FDA 2-4%/yr gastric ulcers
- Strictures, bowel obstruction

7

PREVENTING DYSPEPSIA IN ASYMPTOMATIC PATIENTS

- In asymptomatic RA patients, NSAIDs + low-dose H2 blockers increased risk of GI complications
- In the presence of dyspepsia, NSAIDs + H2 blockers improve symptoms
- Therefore, use of H2 blockers with NSAIDs is <u>not</u> recommended unless the patient has dyspepsia
  - *Arch Int Med* 1996;156:1530-1536

8

INCREASED RISK FOR NSAID-INDUCED GI ULCERS

- >60 years of age
- History of peptic ulcer
- Previous treatment, anti-ulcer drugs
- Corticosteroids
- High-dose NSAIDs
- Multiple NSAIDs
- Serious underlying disease

9

PREVENTING ULCERS IN HIGH-RISK PATIENTS

- Traditional NSAID + protective agent
  - High-dose H2 blocker
  - Proton-pump inhibitor
  - Misoprostol
- Highly selective COX-2 inhibitor

10

SUBSTITUTES FOR NSAIDs

- Nonacetylated salicylates
  - Choline magnesium salicylate
- Opiods
  - Oxycodone
  - Fentanyl transdermal patch

11

SUBSTITUTES FOR NSAIDs

- Rheumatoid arthritis
  - Low dose prednisone (5 - 10 mg/day)
  - Early use of remittive drug
- Osteoarthritis
  - Acetaminophen
  - Glucosamine-chondroitin sulfate
  - Capsaicin cream (0.25% - 0.75%)
  - Intra-articular hyaluronic acid injection

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WHAT'S SO GREAT ABOUT NEW NSAIDs?
Here's the rationale --

- COX-1 is in many cells. COX-1 inhibition suppresses beneficial prostaglandins -- may lead to mucosal ulcers, renal failure
- COX-2, in cells at sites of inflammation, induces production of prostanoids that modulate inflammatory response.
- Theory: Control of COX-2 should control inflammation with NO GASTROINTESTINAL SIDE EFFECTS

COX-2 INHIBITORS

- As effective as "traditional" NSAIDs
- No influence on platelet adhesion or adherence
- Displace coumadin
- Meta-analysis: risk of stroke, myocardial infarct in RA (JAMA, 2001)
- Rare GI bleeding, dyspepsia
- Not renal or hepatic sparing

COX-2 INHIBITORS

- *Celebrex* - celecoxib
  - 200- 400 mg/day, BID
  - *Sulfonamide - beware hypersensitivity
  - *FDA label change: GI safety down-graded, = naprosyn or diclofenac
- *Vioxx* - rofecoxib
  - 12.5 - 25 mg/day
  - *Edema, *Suspect risk of thrombosis
- *Bextra* - valdecoxib

NSAIDs - FRIEND OR FOE?

- Benefits
  - Readily available, nonaddicting, effective, relieve pain and inflammation
- Drawbacks
  - Most toxic to those who need them the most (elderly, severe rheumatoid arthritis), side effects may be severe, the newest and safest are expensive

HOSPICE CARE IN THE UNITED STATES

PHILOSPOPHY OF HOSPICE CARE:

AN OVERVIEW

Janice Farmer, MSSA, LISW-C
Bethesda, Maryland

HISTORY

"HOSPICE" LATIN *HOSPITIUM*

Dr. Cicely Saunders England 1940 initiated the concept. Provided a quiet setting for death with dignity.

Hospice Care introduced in the United States in 1974.

2

Philosophy

Emphasis on palliative care, not curative

Recognition that a cure is not always possible

Treatment is to provide comfort care and pain control

3

Palliative Care – Palliation or relief of symptoms

Comfort Care – Physical, emotional and spiritual needs

A recognition by the patient and family that aggressive treatment will not alter prognosis or cure of the disease process.

4

Diseases include--

Cancers

Heart Disease

HIV / AIDS

End Stage Renal Disease

Alzheimer's Disease / Dementias

5

Hospice Care is for patients with a limited life expectancy – 6 months – as diagnosed by physician

Wholistic approach –
Physical – Emotional – Spiritual

Care focus patient / family needs

Supports understanding and acceptance that death is a part of the life process

6

Decisions for Hospice care –
Physicians discusses with patient and family

Referral is initiated
Admission includes an assessment of:
Diagnoses / physical need
Emotional / Spiritual needs
Family participation

7

Payment for services:

Private Insurance
Medicare (for patients over 65 years)
Medicaid (low income)
Private pay
Donations from Hospice Volunteer fundraisings

8

Challenge for physicians

Traditionally physicians focus on treatment with the goal to cure the disease process.

Hospice education for physicians includes:
The recognition that a disease process not responding to treatment does not mean treatment failure.

The need to reassure patients that palliative care is not "abandonment" by the physician.

9

Challenge for Patients and Families

Understanding and accepting that palliative care is a form of treatment

It is difficult for patients and family to talk about death

Planning for death is not "giving up on life"

10

Interdisciplinary (Medically Directed) Team
Both for Home visits and Facility

Registered Nurse
Social Worker
Chaplain
Home Health Aid/Nurse Assist
Physician
Volunteer

11

Individualized care plan based on patient's physical, emotional and spiritual needs.

Includes:
Education to help families provide necessary care and to help family understand physical and emotional changes as death approaches

12

Role of Hospice Nurse

- Regularly scheduled visits – assesses patient/family needs
- "On Call" skilled nursing available 24 hours every day
- Provides expert pain management
- Keeps primary physician and Interdisciplinary team informed of patient's condition
- Education on end of life issues
- Initiates Respite Care

13

Role of Social Workers

Provides emotional support to patient / family
Counseling of patient / family
Encourages communication
Listening
Bereavement Needs
Assists with reality issues
Coordinates Respite Care
Assists with end of life tasks

14

Role of Home Health Aides / Nurse Assistants

Assists with daily care needs, bath, bed changes, meals

Assists with routine tasks

Helps with Respite care, giving family caregivers time for their own personal needs

15

Role of Chaplains

Provides spiritual support to patient / family

Encourages communication

Listening

Assists with memorial / funeral services

Counseling – end of life needs

16

Role of Volunteers

Assists family with tasks as minimal shopping, bill paying, etc

Provides limited respite

Provides diversional activities / reading

Organizes fund-raising events

17

Patient care services are provided in:

- Private homes of the patient or caregiver
- Nursing / Convalescent Homes
- Hospice Care facilities

Focus is for patient and family to feel a sense of control

18

When the Patient Receives Hospice Care in the Home

All Medications, supplies, equipment needed for comfort of patient is provided

Homes may be supplied with hospital beds, bedside commodes, oxygen, dressings, shower/bath equipment, wheelchairs, walkers

19

Death

Hospice Interdisciplinary team available to support patient and family

Assistance given in memorial service or funeral arrangements

20

Bereavement

Hospice Care includes continuing contact and support to surviving family members and caregivers

Support provided includes support groups and individual counseling for about one year

Referrals made for counseling if caregivers are experiencing "complicated" grieve

21

Pediatric

Specially trained Interdisciplinary team

Sensitivity to parents and sibling needs

Recognition of intensity of emotional and physical needs of the pediatric patient and family

22

In summary

Life threatening disease process and decisions for palliative / comfort care is a difficult and stressful time for patients and families

Quality of family relationships, positive and negative, intensifies

Preparation and ongoing education of the Hospice Interdisciplinary Team is critical for the prevention and relief of suffering

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Web sites

American Academy of Hospice and Palliative Medicine (AAHPM)

Center to Advance Palliative Care
CAPC Manual

San Diego Hospice & Palliative Care
Center for Palliative Studies at San Diego Hospice

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ДЕМОНСТРАЦИОННЫЕ МАТЕРИАЛЫ

к докладу профессора И.Г.Низамова
на Республиканской конференции
«Профилактика хронических заболеваний как актуальная проблема общественного здравоохранения (кардиологические, ревматологические, фармакологические и управленческие аспекты)»

21-22 апреля 2003г.

Visuals for the presentation of Professor I.G. Nizamov at the Republican Conference "Prevention of Chronic Diseases as the Major Public Health Problem" (cardiology, rheumatology, pharmacology and managerial aspects)

April 21-22, 2003

Cover sheet: Visuals for the presentation of professor I.G. Nizamov at the Republican conference «Prevention of Chronic diseases as the major public health problem (cardiology, rheumatology, pharmacology и managerial aspects)» 21-22 April 2003.

Page 1.
Demographic processes in Russia (per 1 000 population)
Columns:

Years	Birth rate	Mortality rate	Natural increase in population

Page 2.
Sanitary-demographic parameters in the Republic of Tatarstan (per 1000 population)
Columns:

Years	Birth rate	Mortality rate	Infant Mortality	Natural increase in population

Page 3.
Natural changes in population of the Republic of Tatarstan (per 1 000 population).

Page 4.
Coefficients of natural changes in population of the Republic of Tatarstan.
Upper line – mortality rate
Lower line – birth rate

Page 5.
Maternal mortality in the Republic of Tatarstan (per 100 000 infants born alive)

Page 6.
Infant mortality in the Republic of Tatarstan (per 1 000 infants born alive).

Page 7.
Causes of death in the Republic of Tatarstan (2001, % of total)
1. Diseases of cardio-vascular system – 59,1%
2. Traumas, poisonings and other external causes – 14,2%
3. Oncology – 13,4%
4. Respiratory tract diseases – 4,5%

Total 91,2%

Page 8.
Life expectancy in Russia
Columns:

Years	All population	Men	Women

Page 9.
Mean life expectancy in Russia (including Tatarstan) – in years
Columns:

Years	All population		Difference	Men		Difference	Women		Difference
	RF	RT		RF	RT		RF	RT	

RF – Russian Federation
RT – Republic of Tatarstan
The data (prognosis) presented form the Journal "Healthcare of Russian Federation", 2001, №6, P.19-27

Page 10.
Demographic tree of the Republic of Tatarstan (2002).
Men (left), Women (right).

Page 11.
Main causes of deterioration of health of the population

1. Bad life conditions because of economics inefficiency and huge external expenses in the cold war period
2. Insufficient (absolutely insufficient) funding of the healthcare system
3. Low efficacy of treatment and preventive activities in preventing morbidity and disability of preventable causes
4. Irrational management of resources (material and human) due to highly centralized administration.

Page 12.
Number of abortions performed in medical facilities of the Republic of Tatarstan (1994-2001)

1. Absolute number, including mini-abortions
2. Per 1 000 women 15-49 years, including mini-abortions
3. Number of abortions per 100 infants born alive

Демографические процессы в России
(на 1 000 населения)

Годы	*Рождаемость*	*Смертность*	*Естественный прирост*
1980	15,9	11,0	4,9
1981	16,0	10,9	5,1
1982	16,6	10,7	5,9
1983	17,5	11,0	6,5
1984	16,9	11,6	5,3
1985	16,5	11,7	5,2
1986	17,2	10,4	6,8
1987	17,1	10,5	6,6
1988	16,0	10,7	5,3
1989	14,6	10,9	3,7
1990	13,4	11,2	2,2
1991	12,1	11,4	0,7
1992	10,7	12,2	-1,5
1993	9,4	14,5	-5,1
1994	9,6	15,7	-6,1
1995	9,3	15,0	-5,7
1996	8,9	14,2	-5,3
1997	8,6	13,8	-5,2
1998	8,8	13,6	-4,8
1999	8,3	14,7	-6,4
2000	8,7	15,4	-6,7
2001	9,1	15,6	-6,5
2002	9,8	16,3	-6,5

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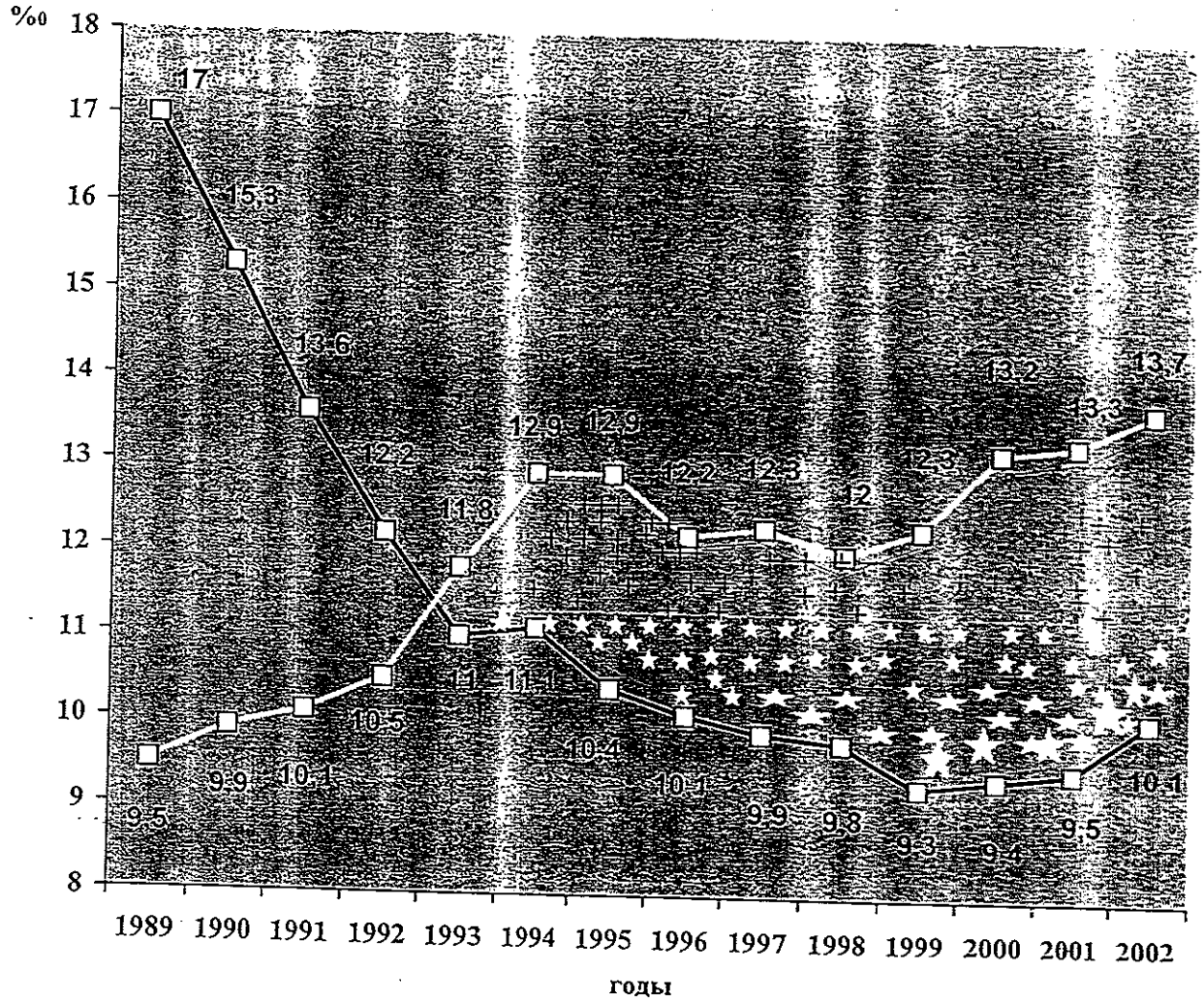
Санитарно - демографические показатели в Республике Татарстан
(в случаях на 1000 населения)

Годы	*Рождаемость*	*Смертность*	*Младенческая смертность*	*Естественный прирост*
1989	17,0	9,5	15,9	7,5
1990	15,3	9,9	16,8	5,4
1991	13,6	10,1	17,8	3,5
1992	12,2	10,5	17,1	1,7
1993	11,0	11,8	20,2	-0,8
1994	11,1	12,9	18,5	-1,8
1995	10,4	12,9	18,5	-2,5
1996	10,1	12,2	17,5	-2,1
1997	9,9	12,3	16,9	-2,4
1998	9,8	12,0	15,3	-2,2
1999	9,3	12,4	14,3	-3,1
2000	9,4	13,2	14,8	-3,8
2001	9,5	13,3	12,6	-3,8
2002	10,1	13,7	12,0	-3,6

256

Естественное движение населения Республики Татарстан (показатели на 1 000 населения за 1989 – 2002гг.)



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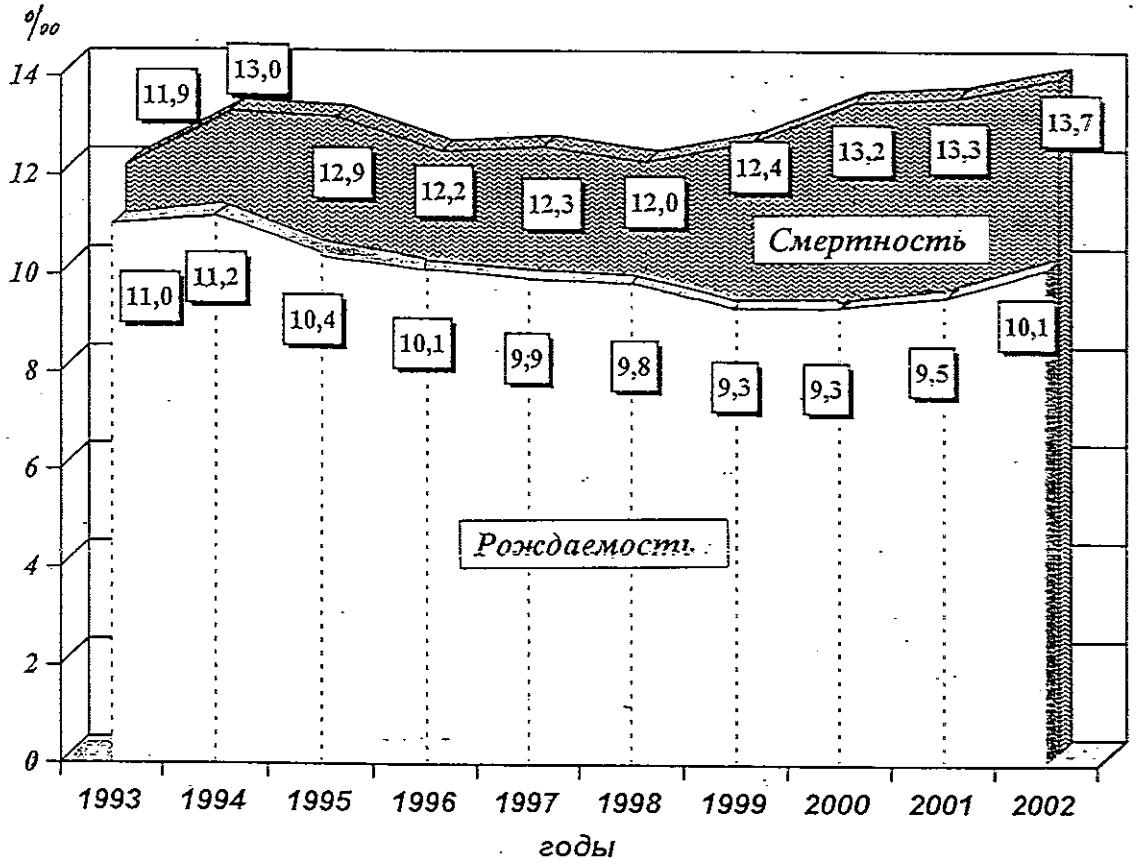
Коэффициенты естественного движения населения Республики Татарстан



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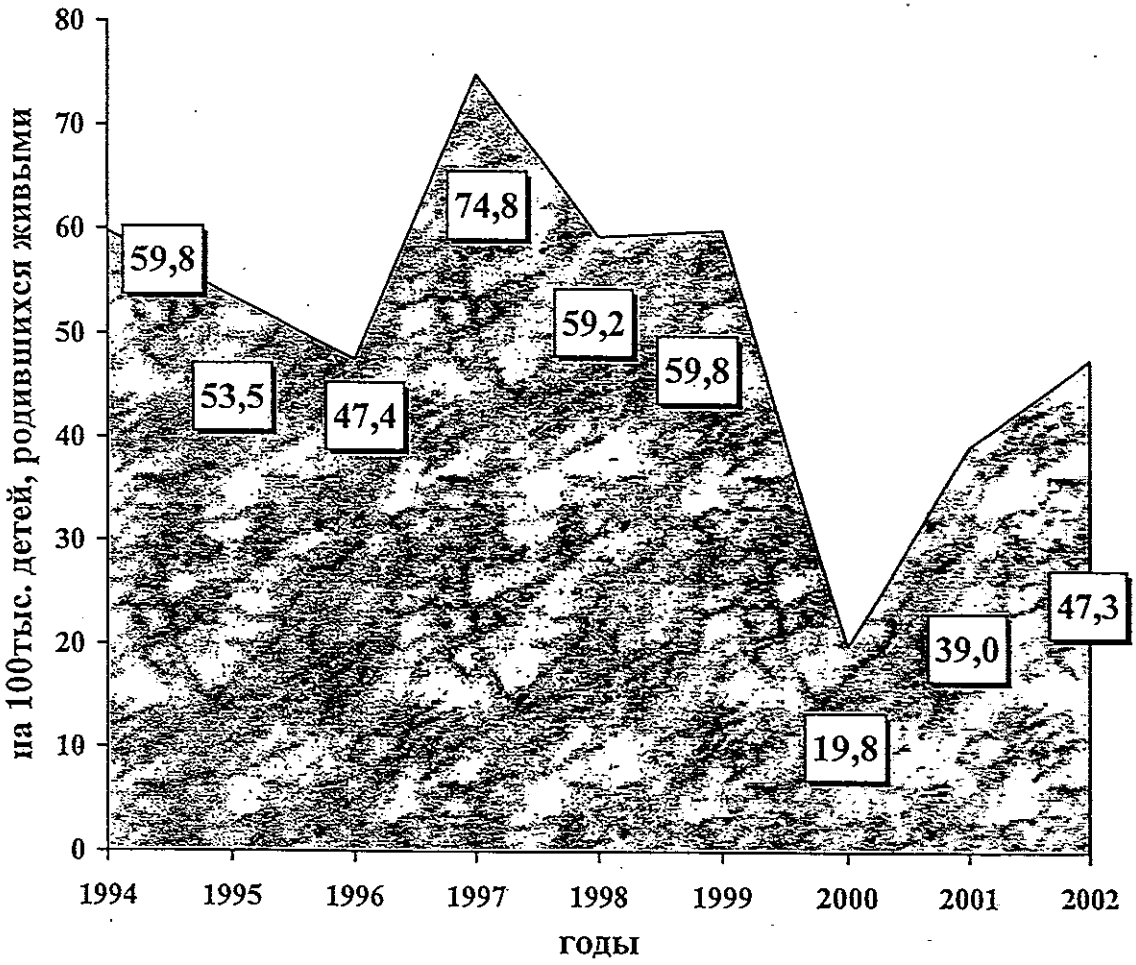
Материнская смертность в Республике Татарстан



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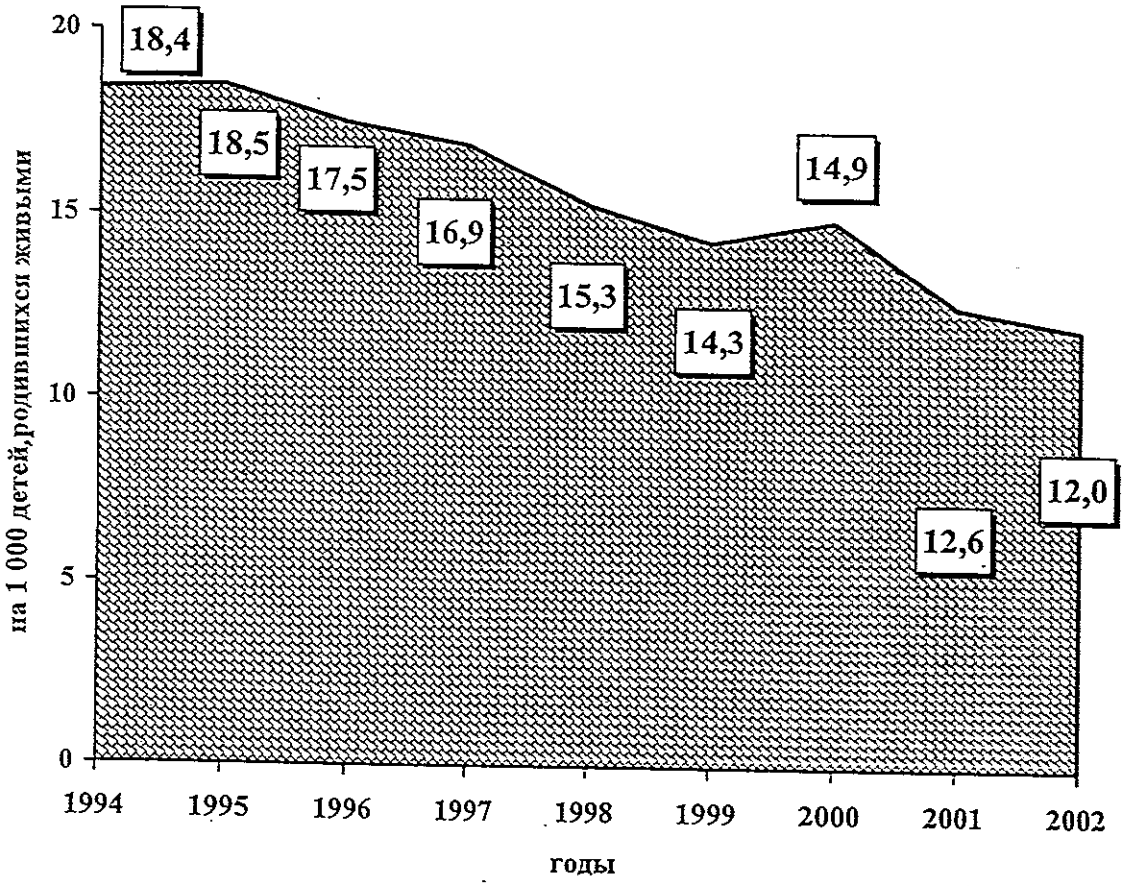
Младенческая смертность в Республике Татарстан



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СТРУКТУРА

причин смертности в Республике Татарстан

(2001г., в % к итогу)

1.	Болезни системы кровообращения -	59,1%
2.	Травмы, отравления и внешние воздействия -	14,2%
3.	Новообразования -	13,4%
4.	Болезни органов дыхания -	4,5%
	Итого	91,2%

СРЕДНЯЯ ПРОДОЛЖИТЕЛЬНОСТЬ ПРЕДСТОЯЩЕЙ ЖИЗНИ НАСЕЛЕНИЯ РОССИИ

(в годах)

ГОДЫ	Все население	Мужчины	Женщины
1896 - 1897 (по 50 губерниям Европейской России)	32,3	31,3	33,4
1926 - 1927 (по европейской части СССР)	44,4	41,9	46,8
1938 - 1939	46,9	44,0	49,7
1955 - 1956	67,0	63,0	69,0
1971 - 1972	69,5	64,5	73,6
1984 -	67,7	62,4	72,6
1986-	69,6	65,0	73,6
1987 -	69,8	65,1	73,8
1988 -	70,0	65,0	74,0
1990 -	69,2	63,8	74,3
1991 -		63,5	74,3
1992 -		62,0	73,8
1993 -		58,9	71,9
1994 -	64,0	57,6	71,2
1995 -	64,6	58,3	71,7
1996 -	65,9	59,6	72,7
1997 -	66,6	60,8	72,9
1998 -	67,0	61,3	72,9
1999 -	65,93	59,93	72,38
2000 -	65,27	59,00	72,20
2001 -	65,3	59,7	72,2
2002 -	65,9	60,0	72,3
2003 -	66,1	60,2	72,5
2004 -	66,4	60,5	72,6
2005 -	66,6	60,8	72,8
2006 -	66,8	61,0	72,9

Средняя продолжительность предстоящей жизни населения России (в т.ч. Татарстана) – *в годах*

Годы	Все население		*Разница*	Мужчины		*Разница*	Женщины		*Разница*
	РФ	РТ		РФ	РТ		РФ	РТ	
1997	66,6	68,2	*1,6*	60,8	62,1	*1,3*	72,9	74,3	*1,4*
1998	67,0	68,8	*1,8*	61,3	62,6	*1,3*	72,9	74,3	*1,4*
1999	65,9	68,4	*2,5*	59,9	62,2	*2,3*	72,4	74,7	*2,3*
2000	65,27	67,54	*2,27*	59,0	61,06	*2,06*	72,20	74,47	*2,27*
2001	65,3	67,6	*2,3*	59,7	61,6	*1,9*	72,2	74,2	*2,0*
2002	65,9	67,9	*2,0*	60,0	61,8	*1,8*	72,3	74,4	*2,1*
2003	66,1	68,1	*2,0*	60,2	62,0	*1,8*	72,5	74,5	*2,0*
2004	66,4	68,2	*1,8*	60,5	62,2	*1,7*	72,6	74,6	*2,0*
2005	66,6	68,4	*1,8*	60,8	62,4	*1,6*	72,8	74,7	*1,9*
2006	66,8	68,5	*1,7*	61,0	62,5	*1,5*	72,9	74,8	*1,9*

Прогноз представлен из журнала "Здравоохранение РФ" 2001, №6, стр.19-27

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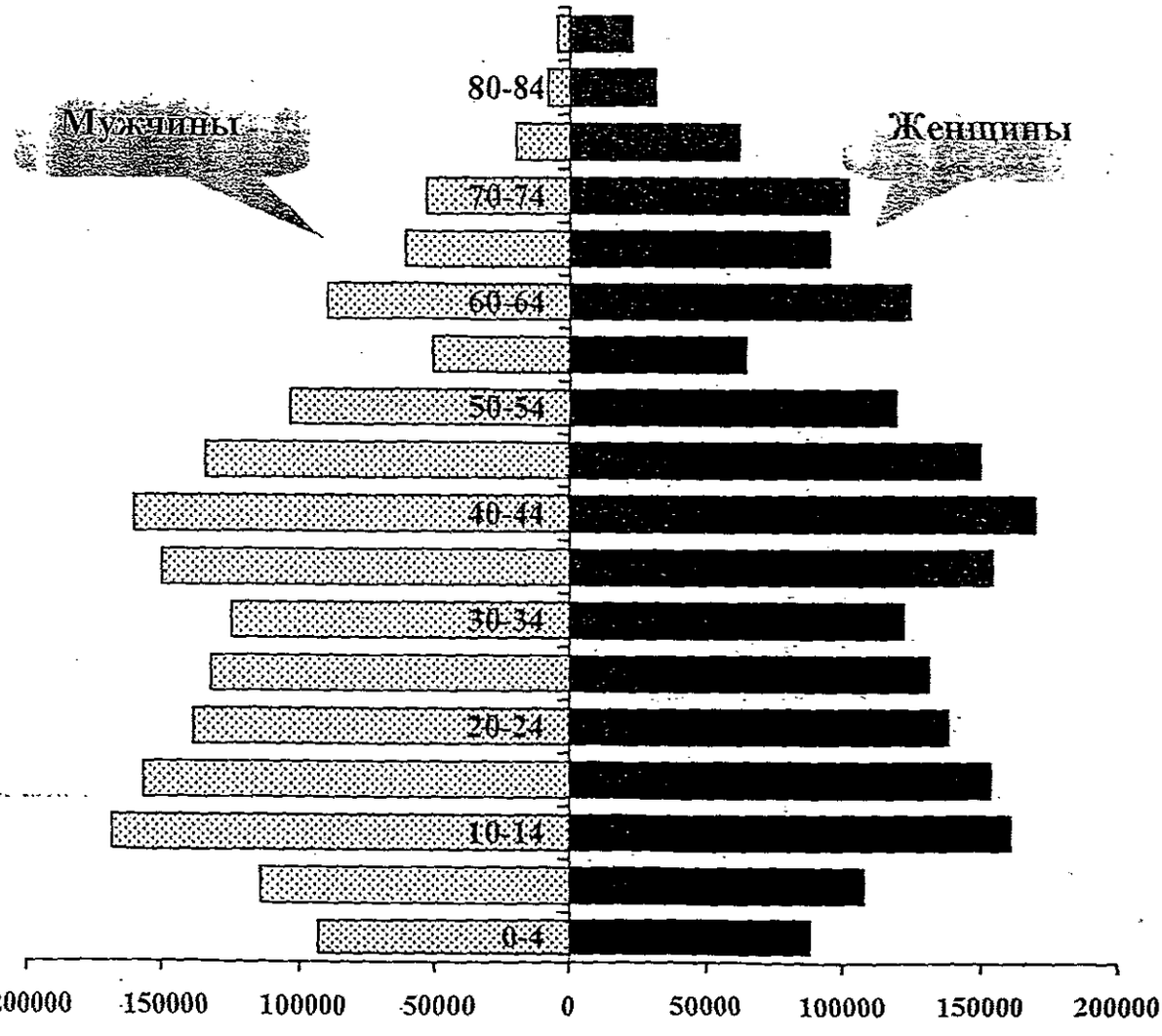
Демографическое дерево Республики Татарстан (2000г.)



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Общие причины ухудшения состояния здоровья населения

1. Ухудшение условий жизни из-за неэффективного функционирования экономики, огромных внешних расходов в период холодной войны.

2. Недостаточное (крайне) финансирование здравоохранения.

3. Низкая эффективность лечебно-профилактических мероприятий по снижению заболеваемости и потерь трудоспособности от устранимых причин.

4. Нерациональное управление материальными и кадровыми ресурсами вследствие жесткого централизованного администрирования.

Число абортов, произведенных женщинам медицинскими учреждениями РТ (1994 –2001 гг.)

		1994г.	*1995г.*	*1996г.*	*1997г.*	*1998г.*	*1999г.*	*2000г.*	*2001г.*
1	Абсолютное число		74 953	77 331	72 222	71 822	67 414	63 518	59 906
	в т.ч. мини-аборты		24 340	24 390	23 211	22 739	23 262	22 049	20 188
2	На 1000 женщин 15-49 лет	99,5	77,2	78,9	73,0	72,0	66,7	62,6	58,6
	в т.ч. мини-аборты	-	25,1	24,9	23,5	22,8	23,0	21,7	19,8
3	Число абортов на 100 детей, родившихся живыми	222	192	204	195,6	194,9	194,4	180,5	167,9

Eurasian Medical Education Program

Continuing Medical Education for Russian Physicians

American College of Physicians

Richard G. Farmer, M.D., MACP
Medical Director

1

Public Health - Definition

- Public health is a series of activities to promote health, to prevent disease and injury, to prevent premature death, to insure positive well-being, which is population-based. It is NOT diagnosis, treatment and rehabilitation of individuals from disease – that is medical care.
- The U.S. only commits 3% of the $1.2 trillion health budget to public health.

2

The 20th Century

- **Life Expectancy** – (47 to 77) 30 years of life added. High-tech medicine has helped, but public health improvement accounts for 25 to 30 years.
  1. Immunization – smallpox/polio to be eradicated
  2. Infection Control – water good, sewage treatment, antibiotics, TB 20,000 lives 1953 – today 2,000

3

The 20th Century

3. Heart Disease – 50% death rate reduction from 1965 strokes – 60% decline
   *NEJM – Monograph by Eugene Braunwald, MD
   - Better medical and emergency treatment
   - Diet weight control, high blood pressure management
   - Smoking reduction from 55% to 25% (male)
4. Better fortified and safer foods – goiter, pellagra and rickets no longer endemic
   *Food Safety – Food and Drug Administration

4

The 20th Century

5. Workplace safety – (1900-25) 356 mine disasters (5 or more killed) – (1975-2000) 14 mine disasters
   - Occupational illness declined (silicosis decline)
6. Motor vehicle safety – deaths 31/100,000 (1937) to 16/100,000 (today)
   - Seatbelts, safer cars and roads, DWI laws
7. Tobacco control – 55% (1950) – 25% (2000) in males
   - Surgeon General report in 1964 – tax increases – litigation and political advocacy

5

The 20th Century

8. Childbirth safety – 1913 leading cause of death for women in reproductive years (after TB)
   - Infant mortality reduction 90%
9. Family planning – 3.3 births/woman in 1917 to 2.1 births/woman today
   - Liberated women – allowed child spacing
10. Flouridation – since 1945 – today almost cavity-free generation

"What an incredible difference the 100 years have made."

6

Sources of Public Health Data in US

US Department of Health and Human Services

Center for Disease Control and Prevention

National Center for Health Statistics

State Department of Health

CDC – Investigating Infectious Terrorism Assessment

7

Death Rates, Life Expectancy, Infant Mortality, US

Measure	2000	1999
All Deaths	2,303,698	2,391,399
Death Rate (100,000 pop.)	872.4	881.9
Male	1,042.7	743.6
Female	739.8	743.6
Life Expectancy	76.9	76.7
Male	74.1	73.9
Female	79.5	79.4
Infant Deaths	27,987	27,937
Infant Mortality Rate (1,000 births)	6.9	7.1

8

DEATH AND DEATH RATES, US 1999 & 2000

All causes – 2.4 million

Rate per 100,000 population 873 in 2000 (882 in 1999)

Causes	2000 Rate	1999 Rate
Heart disease	258	268
Cancer	200	202
Cerebral vascular disease	60	62
Chronic respiratory disease	45	46
Accidents	34	36
Diabetes	25	25

9

INFANT MORTALITY, US 1999 & 2000

Under one year of age		
All causes	27,987 in 2000	27,937 in 1999
Rate per 1000 live births	6.9 in 2000	7.1 in 1999
Under one month of age		
All causes	18,737 in 2000	18,728 in 1999
Rate per 1000 live births	4.6 in 2000	4.7 in 1999
Black race only		
Under one year rate	14.0 in 2000	14.6 in 1999
Under in one month rate	9.3 in 2000	9.8 in 1999

10

2001 Public Health Data

- 3074 deaths from terrorism (9 / 11)
- HIV death rate decreased 3.8 %
  6th leading cause of death ages 25 – 34
  Rate decreased by 47.7 % since 1996
- Drug-induced deaths decreased by 5.7 %
- No change in death rates from alcohol, firearms, injuries

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2001 Death Rates, Life Expectancy, and Infant Mortality

•Death Rates: Male 1029, Females 722

•Life Expectancy: Male 74.4, Female 79.8

•Infant Mortality 6.9

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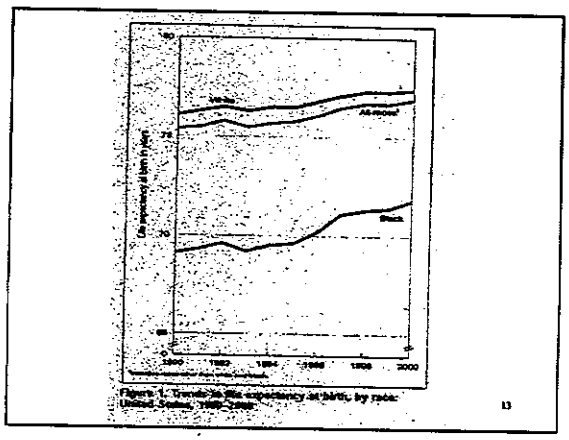

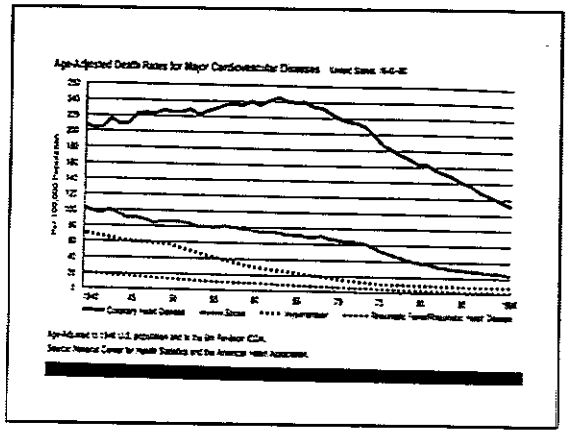

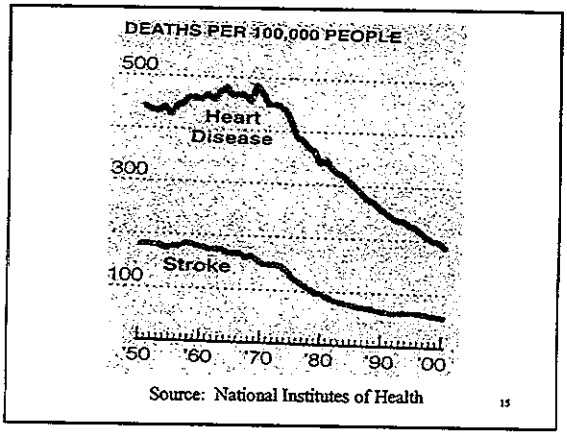

Source: National Institutes of Health

The 20th Century

- **Challenges for the future**
  1. Universal health insurance with a comprehensive primary care system
  2. Closing the health gap between rich and poor – whites and minorities
  3. Containing emerging infections
  4. Continued assault on heart disease

The 20th Century

- **Challenges for the future, continued**
  5. Raising our children out of poverty and tending to their development and emotional needs
  6. Improving lifestyles – weight, alcohol and tobacco consumption, exercise, sexual behavior, illicit use of drugs and firearms
  7. Improved health literacy

Chronic Ischemic Heart Disease

- Global epidemic looming
- 12,000,000 Americans have CAD
  - 6,300,000 with angina
  - 7,200,000 with prior MI
- Estimated cost in US: $118 billion /year
- Increasing in prevalence worldwide as infectious diseases and nutritional disorders overcome

Cardiovascular Diseases in U.S.

Optimistic Trend

- 25 – 30 % reduction in mortality each of the past three decades
- Risk factor modification in high risk individuals
  - Elimination of smoking
  - Improved diets
  - More active life styles
  - Attention to blood pressure control

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Cardiovascular Diseases in the U.S.

Ongoing Concerns

- Still # 1 cause of death in both men and women from childhood on, almost 1,000,000 per year
- ½ of patients experiencing heart attacks or sudden death have had warning symptoms
- The majority of patients who are discharged from hospitals after MI are not on optimal medical therapy

20

Cardiovascular Diseases in U.S.

- Estimated: Two-thirds of reductions because of better medical care
- Estimated: one-third of reduction because of risk factor modification
- Absolute number of coronary deaths unchanged – occur at older age

21

Cardiovascular Diseases in U.S.

- Effective Therapies – Primary Prevention
  - Aspirin
  - Statin drugs
  - Risk factor modification
  - Active lifestyle

22

Public Health Implications of Excessive Alcohol Consumption

US Data:

- 8 million alcohol dependence
- 5.6 million alcohol abuse
- 66.5 million smokers
- 16 million – illicit drug use

- Factor in 25% of all deaths
- Ages 12-20 drinkers – 20% of total
- "Excessive" = >2 drinks/day (men); > 1 drink/day (women)

JAMA 289:1031, 2003

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American College of Physicians Preventive Service Recommendations

- Blood pressure
- Height and weight
- Cholesterol (total, HDL)
- Fecal occult blood
- Sigmoidoscopy, colonoscopy
- Pap smear
- Mammogram/exam
- Prostate/PSA
- Bone densitometry
- Vision/hearing
- Rubella immunization for pregnancy
- PPT (TB skin test)
- STD testing (and HIV)

24

American College of Physicians
Immunization – Adult Recommendations

-Influenza >50, yearly

-Pneumococcal >65

-Hepatitis A and B – all

-Tetanus – Diptheria – every 10 years

-MMR – once

25

Preventive Services Recommendations
(United States)
US Preventive Services Task Force

1. Breast Cancer – Clinical breast exam and/or mammography every 1-2 years, after 40
2. Prostate Cancer – Digital exam and PSA aids early detection; ? on outcomes
3. Colorectal Cancer – Effective in reducing mortality; early detection of polyps
4. Depression – Identification in primary care settings and treatment decreases morbidity

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Clinical Preventive Services
Agency for Healthcare Research and Quality
US Dept of Health and Human Services

- Lipid Disorders
- Hearing Disorders
- Mental Disorders
- Substance Abuse
- Adult Diabetes
- Diabetes in Pregnancy
- Osteoporosis
- STDs
- Chemoprevention: HRT, Aspirin

27

<u>Screening</u>

Examination of a group to separate well persons from those who have an undiagnosed pathologic condition or who are at high risk

Dorland's Medical Dictionary 25th Edition

<u>Case Finding</u>

Utilizing patient demographics, risk factors and symptoms to determine whether to apply a test to an individual to detect disease

29

<u>Effective Screening Criteria</u>

<u>Disease Criteria:</u>

1. Serious consequences (high morbidity or mortality)
2. Acceptable therapy that is more effective than symptom-diagnosed disease
3. High prevalence of a long preclinical phase that is detectable by the screening test

Hennrud, Mayo Clin Proc., 2000

30

Screening Measures

- Blood Pressure Measurement
- Blood Sugar Determination
- Blood Lipid (Cholesterol) Determination
- Glaucoma Testing
- Cancer Screening
  - Breast – Mammography
  - Colorectum – Occult Blood, Endoscopy
  - Cervix – Papsmear
  - Prostate – PSA

U.S. Prevention Services TaskForce

31

CDC Updated Interim Case Definition for

SEVERE ACUTE RESPIRATORY SYNDROME (SARS)

Suspected Case

Respiratory illness of unclear etiology, with onset since February 1, 2003 and the following criteria:

- Temperature > 100.4 F (>38.0°C)
- 1 or more clinical signs of respiratory disease (for example, cough, shortness of breath, hypoxia, by X-ray pneumonia or ARDS)
- Trip to the suspicious or documented SARS area (excluding the areas of secondary diseases, restricted by medical personnel or direct household contacts) 10 days before the symptoms

JAMA, April 17, 2003 32

CDC Updated Interim Case Definition for

SEVERE ACUTE RESPIRATORY SYNDROME (SARS)

- Close contact during 10 days before the first signs of disease with the respiratory sick patient and the trip to the SARS area or contact with the person, investigated or suspicious for SARS
- March 22, 2003 – Cases of suspicion or radiographic signs of pneumonia or RDS, or symptoms of idiopathic RDS on autopsy – probable cases by the WHO definition.
- Suspicious countries: Hong-Kong, Guangdong province, China, Hanoi, Vietnam and Singapore.
- Close contact is defined: taking care of, live with, have direct with respiratory secrets and/or other biological liquids of the patient suspicious for SARS

JAMA, April 17, 2003[33]

"The doctor of the future will give no medicine but will interest his patients in the care of the human frame, in diet, and in the cause and prevention of disease."

Thomas A. Edison

Quoted by Hemsrud, Mayo Clinic Proc., 2000

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1

Medical Education in the United States

1. **Undergraduate - College or University**
   - Ages 18-22 (4 years)
   - Science courses, history, literature, math, language, writing; AB, BS degree
   - Apply to medical school (125 in US – average size about 100/year)
     - Acceptance based on grades in college and standardized test, plus experience, interviews
     - Approximately 1 in 6 accepted
     - Cost about $25,000 per year

2

Medical Education in the United States

2. **Medical School (MD degree)**
   - Ages 22-26 (4 years)
   - Often different location from undergraduate
   - First 2 years basic science – lectures, laboratory work, introduction
   - 3rd and 4th years – "clinical" in hospital and outpatient settings
   - Progressive patient responsibility (with supervision)
   - Exams, standardized national testing

3

Medical Education in the United States

3. **Internship and Residency (4 years)**
   - Ages 26-30
   - Internal medicine and sub-specialties
   - Family medicine
   - Surgery and sub-specialties
   - Pediatrics and sub-specialties
   - Radiology
   - Pathology
   - Anesthesiology
   - Neurology
   - Psychiatry
   - Dermatology

4

Medical Education in the United States

Medical Residency Features (3 years)

- Hospital (In-patient)
  - Attending (faculty) rounds
  - Case presentations
  - Seminars (subject-oriented)
  - Interactive role-playing
  - Grand Rounds (lectures)
  - Critical Care (ICU)
- Ambulatory (Out-patient)
  - Continuity clinic (same patient, over time)
  - Core Curriculum (24 month cycle)

5

Medical Education in the United States

Medical Residency Features , cont.

- Elective Programs: Specific Diseases or Clinical Situations
  - Procedures (flexible sigmodoscopy, testing, treadmill)
- Conferences
  - Journal Club
  - CPC
- Sub-specialty Rotations
  - Cardiology, gastroenterology, endocrinology, infectious disease, hematology/oncology, rheumatology, etc.
- Bioethics
- Clinical Investigation/Research
- Affiliated Hospitals

6

Medical Education in the United States

4. **Surgical Specialties**

- Duration: 4-7 years (ages 27-34)
  - General surgery
  - Thoracic surgery
  - Cardiovascular
  - Neurosurgery
  - Orthopaedics
  - Gynecology
  - Urology
  - Opthamology
  - Otolaryngology

7

Medical Education in the United States

5. **Medical Specialties (Fellowship)**

- Duration: 2-4 years (ages 30-34)
  - Cardiology
  - Gastroenterology
  - Pulmonary/Critical Care
  - Hematology/Oncology
  - Nephrology
  - Endocrinology
  - Infectious Diseases
  - Rheumatology

8

Medical Education in the United States

6. **Continuing Medical Education**

- Conferences, lectures, seminars
- Duration: days or weeks
- Requirement generally 50 hours over a 2 year period

9

Medical Education in the United States

Regulation

1. **Licensure – to practice medicine**
   - Given by individual states and renewed every 2-3 years
   - Pass exam; obtain CME
   - Ethical standards (license can be revoked by state board)
   - Supervision by Medical Board of Physicians and others

10

Medical Education in the United States

Regulation, cont.

2. **Certification of Specialty**
   - National exam by specialty organizations (NOT government)
   - All specialties, including general practice, family medicine, primary care, as well as traditional specialties
   - Time limited; renew with exam

11

Medical Education in the United States

Regulation, cont.

3. **Medical Schools and Residency**
   - Programs are accredited by national organization – private, NOT government
   - Standards are developed and reviewed
   - 425 programs in Internal Medicine

12

Core Clinical Competence in Internal Medicine

1. **Patient Care**
   - Health promotion, disease prevention, treatment
2. **Medical Knowledge**
   - Critical evaluation, basic and clinical science
   - Critical problem-solving and decision-making
3. **Interpersonal and Communication Skills**
4. **Professionalism**
   - Ethical practices, compassion, sensitivity
5. **Practice-Based Learning and Improvement**
6. **Systems-Based Practice**
   - Continuity of care

13

Eurasian Medical Education Program

5 Years in Russia: 1998 – 2003
Kazan, Ekaterinburg, Khabarovsk, Tula, Birobijan

Richard G. Farmer, MD, MS, MACP
Medical Director

1

Continuing Medical Education

- *Lectures* – 35 programs: 5,000 Russian doctors
- *Train-the-Trainers* – slides, handouts and lectures by Russian professors, using EMEP information, to more than 1,500 Russian physicians each year
- *Polyclinic Visits* – direct patient contact, data collection programs, 7 locations
- *Visiting Professors* – 22 members of the American College of Physicians

2

Program Emphasis

- Prevention, early detection, management, prevention of complications, continuity of care of diseases that can cause premature death
- Cardiovascular disease, diabetes, tuberculosis
- Women's health, public health, public education

3

Tuberculosis

- 8 visits of Russian physicians to the US for training in DOTS and laboratory procedures – formal programs in Newark, Baltimore and Denver
- As a result of EMEP, DOTS officially established in Sverdlovsk by government decree
- Laboratory procedures based on culture and sensitivity developed
- Sverdlovsk Oblast – more than 1,500 Russian doctors trained in DOTS using EMEP materials
- Collaboration developed between prison and civilian tuberculosis treatment programs

4

Data Collection: Cardiovascular Disease and Diabetes

- **5 programs are on-going**
  - **Cardiovascular:**
    - 3 programs over 3 years, involving more than 750 patients
    - Significant increase in compliance with medication
    - Significant improvement in blood pressure control
    - Decrease in sick leave and disability
    - Great decrease in hospitalization
    - Improvement in lifestyle (exercise, diet)
    - Some decrease in smoking

5

Data Collection: Cardiovascular Disease and Diabetes

- **Diabetes:**
  - 2 programs over 3 years, involving more than 10,000 patients
  - Dramatic decrease in ketoacidosis
  - Dramatic decrease in hospitalization
  - Dramatic decrease in mortality
  - Improvement in patient compliance with medications, diet and lifestyle

6

Osteoporosis:
A Public Health Problem

In honor of

Professor Mars K. Mikhailov
Rector, Kazan State Medical Academy
By Sara E. Walker, MD, MACP

OSTEOPOROSIS

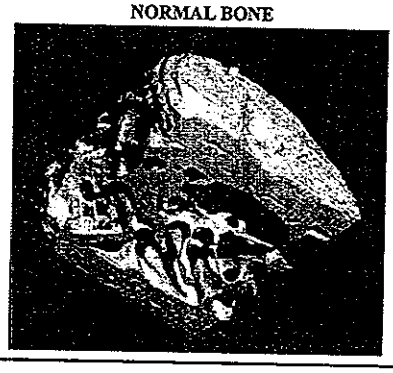
Definition:

- Loss of inorganic mineral
  - Ca and PO4 hydroxyapatite crystals
- ***and*** organic matrix
  - collagen and other proteins

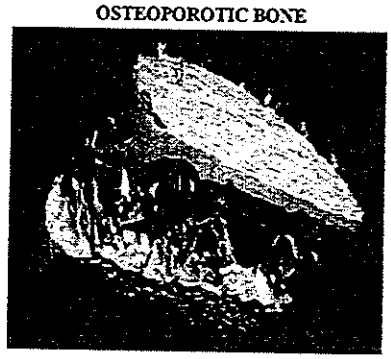
Result:

- Low mass, fragile bones, fractures

NORMAL BONE

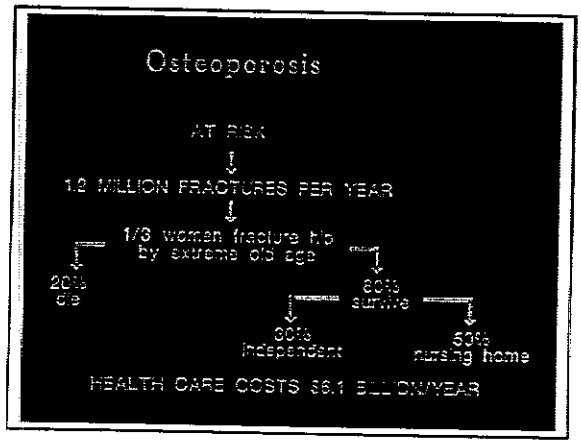


OSTEOPOROTIC BONE

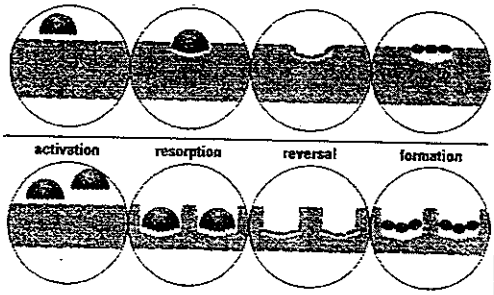


OSTEOPOROSIS
An International Problem

- Most common metabolic bone disease worldwide
- Affects 200 million people
- After 50 years of age, exponential increase in fractures:
  - Women 40%, Men 13%



BONE REMODELING CYCLE



Primary Osteoporosis: Risk Factors

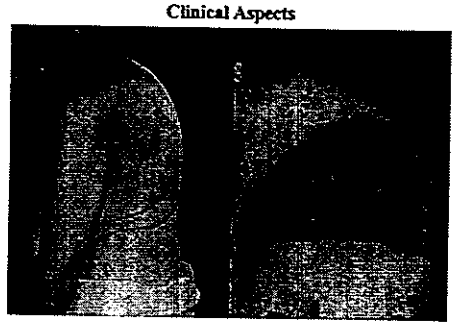
- Female
- Postmenopausal state
- Increasing age
- Inadequate calcium intake
- Relative inactivity
- Small skeleton
- White or Asian race
- Relative leanness
- Tobacco use
- Alcohol abuse

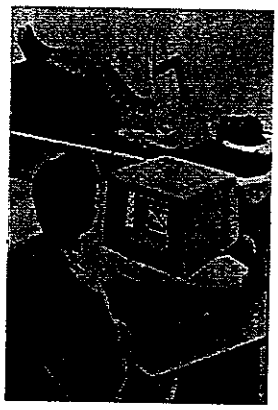
Secondary Osteoporosis: Risk Factors

- Early surgical menopause
- Hyperthyroidism
- Malabsorption
- Corticosteroid use (past or current)
- Rheumatoid arthritis
- Hyperparathyroidism
- Chronic uremia
- Other chronic illness

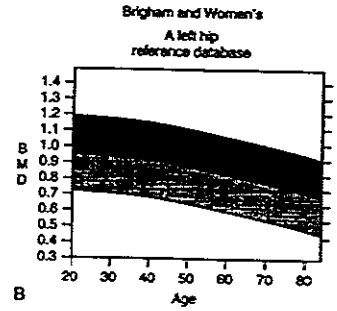
OSTEOPOROSIS

Clinical Aspects





BONE MINERAL DENSITY MEASUREMENT



2B

BONE MINERAL DENSITY MEASUREMENT

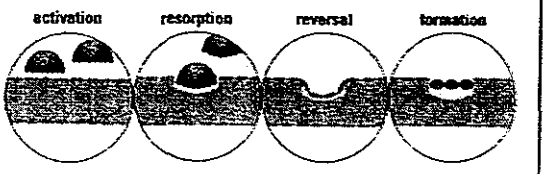
BMD (Total[L]) = 0.596 g/cm²

Region	BMD	T	Z	
Neck	0.444	3.65 52% (25.0)	1.42	74%
Troch	0.491	2.10 70% 25.0	0.41	92%
Inter	0.720	2.45 65% (35.0)	0.72	87%
TOTAL	0.596	2.83 63% (25.0)	0.87	85%
Ward's	0.263	4.03 36% (25.0)	1.08	67%

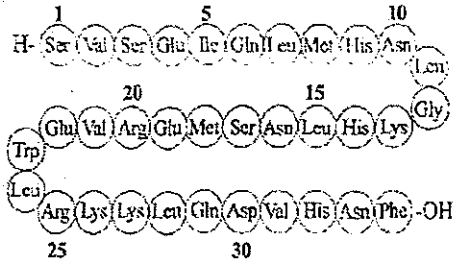
T = peak BMD matched
Z = age matched

NHA 02/01/97

EFFECTS OF ANTIRESORPTIVES



TERIPARATIDE (rDNA) RECOMBINANT HUMAN PARATHYROID HORMONE (1-34)



EFFECTS OF PARATHORMONE