

University Services Agreement
Annual Report FY 1972

AID/CSD-2956

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On June 30, 1971, the Agency for International Development granted to Johns Hopkins University the sum of \$716,521 under Grant AID/CSD-2956 to provide for the development and implementation of various population/family planning activities. Out of the total sum, \$443,461 was provided for core support for project development implementation and evaluation for a three year period from 6/30/71 to 6/29/74. The remaining \$273,060 was allocated for the implementation of four separate projects.

This report will be divided into three parts. Part I will describe the overall activities of the core staff and utilization of core expenditures, including a list of projects that have been developed during FY 1972. Part II will summarize briefly the current status of the four projects which were funded with the initial implementation of this grant, and Part III will outline a work plan and proposed budget for FY 1973.

I. Core Activities

The activation of core activities under this grant was delayed for five months until a letter was received from Dr. Ravenholt on November 29, 1971, outlining the procedures and current requirements prescribed by AID for project development. With the receipt of Dr. Ravenholt's letter, an announcement was distributed to the faculty throughout the University on December 3, 1971, informing them of the University Services Agreement and soliciting their interest in developing research projects under the terms of the grant. A copy of this announcement is attached in Appendix A.

A listing of the expenditure of the core funds during FY 1972 is given in Table 1. Total expenses amounted to \$28,283. Personnel funded included the Director, the Associate Director for Administration, and Administrative Secretary, and the Secretary to the Director. Domestic travel costs primarily involved expenses for meetings with AID in Washington or with directors of population programs in other universities. Six international trips were funded under core support as listed in Table 1. This did not represent all international travel involving project development, as Dr. Taylor, Dr. Wright and Dr. Reinke were actively involved in project development during the course of trips for other purposes to Africa, Asia, and the Middle East.

Table 2 summarizes fourteen project proposals developed and submitted to AID during FY 1972. Seven of these proposals are from the Department of Obstetrics and Gynecology, three have been approved, four were not approved as they were subsequently included as a part of a separate grant to the Department of Obstetrics and Gynecology by USAID. Three proposals have been submitted from the Department of International Health. One in Korea has been disapproved by AID, and two in Iran are awaiting decision. Three proposals were submitted by the Department of Population Dynamics. One has been disapproved, and two are pending decision. One proposal from the School for Advanced International Studies in Washington, D. C., has been approved.

The following general comments are in order. Activity on this project was not as great as it could have been in the first year because of the

five month delay in receiving guidelines for project development. The University has experienced substantial difficulty in developing projects under the guidelines developed by USAID. Part of these difficulties are due to administrative technicalities, and part are due to the realities of collaborative international research projects. The administrative difficulties primarily center around problems of obtaining clearance for travel to the various LDC's after an invitation had been extended by an agency within the country. Additional difficulties have been, and are continuing to be experienced, in getting Mission clearance and approval for the implementation of a project once it has been developed jointly with the LDC agency. While recognizing the necessity for these administrative clearances, it would appear that this could be expedited if two things were defined - first, who is responsible for obtaining the clearance? When the University has been asked to obtain the clearance from the Mission, this has been unsuccessful since requests from the University to the Mission apparently have low priority and appear at times, to have been ignored. Secondly, guidelines should be developed for clearance by the Mission, since some Missions see this responsibility only in terms of giving administrative approval, while others have taken upon themselves to examine, criticize, and even revise technical aspects of the project proposals.

The realities of developing and implementing overseas projects have made it difficult, if not impossible, to precisely follow the AID guidelines. This is in particular reference to the instruction to develop a statement of priority need by the LDC and a summary statement showing what the LDC and other organizations are doing in relation to these needs. It has been our experience that many LDC institutions have not gone into the long range planning required to assess priority needs. This may be because of the futility of such a planning exercise if funds for implementation are not forthcoming. Projects, therefore, often are developed based on a mutual consensus between the institution and Johns Hopkins relative to what needs the institution has that may be fulfilled by the capabilities available at Johns Hopkins University. Additional practical problems have been encountered relative to the time frame and funding limitations. This is particularly true in cases of projects that are expected to have a multiplier effect or a long range impact. It is assumed that some of these difficulties may be alleviated with the revision of the Agreement to include institutional development grants.

II. Report on Sub-projects

The following four sub-projects were approved and funded at the time of the initiation of the grant:

JHU 1-1 Dr. Nan Lin, 30 months, \$123,071

JHU 1-2 Dr. G. S. Jones, 6/30/71 - 5/31/72, \$49, 995

JHU 1-3 Dr. I. M. Cushner, 6/30/71 - 5/31/72, \$49,998

JHU 1-4 Dr. I. M. Cushner, 6/30/71 - 5/31/72, \$49,996

The first project, JHU 1-1, listed above as Dr. Nan Lin, was an AID approved proposal for a cross-cultural study in two countries (Korea and Sal Salvadore) of the difusion of family planning innovations. Before the project

could be started, a number of problems developed which resulted in the re-writing of several amended proposals. After first one country and then the other country was withdrawn from consideration, it was mutually agreed that the project would be dropped.

Detailed reports on the progress on projects JHU 2, 3, and 4, from the Department of Obstetrics and Gynecology, are attached in Appendix B. These reports summarize the activities as of April 28, 1972. Extensions until September 30, 1972, have been requested and granted. Final reports with a summary of the expenditures will be presented as of that date.

III. Proposed Program for FY 1973

A summary of the proposed budget for FY 1973 is given in Table 3. It will be noted that in addition to salary support for the Director and Associate Director and secretarial staff, eight faculty members are listed for 10 percent of their time. This support is to compensate them for time spent in the formulation of programs and projects, including the development and exploration of ideas leading to the preparation of proposals and projects and the evaluation of project accomplishments. Each of these faculty members serves on committees to review proposals and are consulted from time to time during the course of project development.

Dr. McCord is listed for 50 percent time. This is to cover his support for a period of three to six months while he is involved in project development in Bangladesh.

Under equipment an MTST is listed. This is required, both to handle the drafting and redrafting of project proposals and project reports, as well as the voluminous correspondence involved in project development. The calculators are for the administrative staff.

The proposed international travel lists investigators and countries where correspondence is currently active, regarding potential project development, and overseas travel anticipated for FY 1973.

Table 1.

U.S.A. Budget - Expense Summary F.Y. 1972
6/30/72

I. Personnel Funded

A. Name	Title	%Time	Amount
W. H. Mosley	Director	20	6050.00
H. Chuck	Asst Director	50	6000.00
D. Chagetas	Secretary	50	532.00
M. Pramschufer	Secretary	20	1200.00
			<u>13782.00</u>

B. Faculty Time - Project Development

R. D. Wright	Professor	3	871.00
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Total Personnel 14653.00
Fringe 2052.00

Total 16705.00

II. Supplies 54.00

III. Consultant Dr. Rice-Wray 44.00

IV. Travel - Domestic

1. Date	Name	Purpose	Place	Cost
11/30/71	W. H. Mosley	Consultation &	Washington, D.C.	
	H. Chuck	meeting with Univ..	"	
	C. E. Taylor	of Mich., Univ. of	"	
	W. Reinke	N. Carolina & AID.	"	121.52
12/7/71	H. Chuck	Consultation	"	13.60
2/7/72	Nan Lin	"	Balto/Wash.D.C.	113.29
3/9/72	W. H. Mosley	Coordination of		
		Programs with schools		
		of Public Health	Hawaii	59.41
3/16/72	H. Chuck	Consultation	Washington, D.C.	16.87
5/31/72	Nan Lin	"	Balto/Wash, D.C.	87.50
6/1/72	H. Chuck	Present proposals	Washington, D.C.	14.00
6/6/72	H. Chuck	Present proposal	"	
		(SAIS)	"	13.00
6/18-20/72	W. H. Mosley	Meeting of Directors		
		of Family Planning		
		Programs - Pop. Centers	Washington, D.C.	73.40
6/18-20/72	H. Chuck	"	"	<u>77.47</u>

Total 503.06

Continued . . .

Travel - Continued

International

<u>Date</u>	<u>Name</u>	<u>Purpose</u>	<u>Place</u>	<u>Cost</u>
3/13-20/72	L. P. Chow	Develop Project w/ Haile Sellassie University	Addis Ababa	682.72
3/18-4/1/72	D. Sich	Develop Project w/ Yonse University	Seoul, Korea	1394.70
3/19-25/72	W. H. Mosley	Develop Project w/ Dr. Rice-Wray	Mexico	378.37
3/24-4/9/72	H. Ronaghi	Consult with AID & Univ. No. Carolina & Johns Hopkins regarding proposals	Iran	1210.84
4/7/72	C. Wheelless & B. Thompson	Demonstrate Laparoscope	Kathmandu & Bangkok	2282.00
5/19-25/72	W. H. Mosley	Discuss Project collaboration w/ Pres. & Dean at A.U.B.	Beirut	148.50
	Visa Services			<u>15.25</u>
				6112.38
Indirect Costs	33.2%	Salaries and Wages		4865.00
			Total	28283.00

Table 2.
List of Project Proposals Developed During F.Y. 1972

BEST AVAILABLE COPY

Investigator	Title of Project	Place	Amount Requested	Date Submitted	AID Action
J. Jones J. Wentz	Luteolytic Action of PGF ₂ in Human Pseudopregnancy	JHU Hosp. USA	50,000.00	Jan. 17, 1972	Approved
Wheelless	International Sterilization Training	Various Countries	49,683.00	Jan. 31, 1972	Approved
J. Wentz	Efficacy of Intra-Amniotic Urea in Mid-Trimester of Pregnancy	JHU Hosp. USA	50,000.00	Jan. 31, 1972	Not Approved 7/10/72
J. Wentz	Evaluation of Abortifacient Activity of PGE ₂	JHU Hosp. USA	50,000.00	Jan. 31, 1972	Not Approved 7/10/72
J. Jones J. Wentz	Luteolytic Action of Intravaginal Prostaglandin F _{2a}	JHU Hosp. USA	50,000.00	Feb. 16, 1972	Not Approved 7/10/72
J. Wentz J. Jones	Prostaglandin F _{2a} for Menses Induction	JHU Hosp. USA	100,000.00	March 7, 1972	Not Approved 7/10/72
Wheelless	Clinical Trial of Tubal Sterilization by Hemoclips	JHU Hosp. USA	123,450.00	April 5, 1972	Approved
D. Wright	Family Health Planning Medical Students	Pahlavi Univ. Iran	150,000.00	April 27, 1972	Pending
D. Wright	Expansion of Family Planning Service in Iran National Health Corps	Pahlavi Univ. Iran	150,000.00	May 11, 1972	Pending
E. Taylor Sich	Introducing Family Health Workers in Rural Korea	Yonsei Univ. Seoul	150,000.00	May 12, 1972	Not Approved (Verbal)
P. Chow	Population Dynamics and M.C.H. in Rural Ethiopia	Haile Sellassie University Addis Ababa	150,000.00	May 18, 1972	Pending
H. Mosley	Organization, Automation & Analysis of Patient Record Files of a Family Planning Program	Asociacion Pro Salud Mexico City	150,000.00	May 18, 1972	Not Approved (Verbal)
Sirageldin W. Osborn	Survey Method in Family Planning Research and Evaluation	JHU School of Hygiene USA	98,373.00	June 6, 1972	Pending
		S A T S.	70,000.00	June 9, 1972	Approved

Table 3.

Proposed Budget F.Y. 1973

I. Personnel			
<u>Name</u>	<u>Title</u>	<u>% Time</u>	<u>Amount</u>
W. H. Mosley	Director	20	6600.00
H. Chuck	Assoc. Director	50	9500.00
R. Rider	Professor	10	2900.00
L. P. Chow	Assoc. Professor	10	2500.00
J. Kantner	Professor	10	2900.00
R. Wright	Professor	10	2400.00
I. Sirageldin	Assoc. Professor	10	2100.00
W. Reinke	Professor	10	2600.00
G. McCord	Assoc. Professor	50	15625.00
L. Green	Assoc. Professor	10	1900.00
J. Newman	Asst. Professor	10	1550.00
Release Time (FTE)	Professor	100	25000.00
M. Pramschufer	Secretary	25	1396.00
D. Chagetas	Secretary	50	2593.00
Total Personnel			79564.00
Fringe			11139.00
Total			90703.00
II. Supplies			1500.00
III. Equipment	(MTST)	\$1800.00	
	Calculator(s)	700.00	2500.00
IV. Proposed Travel - Project Development & Administration			
Domestic -	750.00		750.00
International -			
	W. H. Mosley	Indonesia, Thailand	2500.00
		Bangladesh	1350.00
		Mexico	400.00
		Lebanon	1000.00
	L. P. Chow	Indonesia, Ethiopia	1400.00
	I. Sirageldin	Egypt, Tonga	1600.00
	R. Rider	Korea	1400.00
	C. E. Taylor	Bangladesh	1350.00
	G. McCord	Bangladesh (allowance)	3000.00
	R. Wright	Iran	1200.00
	C. Wheelless	Panama, Costa Rica	500.00
	L. Green	Colombia	600.00
	W. Reinke	Kenya	1400.00
	H. Chuck	Iran, Afghanistan, Ceylon	1400.00
	T. Baker	Manila, Indonesia	2000.00
			21100.00
V. Program Support			15000.00
VI. Consultants			4000.00
VII. Indirect Costs	41.12 Salaries & Wages		32717.00

THE JOHNS HOPKINS UNIVERSITY

SCHOOL OF HYGIENE AND PUBLIC HEALTH

DEPARTMENT OF POPULATION DYNAMICS

615 North Wolfe Street • Baltimore, Maryland 21205

December 3, 1971

Memorandum to: Department Chairmen
Members of the Population Advisory Committee

From : W. Henry Mosley, M.D.

Subject : Support for Development of Project Proposals under the
University Services Agreement

We have just received notification from USAID regarding the procedures for submission of project proposals under the University Services Agreement. Specifically, this notification permits us to utilize the project development monies provided for the specific purpose of developing projects that meet the objective of the University Services Agreement.

To review briefly the terms of this Agreement, AID has granted Johns Hopkins University the sum of \$443,461 over a three year period to develop and implement population/family planning activities. The purpose of the grant as stated by the Agreement is:

"The objective of this grant is to assist the less developed countries to obtain answers to problems which impede the more effective and efficient operation of their population/family planning program. This grant provides funds for grantee core staff to develop and manage a variety of small scale, short duration experimental test projects or surveys designed to make a positive, tangible and direct impact in various categories of the field of population and family planning, including:

- a) Technics of fertility regulation
- b) Demographic data and measurement technics
- c) Analysis of the interrelations of economic, social, and demographic variables
- d) Evaluation and methodology and its application
- e) Improvement of family planning services delivery systems
- f) Improvement of information/education programs
- g) Strengthening of institutional capabilities in less developed countries
- h) Training and employee development."

The core support provided in this grant is specifically for development of project proposals in the areas listed above. The projects are expected to be of limited size and duration, innovative and experimental. They will be expected to include a majority located in less developed countries and expected to reflect host country priorities and to be developed jointly with host country personnel and institutions. The individual projects developed utilizing the core support are expected to be small, not to exceed \$50,000 per year, and short range, not to exceed three years.

The specific details regarding the utilization of the core support to develop projects are given in the letter of November 29 from Dr. Ravenholt

(attachment 1) which includes a format for the proposals.

In essence, there is now money available for investigators who wish to travel to less developed countries (LDC's) in order to develop collaborative research projects with government, public, or private institutions within these countries. The core support not only pays for travel and per diem expenses but also will pay the cost of salary for staff while they are actively involved in project development.

AID has indicated that as much as \$750,000 may be available to support specific projects developed under this Agreement during this fiscal year. Thus, this memo is a request to all investigators interested in developing research projects in the area of population and family planning, relevant to the problems of less developed countries, to contact me as soon as possible.

"Abortifacient Activity of Prostaglandin F_{2a} in the First Trimester"
"Abortifacient Activity of Prostaglandin F_{2a} in the Second Trimester"
AID/csd-2956 - Dr. Anne Colston Wentz

The objectives of these two projects were to investigate and evaluate prostaglandin F_{2a} under controlled circumstances as an abortifacient agent. The original project was written to investigate prostaglandin as an intravenously administered abortifacient, but permission was obtained from the Agency for International Development to extend these studies to other routes of administration as these became available. Thus, controlled and comparative data were to be obtained on three routes of administration, to ascertain that most applicable for use both as an abortifacient technique in the United States, and in lesser developed countries.

The original project was to evaluate the efficacy and tolerance of prostaglandin utilization in approximately 100 to 120 patients. The results obtained from the administration of prostaglandin to these patients were to be compared to the results obtained from saline injection, and to attempt a comparative study to give valid data on the relative efficacy, morbidity, and tolerance of the two methods.

Three modes of administration of prostaglandin F_{2a} have been evaluated by one physician, and cared for by the same staff of nurses and coordinator. Thus, valid comparative data have been obtained.

To date, over 30 patients have received prostaglandin intravenously, 21 intravaginally, and over 60 by the intra-amniotic route of administration.

The intravenous route has been associated with a 70% incidence of abortion, and has proved quite acceptable. Side effects do occur, predominantly vomiting, diarrhea and fever, but these are self-limited, and are not of particular concern either to physician or patients. The average time from drug administration to abortion has been approximately 22 hours, and patients have aborted completely if greater than 16 weeks gestation. The intravenous route appears to have fair reliability and reproducibility, and is indicated in certain situations. The intravenous route, for instance, offers a solution for the patient with a failed saline injection, or a failed prostaglandin termination by another method. In addition, it has been demonstrated that fetal tissue obtained from prostaglandin abortion is not damaged by the prostaglandin, as it is with saline injection, and is therefore suitable for tissue culture and karyotype techniques. Thus, the intravenous route of prostaglandin administration is indicated in patients in whom there is a need for study of products of conception.

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The intravaginal route of administration has been tested in 21 patients, in a preliminary evaluation of prostaglandin tablets. These tablets contain 50 mg. of prostaglandin F_{2a}, and have been administered every one to two hours. The success rate has been 95%, but side effects have been a limiting factor in this route of administration. Nausea, vomiting, diarrhea and fever have occurred in well over 50% of patients, and have increased the utilization of both physician and nurse time. In contrast, the patients did feel that the method was not only efficient, but acceptable, and they tended to minimize the side effects experienced when interviewed at the four week clinic checkup. The intravaginal route of administration indicates that self-administration by this route is a possibility, and that there is a necessity for continued research into new delivery systems, and into the utilization of different prostaglandin analogues. The route is certainly more convenient and less uncomfortable than a protracted intravenous infusion, and is adaptable to self-administration.

The intra-amniotic route of administration appears to be the most favorable for immediate utilization. Although the recommended dosage has not been completely settled, it would now appear that convenient as well as efficacious regimens have been developed. The intra-amniotic route of administration requires the introduction of a polyethylene catheter in certain selected patients, specifically those greater than 16 weeks gestation, and those who are nulliparous, but a supplementary dose of drug at approximately eight hours after the initial appears to effect abortion in most patients. Therefore, an initial dose, and a supplementary dose at six to eight hours appears to be sufficient in well over 90% of patients, and efficacy rates have approached 95%. We have aborted 60 patients using this method, with varying dosage regimens, and have found that method to be associated with a low incidence of side effects, a high degree of efficacy, and a marked degree of patient acceptance and tolerance. It would appear that this method will shortly be applicable to widespread use, and Phase III clinical trials will be starting shortly.

At the present time, a paper on the intra-amniotic utilization of prostaglandins is in press, one on the intravaginal route is submitted for publication, and we are preparing a paper on the hormonal values in patients aborted using the intravenous route. We have performed studies utilizing the Rhesus monkey to evaluate the effect of hypertonic saline injected into the myometrium, in comparison with intramyometrial administration of prostaglandin. Prostaglandin F_{2a} causes no gross or histologic change, in the muscle, in contrast to hypertonic saline, which produces extensive necrosis. These findings have been accepted for publication.

The necessity for evaluation of prostaglandin E₂ as an abortifacient is obvious. This prostaglandin appears to have certain advantages over prostaglandin F_{2a}, specifically a lower dose, increased duration of action, and a possible cervical dilatation action. It has been reported to be associated with a decreased incidence of side effects. Continuing such investigations utilizing prostaglandin analogues is also a necessity, as these analogues, or different formulations of currently-used prostaglandins, may offer more convenient delivery systems, with increased duration of action and decreased side effects. It is apparent that prostaglandins offer extensive advantages over currently used methods, without many of the hazards of currently accepted techniques. The primary advantage of prostaglandins is in their almost immediate induction of labor, the decreased latent time to abortion, and therefore a decreased utilization of hospital beds and of professional and nurse time. The utilization of prostaglandin also offers an approach to the patient between 12 and 16 weeks gestation, for whom no method of pregnancy termination is currently available.

AGENCY FOR INTERNATIONAL DEVELOPMENT

"Clinical Efficacy of Prostaglandin F_{2a} as a Luteolytic Agent"
AID/csd-2956 - Dr. Georgeanna Seegar Jones

The aim of the study was to establish whether intravenously administered prostaglandin F_{2a} has a luteolytic effect in the nonpregnant human. The long-term objective was to demonstrate the safety and non-toxicity of the agent, and to aid in its development as an ideal contraceptive agent.

The study was designed to investigate the effect of an intravenous prostaglandin infusion on selected days of the luteal phase in 20 human, non-pregnant volunteers. The hypothesis was that prostaglandin administration would induce menses in those patients in the luteal phase, but not those in the peri-ovulatory period.

22 human, nonpregnant volunteers have completed control and experimental cycles in this project. Control cycles included the establishment of each volunteer's individual parameters of normality, including basal body temperature chart, urinary pregnanediols, and additional blood assays for progesterone, estradiol, and estrone. Two women received infusions at mid-cycle, presumably prior to ovulation. Two patients were infused on the day of onset of menses. One volunteer received a sham infusion. The remaining volunteers were infused on selected days of the luteal phase, specifically Days 0 + 5, 0 + 8, and 0 + 11. All volunteers continued basal body temperature charts through the next cycle, in order to ascertain if any effect on ovulation occurred.

All infusions have been completed, and the data are now being tabulated and correlated. Still to be completed are the blood assays of progesterone, LH, estradiol and estrone, which were not to be included in the original protocol, but appeared to be necessary for proper completion of the study.

In general, there was no significant differences between the control cycle and the infusion cycle. If any trends could be imagined, it would be that those infusions given between Days 21 and 23 seemed to be associated with a one-day shortening of the luteal span by basal body temperature, with no change in serum progesterone and urinary pregnanediol values. When infusions were given between Days 24 and 27, there appeared to be no change in the luteal span, and a slight decrease in the serum progesterone during the experimental cycle. None of these changes were of a sufficient degree to be significant, nor did the three parameters examined vary simultaneously. It is expected that when the complete data are evaluated, that there will be demonstrated no significant change in blood hormonal levels between experimental and control cycles.

Side effects were carefully monitored during prostaglandin infusion and the patients followed for a subsequent cycle. Eight of 22 women vomited, and 12 women experienced watery diarrhea. The diarrhea was readily controlled by the use of Lomotil. Fever of 101.6 was observed once, and, while four additional patients showed temperatures of over 100°F., all fevers subsided rapidly following discontinuation of the infusion. 17 of 22 patients showed a local tissue

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Prostaglandin F_{2a} as a luteolytic agent

reaction at the site of the needle which was transient. Chills occurred three times, twice in the absence of fever. Respiratory symptoms, consisting of excessive phlegm, and the necessity to clear the throat, occurred in 12 women. These symptoms were so mild, they were frequently unnoticed by the participants and recorded only by the research nurse. Five women reported excessive thirst, and a tabulation of urine volumes during the infusion illustrated that a diuresis was stimulated during the time of infusion.

18 women had lower abdominal cramps characteristic of menstrual cramps, and 14 had associated vaginal bleeding during the infusion. Five women experienced headaches, and 14 had changes in sensorium. Depression and lethargy appeared to be the most prevalent changes with an inability to maintain an interest in reading, knitting or conversation. Patients felt that questioning was troublesome, whereas prior to the infusion, conversation and questions had been welcomed.

Tentative conclusions of this project are that at the dosage levels utilized, prostaglandin F_{2a} has no effect on the functioning corpus luteum. Prostaglandin F_{2a}, in contrast, does induce uterine contractions, and may induce menstrual-like bleeding, probably because of an oxytocic effect on the uterus.

Data obtained from this project will be presented at the American Gynecological Society meeting in May. A paper is in preparation.

Several studies have been performed in conjunction with the above project. The evaluation of the effect of prostaglandin in secretion and release of cortisol has been performed, and these data will be presented at the Endocrine Society Meeting in June. A paper is in preparation. In addition, studies evaluating prostaglandin blood levels in patients with dysmenorrhea have also been performed.

The necessary direction of continued research will be in investigation of prostaglandin F_{2a} as a contraceptive agent. Even if there is no luteolytic effect induced by prostaglandin, still the administration of prostaglandin in the early gestation might well interrupt the implantation because of the oxytocic effect of prostaglandin. This activity must be investigated, as prostaglandin administration shortly after the first missed menses might well result in termination of pregnancy.