

LOW BIRTH WEIGHT RESEARCH COMPONENT OF IMCN PROJECT

CONSULTANCY REPORT
FOR USAID/INDIA

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SEPTEMBER 1982

I. ANALYSIS

A. Background

In April 1981 Dr. Julia A. Walsh, Consultant, undertook an assessment of the previous and current work and the prospects for further research in India on the causes of prematurity, low birth weight, and infant mortality. In addition to performing a careful review of published materials, she visited a number of centers where research in these areas was underway and discussed current activity and plans with active investigators. She summarized her review and impressions in a Consultant Report for USAID India (April 5-26, 1981) hereafter referred to as the "Walsh Report".

The Walsh report focussed on Indian investigations of those factors that had been identified as possible determinants of low birth weight (LBW). The investigations described in it appeared to support a role for many of the factors also implicated in studies in the developed world (maternal height and weight, age, parity, toxemia, hemorrhage, and prior LBW), as well as suggesting some relatively more important in the under-developed world (extremely low maternal weight, iron and folate deficiency, anemia, and other nutritional influences as well as strenuous physical exertion). However, almost no work had addressed the issue of genitourinary (GU) infections, a set of factors long thought to be determinants of LBW and/or prematurity in the US and elsewhere in the West. Nor had adequate attention been paid to the possible influence of other important infections such as malaria and tuberculosis. Unfortunately, even in the studies where very careful effort was made to link a given factor to adverse outcome, rarely was any attempt made to control for confounding or to examine possible

interaction of multiple factors. Indeed, only infrequently did the published reports reflect concern with these phenomena.

It was clear from the Walsh report that there was a need to extend the inquiry on adverse pregnancy outcome to include questions on GU infections and others in a more comprehensive approach. It was equally clear that if any relationship could be confidently established, there might be opportunity for substantial health impact through treatment of infection. So Dr. Walsh proposed an analytic investigation to be followed by a clinical trial of chemoprophylaxis of whatever infection was shown to be involved. USAID approved the recommendation to support investigation of the role of infection as part of their existing proposed Integrated Maternal and Child Nutrition (IMCN) project, through the Indian Council of Medical Research (ICMR), provided such a study proved feasible. ICMR welcomed the idea of USAID assistance for a longitudinal study of the effect of maternal GU infections on fetal outcome in both well and malnourished women. Accordingly, USAID requested a consultation by Drs. E. Russell Alexander, Professor of Pediatrics, University of Arizona at Tucson, and Richard A. Kaslow, Chief, Epidemiology and Biometry Section, NIAID, NIH, to develop plans for such an investigation trial of chemoprophylaxis of whatever infections were shown to be involved.

B. Recent Activities and Advances

One of the most significant activities since Dr. Walsh's visit has been the initiation of an ICMR-sponsored national collaborative population based study of reproductive events based on periodic followup of all reproductively active women in each of seven cohorts of about 20,000 persons each to identify high risk cases. The main interest among maternal factors is on the role of

nutrition/anemia; no infection data will be collected. The importance of the effort is that a rather rigorous approach to design, execution, and analysis should assure high quality and comparability and thereby, hopefully, provide an accurate picture of adverse pregnancy outcome in both urban and rural settings. Additionally, all children will be followed for 1 year after birth, so relatively detailed information on growth and development, major illnesses and causes of death should become available. A midpoint review of this ambitious project was provided for us by Dr. Santosh Bhargava, who is the principal investigator and the overall coordinator, at a meeting summarized below.

Other observation as well as intervention studies on LBW, mostly on nutritional effects, have been conducted in certain of the centers visited during the consultation and elsewhere. For example, Dr. Vijay Bhargava, the neonatologist at the Institute of Medical Sciences, BHU, Varanasi, continues his interesting work on the role of anemia and its interaction with other maternal and nutritional characteristics in intrauterine growth retardation (IUGR). His and others work emphasizes the importance of distinguishing between IUGR and premature labor as causes of LBW. This is noteworthy simply because LBW in the US and other western countries where infection has been implicated is generally more closely associated with prematurity than may be the case in India so the relative importance of the causes, including GU infection, may well differ geographically.

There have also been a few pertinent developments in the research on the maternal infection-pregnancy outcome issue in the US. First, further observations on prevalence of previously suspected organisms, without careful control of other important factors in the relationship have, not

surprisingly, continued to yield inconsistent results from one study to another. Second, better microbiologic description of the genital tract flora in and outside of pregnancy leaves open the possibility that pathogenic agents not previously considered in this context (e.g. Gardnerella vaginalis or anaerobic organisms) could play a role. Third, very preliminary data from microbiologic studies in San Diego suggest that different bacteria produce varying amounts of phospholipase A, an enzyme involved in metabolism of a precursor for prostaglandins, a potent stimulant of uterine contraction. Apropos of the earlier question raised about prematurity vs. low birth weight, such a mechanism might be more consistent with a relationship to prematurity than to IUGR. Lastly, there is early evidence that an immune response demonstrating recent primary infection with mycoplasma or chlamydia may correlate better with LBW than mere presence or absence of the organisms. In short, our understanding of the role of infection is still evolving. The prospects are still uncertain, even under the best circumstances of scientific research, for early resolution of whether and which infections are major causes of LBW. For India it may be even harder to answer for reasons that will become clearer in the summaries of our visits to potential research centers. Briefly, in India experience with design, execution, and analysis of large scale population studies is meager, and the physical obstacles (See below) are considerable.

C. Meetings and Visits to Centers/Individuals (see Appendix A for names of individuals visited)

ICMR - Alexander and Kaslow

At a meeting prearranged at ICMR on September 6-7, 1982 we met with professionals from ICMR and from two institutions that had expressed interest

in the project by submitting preliminary proposals outlining their approach. The description of their institutions and capacities are included in the section on the site visits. What became clear in the earliest discussions and descriptions of the ongoing work in maternal and child health was that each center had both strengths and weaknesses unlikely to be overcome solely by financial support for the project. Some of the problems that might confront these two institutions (and almost any other where field studies might be undertaken) were highlighted very well by Dr. Santosh Bhargava, the principal investigator in the ICMR-sponsored centers prospective pregnancy outcome study mentioned earlier. In part, they include problems in:

1. Design -

a. Inadequate biostatistical support

b. Unfavorable population characteristics

- Underestimate of the number of pregnancies available for enrollment.
- About 40% enrolled in the first and 35% more in the second trimester, on the average.
- Loss to follow up because some rural women deliver in urban health care facilities, and because of migration within urban slums.

2. Subject cooperation

a. Internal examination)

b. Clean-voided specimen)

c. Venipuncture)

} Difficult outside the hospital setting.

3. Logistics/support

a. High turnover of professional staff.

b. Inefficiency or inadequate ground transportation.

c. Portable scales unavailable for maternal weight.

King Edward Memorial Hospital, Pune - Alexander and Kaslow

The enthusiasm about the problem and the proposed research was as high here as at any of the institutions. Moreover, the research orientation and commitment are quite strong here as well. Experience in field and clinical investigation on the part of the professionals who would be involved is another advantage. Although their five-year relationship with the villages in the VADU project certainly favors the accomplishment of the most difficult field components of the study, even there the formidable obstacles common to all the institutions will challenge their capabilities. The major weakness of the institution, they are frank to admit, is the microbiology laboratory. Minimal equipment and absent research expertise makes them dependent for training and technology transfer on another institution. Proximity to the National Virological Institute, with which working relationships are already established, may offset this deficiency.

Jawaharlal Institute of Post-Graduate Medical Education and Research (JIPMER)

Pondicherry - Alexander and Kaslow

Here, too, the interest in the proposed research is quite high. The clinical competence and dedication to service are great. In fact, it appeared to us that the taxing demands for service and teaching made on the clinical investigators who are likely to be crucial to the success of the project might occasionally compete for time with the tasks of the study. Heavy service demands are common in India, but they are more worrisome where past experience and involvement in field investigation so critical to these studies seems thin. The strength of JIPMER for this project lies in its rather well equipped and broad-based laboratory which includes basic virology capabilities.

The staff are young and eager and would probably acquire the technical skills quickly. There is also some microbiologic research underway.

Christian Medical College, Vellore

Alexander and Kaslow

The purpose of the visit to Vellore was somewhat different from the purpose of the other visits. Dr. Jacob John's laboratory had been proposed as a possible reference laboratory for the chlamydia and mycoplasma technologies needed for the project, which are not currently available, so the emphasis during the visit was an evaluation of that laboratory's capabilities and needs. Dr. John's creative leadership and experience coupled with the longstanding capabilities of introducing new techniques into India make his laboratory attractive as an Indian reference center. Although the laboratory facility has the basic necessities, some of the equipment is outdated and/or irreparable. Also, the need for additional laboratory space might require some remodeling effort. None of these needs is likely to entail any major capital expenditures.

From discussions with people in the other sections of the microbiology laboratory, it appears that they, too, would be capable of serving the reference function for other microbiologic studies. We did not sense or elicit any special commitment to this function.

As for the other elements of a clinical field investigation, the field and research activities of the hospital and university are fairly well developed, but it was not clear how easy it would be to graft a laboratory based epidemiologic research project onto the existing community outreach program.

We did not detect as high a level of interest or commitment as elsewhere in the population aspects of the project on infection and LBW among the key professionals in the pertinent disciplines other than microbiology.

Institute of Medical Science
Banaras Hindu University, Varanasi - Kaslow

The IMS in Varanasi is one of the centers participating in the 7-center ICMR project on pregnancy outcome. As such it has developed the framework for community/rural - based field study although the absence of the principal investigator left uncertain the degree of interest there would be. The field research work with laboratory components suggests an adequate experience in this key aspect. Similarly, the microbiology laboratory unit contains the elements - equipment, staff, interest - needed for the study. However, the principal professionals at the Institute in Varanasi are deeply involved in their high quality research on anemia and nutritional aspects of perinatal medicine. Since no department seemed generously staffed, one has the sense that a major additional research effort might be a real distraction and thus a disservice both to the proposed research and to their ongoing work.

Christian Medical College
Ludhiana - Kaslow

There has been a strong community-based health project at Ludhiana for several years under the vigorous direction of the Department of Preventive and Social Medicine, and it would provide a firm foundation on which to build

the field component of the maternal infection study. The central facility (Brown Memorial Hospital) and the peripheral community hospital visited are both indicative that resources at CMC Ludhiana, are more plentiful than at many other institutions. The villages themselves are also economically more advanced. A solid research orientation is matched by a healthy atmosphere of discipline. However, again, although there are very able professionals in the clinical and other departments, concern arises about the participation of those who already have heavy time commitments to other activities - whether clinical, research, or teaching. In microbiology in particular the very active and capable director of the laboratory spends half of the year in India and the other half in England. The laboratory is admittedly short-staffed for now, although at least one new professional is scheduled to join soon. If proper professional staff commitments to this collaborative type of research could be affirmed, the center would be quite suitable for the work.

Post Graduate Institute, Chandigarh - Kaslow

The modern, sophisticated facility in Chandigarh seemed to be the most academically-oriented institution visited. The clinical staff in the critical departments are actively involved in research and can probably devote a greater portion of time to it because of the seemingly lesser service obligations. They seemed fairly receptive to the proposed research as outlined, remaining appropriately skeptical about any study that would not examine all the major variables. Their microbiology laboratories are extremely well organized and equipped compared to the other laboratories we saw. Indeed, in some ways these laboratories rival the CMC facilities in Vellore as possible reference laboratories. They are busy but relatively well staffed. And again

research obviously occupies a substantial portion of their time. For example, they are doing mycoplasma cultures now and are planning chlamydia work. The field and community activities are also well established due to their involvement in the ICMR 7-center study and in separate, longer-lived projects (e.g. on intervention for high risk mothers and infants). Although activities of the community program were not personally observed, it did not appear as if the field activities have quite the generous support that the hospital-based research has. But the uncertain capabilities here are not so much greater than at the other centers as to offset the obvious advantages.

II. PROJECT DESCRIPTION

A. Chronology

Due to the major uncertainties involved in the proposed research and obstacles to be overcome, the project should be phased so that successful completion of one phase would be a prerequisite for proceeding to the next. We recommend the following approach and time table:

- Phase I (Preparatory) - 11/82 - 9/83.

During this period the laboratory training and preparations and the agreements and other documents necessary for the prevalence of infection study will be completed (Appendix B)

- Phase II (Prevalence Study) 10/83 - 12/84

Women presenting for prenatal care in the hospital and if possible in a community setting will have pertinent cultures and serology performed in order to determine what infections may be of significance during pregnancy. Nutrition and other factors as well as outcome (birthweight) will be

examined but not with any test of hypotheses in mind (Appendix B)

- Panel Meeting to assess progress and prospects for next phases 1/85-3/85

- Phase III-IV (outcome and intervention studies) 3/85-5/89

These phases would address the relationship between infection, malnutrition, and LBW by a combination of hypothesis testing of association and intervention. The nature of these studies will depend heavily on new knowledge acquired in the previous phases and in studies done elsewhere. Interventions might include Chemoprophylaxis or treatment of infections and provision of nutritional supplements.

PHASE I

TIME

- | | | |
|----|--|------------|
| 1. | Submission of proposals to selected centers for response and expression of interest. | 11/82 |
| 2. | Selection of reference laboratory(ies) and study centers. | 12/82 |
| 3. | Identification/recruitment of laboratory and other research staff. | 12/82-1/83 |
| 4. | Identification and training of 1 technical person from each reference laboratory. | 3/83-7/83 |

Training would be carried on at the Channing Laboratory Harvard Medical School, in Boston and the Department of Pediatrics/ Microbiology at the University of Arizona, Tuscon.

- | | | |
|----|--|------------|
| 5. | Acquisition of supplementary equipment in reference and study center laboratories. | 4/83-12/83 |
|----|--|------------|

Assembly of study center and reference laboratory investigators, and US collaborators to review progress and write protocol. This would most efficiently be accomplished by a 7-10 day meeting of

a panel consisting of Walsh, Alexander, Kaslow, and Rush; 2 principal investigators from the study centers, the senior investigator from the reference laboratory, and possibly an ICMR representative.

6. Transfer of technology from US to Indian reference laboratory. 7-9/83
7. Brief visit by US collaborator(s) to assess technology transfer. 9/83
8. Trial exchange of standardization specimens between India and U.S. 9/83
9. Training of study center laboratory personnel in India. 9-12/83
10. Training of study center staff and pilot study in interview and examination techniques (e.g. questionnaire administration, clean voided urine specimen collection, speculum examination, and blood collection in hospital setting. 7/83-9/83

PHASE II

1. Hospital prevalence of infection and malnutrition study. 10/83-1/84
2. Data analysis. 2/84-5/84
3. Attempts to replicate interview/exam technique in community/rural setting; establishment of "cold chain" materials and methods, transportation, etc. 2/84-4/84
4. Community/rural prevalence of infection and malnutrition study. 5/84-8/84
5. Data analysis 9/84-12/84

Panel Meeting - Evaluation of Progress and Protocol Design for

Phase III-IV - Outcome/intervention studies

1/85-3/85

PHASE III

Longitudinal infection, malnutrition and pregnancy

Outcome study - approximately

1600 subjects.

Panel Meeting to Assess Progress and Decide on Intervention Trials

3/85-5/89

PHASE IV

Intervention trial-approximately

3,000 subjects.

B. Budget (in \$ 000s)

<u>Phase I & II</u>	\$	\$
*1. Initial equipment and remodeling - 1 reference laboratory and 2 study centers.	15	45
	ea	
2. Personnel training costs		
1 mid-level professional 4 mo @ \$8000/yr. in US; 2 junior microbiologist - Ph. D. types	2	3 4
3. Meeting of Panel		17
4. Lab technical @ ea/yr. 3 centers, 16 mo. Research Coordinator 1/2 time	6	24
5. Research assistants @ 6000 ea/yr. - 3 centers, 16 mo.		24
6. Reimbursement of US training/standardization laboratory expense; shipping of antigens		2
7. Equipment/supplies		
\$230 ea x 300 - 2 hospitals		70
230 ea x 300 - 2 communities		70
8. Shipping specimens and data processing		3
9. Miscellaneous		<u>2</u>
		\$225
 <u>Phase III</u>		
1. Personnel (see Phase I #4,5) \$26,000/yr, 2 yr		75
2. Asst. at 3000/yr. + 5% x 2 yr. @ each center		12
3. Equipment/supplies \$250 ea, 1600 subjects		<u>360</u>
		447

<u>Phase IV</u>		\$
1. Personnel (see Phase III, # 1) +5%		80
2. Assistant (see Phase III, # 2 + 5%)		13
3. Equipment/supplies \$60ce x 3000		180
4. Antimicrobial therapy \$20 x 600 subjects		12
Travel-meetings		<u>55</u>
		340
	TOTAL	\$ 1,012

C. Recommendations for selection of Institutions

1. Reference Laboratory

Either CMC, Vellore, or PGI, Chandigarh is probably capable of serving as a reference laboratory for this project. For practical purposes, PGI may need less preparation and equipment, their staff has slightly more depth, and transportation access is better. Alternatively, both could serve for the respective study centers depending on which are chosen.

2. Study Centers

While it is possible that the project would be performed successfully by any of the institutions visited, we feel the chance of success is, in descending order, as follows:

- | | | |
|-------------|---|---|
| Chandigarh | · | 1 |
| Pune | | 2 |
| Vellore | } | 3 |
| Ludhiana | } | |
| Varanasi | } | 4 |
| Pondicherry | } | |

We therefore recommend that if 2 centers are chosen, they be Chandigarh and Pune.

3. US Collaborators

Assuming that the acceptable arrangement for collaborative research can be established. We believe that such collaboration would be mutually rewarding for all the institutions involved and would improve the prospects for achieving the project goals. The nature of the collaboration in this case depends heavily on interpersonal relationships, and sympathy for the potential difficulties, which exist now with the individuals recommended

for the US consultant panel (see A. Phase I.5). Because there have been 4 consultants on the master project at different times, we discourage potentially confusing involvement of additional US scientists, unless skills outside of those available from previous consultants are needed.

Collaboration would consist of training of Indian researchers at U.S. universities, panel meetings of U.S. and Indian investigators to review project progress at key stages, individual consultations of U.S. collaborators is necessary, and possible exchange of infection specimens and data for cross checking and further processing.

D. Obstacles

At each step in the sequence of the research plan certain obstacles threaten the possibility or validity. Some obstacles would be common to such a complex field study anywhere; a few are peculiar to the circumstances in India.

1. Population Selection

In the ICMR 7-center study on the average about 40% of women present for prenatal care in the first trimester and about 35% more present in the second trimester. Only a small proportion, although not necessarily biased one, would be available early for recruitment, and only about 75-80% would be eligible at all.

2. Training

It is not entirely clear how easily or fast the appropriate field workers can be trained to perform interviews or to get proper samples through a speculum or by Venipuncture/skin prick in women outside the hospital setting.

3. Response rates

Movement of village women from within a study area to a place outside during the latter part of pregnancy e.g. to the parents' home (15-70%) could reduce the followup completeness although it may not significantly bias the results. That inefficiency will be less of a problem in the urban areas. Perhaps the most serious response obstacle is likely to be the refusal of women outside the hospital to permit a speculum examination or blood sampling, especially on more than one occasion. The problems sound more or less uniform in all centers, and overcoming them will require a rather intensive effort. Similarly, there may be important questions of medical history that the women cannot answer accurately (e.g. prepregnancy weight, previous pregnancy (LBW) outcome) or will not answer accurately (e.g. on sexual practices).

4. Specimen preservation

At several points along the chain of preservation of biologic specimens, losses could occur. Local ground transportation can be uncertain, particularly in wet season. A reliable supply of dry ice is not always available. Multiple transfers between airplanes and ground vehicles may account for losses in submissions to the reference laboratory

5. Evaluation/quality control

In a moderately complex field investigation, there will be difficulties in sharing specimens and data with collaborators outside India. If they cannot be obviated from the beginning, these difficulties may compromise the care and thoroughness with which the results are analyzed.

Whether these and other minor obstacles can be circumvented or eliminated without seriously compromising the value of the research will have to be carefully assessed from the earliest stages of the project.

APPENDIX A

Centers and Individuals Visited

Post-graduate Institute of
Medical Education and Research
Chandigarh, Punjab

1. Dr. (Mrs.) Kamla Dhall,
Department of Obstetrics and Gynaecology
2. Dr. Serla Gopalan,
Department of Obstetrics and Gynecology
3. Dr. B.N.S. Walia,
Department of Pediatrics
4. Dr. A. Narang,
Department of Community
5. Dr. Vijay Kumar,
Department of Community
6. Dr. K.C. Agarwal,
Department of Microbiology
7. Dr. R. C. Mahajan,
Department of Microbiology
8. Dr. N.K. Ganguli,
Department of Microbiology
9. Dr. A. Ayyagari,
Department of Microbiology
10. Dr. S. P. Dhir
11. Dr. G.I. Dhall, Dept. of Obstetrics & Gynaecology

Christian Medical College, Ludhiana, Punjab

1. Dr. Betty Cowan, Department of Preventive and Social Medicine
2. Dr. H.N.S. Grewal, Department of Preventive and Social Medicine
3. Dr. Helen Simon, Department of Obstetrics and Gynecology
4. Dr. Paul, Department of Pediatrics
5. Dr. Betty Hobbs, Department of Microbiology

Jawaharlal Institute of Post-graduate
Medical Education and Research
Pondicherry, Tamil Nadu

1. Dr. Rajaram, Department of Obstetrics and Gynecology
2. Dr. Puri, Department of Pediatrics
3. Dr. R. S. Rao, Department of Microbiology

King Edward Memorial Hospital
Pune, Maharashtra

1. Dr. (Mrs.) Banoo Coyaji, Director
2. Dr. Anand Pandit, Department of Pediatrics
3. Dr. Kurus Coyaji, Department of Obstetrics & Gynecology,
Department of Preventive Social Medicine
4. Dr. Kulkarni, Family Planning Officer, Asst. Secretary Health
5. Dr. Rao, District Health Officer

Institute of Medical Sciences
Banaras Hindu University
Varanasi, Uttar Pradesh

1. Dr. K.N. Agarwal, Department of Pediatrics
2. Dr. Vijay Bhargava, Department of Pediatrics
3. Dr. A.M. Deipathi, Department of Pediatrics
4. Dr. P.D. Sharma, Department of Obstetrics and Gynecology
5. Dr. (Mrs.) Agarwal, Department of Preventive and Social Medicine
6. Dr. P.C. Sen, Department of Microbiology

Christian Medical College
Vellore, Tamil Nadu

1. Dr. Jacob John, Department of Microbiology
2. Dr. Marc Steinhoff, Department of Microbiology
3. Dr. Jacob Abraham, Department of Preventive and Social Medicine
4. Dr. P.S. Sundar Rao, Biostatistician

ICMR

1. Dr. Badri Saxena, Senior Deputy Director General
2. Dr. Usha Malhotra
3. Dr. Saxena, Statistician

FORD FOUNDATION

1. Dr. Lincoln Chen
2. Dr. Meera Chatterjee
3. Dr. Usha Shah

OTHERS

1. Dr. Santosh Bhargava, Department of Obstetrics & Gynecology,
Safdarjang Hospital, Delhi
2. Dr. Verma, Department of Dermatology & Venereology, Baroda
Consultant to WHO on Sexually Transmitted Diseases

APPENDIX B

Below is a list, although not necessarily exhaustive, of the kinds of exposure (risk) factors and outcome variables that would be sought under the best of circumstances.

Demographic/Social

Age, sex, caste/religion, income, work habits, dwelling type, cigarette and betel use.

Medical History

Last Menstrual Period (LMP)

pregnancies, # children

Past LBW children, recognized complications, perinatal mortality

Symptoms in past pregnancies - genitourinary, fever

Current Pregnancy -

Fever, Productive cough, skin lesions

Sexual activity - habits by week partners

Examination

- Temperature

- Smear for malaria where history of fever/chills or current fever

- Hemoglobin, Hematocrit, weight, height, fundal height,

Abdominal girth, and other nutritional measures

- Vaginal fluid culture for:

Mycoplasma, ureaplasma

Group B streptococcus

Listeria

Gardnerella vaginalis

Anaerobic organisms

Cervical culture - Chlamydia, gonococcus,

Urine culture -

Quantification and

Identification of usual organisms

esp. E.coli, Klebsiella, Enterobacter, proteus, pseudomonas, enterococcus

Serum specimens (2-3cc) - paired

Syphilis - STS

Mycoplasma Ab, other

Chlamydia - microimmuno fluorescence

Toxoplasmosis

Malaria

Pregnancy Outcome

Spontaneous abortion

Stillbirth

Premature rupture of membranes

Premature delivery

Gestational age

Birth weight

Perinatal, neonatal, and post neonatal mortality

APPENDIX C

Comments on Centers

Pondicherry - They are young, inexperienced in clinical and field investigation; don't appear to have tightly organized field team in village. Too busy with clinical demands, staff thin. Probably not the leadership even though enthusiasm there. Good lab.

Ludhiana - Cowan strong leader, gets things done the way she wants them, not sure she would play by rules/team work, etc. Grewal knowledgeable; junior people around who could do field work. Clinical areas strong but not highly research oriented, not great interest expressed in project. Lab good - Betty Hobbs doing her own thing, half time in London, would need associate for study. Excellent facilities by Indian standards. Most doubtful about blood, GI Specimens. Explicit about no collaboration with Americans.

Vellore

Not great interest in project other than lab, not sure field work as well organized as elsewhere. Facilities aging. Capability and leadership in reference laboratory role unquestioned. Difficulty with transportation from outside. Steinhoff also very good and with support will probably stay around. Real opportunity for capacity building in laboratory. Has some relationship with Pune both KEM and NVI, so connections would seem favorable for support in Pune.

Varanasi

Agarwal and Bhargava both strong in research, the former not very clinically oriented and has little to do with field organization. Both would have trouble giving up time from their own work. One of 7 center group, but PI now away, seems to be running OK by Bhargava. Lab good, setting up virology, no weaknesses or outstanding features. Facilities seem the most frugal and limited. Flexibility greater than other places because of Ministry of Education funding. Not great interest in project unless combined with ongoing studies. Doubt about succeeding over long run here.

Chandigarh

Excellent laboratory, probably better than Vellore as far as depth of staff and facilities. Solid research orientation ___ strong clinical component (Walia and both Dhalls). Had heard and observed that community medicine weaker in support although Kumar is thoughtful and competent. Saxena (ICMR) says thinks support issue may now be cleared up. As one of 7-center projects would hope the training and experience could be mobilized.

Interested in project but cautious. Expect proper proposal will be acceptable to them. Very free about collaboration. Seem to have exemption for sending specimens etc. out. Good transportation access would also make them suitable reference lab as well as study center.

Pune

Strong dynamic leader in BJJ Coyaji and strong field component with good organization. Laboratory is weak point. Could use NVI but haven't discussed, a difficult role to define. If Pune chosen may be Coyaji should explore what NVI would do for them. Probably best to just hire at Pune someone for 2 years to start - doctoral level microbiologist/technician and train at reference lab. Alternative would be to train existing staff but not sure they now have appropriate person. Also probably short staffed for this project. Kurus (Banoo's son) in OB/GYN is not that interested in community work but is well trained and could probably be enticed to take a role by virtue of "research" activity. He is content with beginning project in the hospital. Transportation not too bad. Pandit the very solid neonatologist, moves specimens back and forth to England without much trouble. He seems keen on collaboration and would be good. Minor concern about private 400 bed hospital - can they get enough high risk women to enroll for hospital portion?

Summary of Evaluation of Centers for Proposed Research on Infection and Low Birth Weight

<u>Center Location</u>	<u>Research (10)</u>	<u>Laboratory (30)</u>	<u>Field (40)</u>	<u>Clinical (10)</u>	<u>Interest/Commitment (10)</u>	
Chandigarh	10	27	24	9	8	78
Ludhiana	8	19	26	6	7	66
Pondicherry	6	19	21	7	7	60
Pune	8	12	28	9	9	66
Varanasi	8	20	21	6	4	60
Vellore	9	23	24	6	5	67

Explanation of Table Evaluations

1. Research - history of commitment to research and accomplishments, including specific references in laboratory or field projects relevant to the proposed project.
2. Laboratory - capabilities in routine bacteriology, anaerobic bacteriology, and other special capabilities or studies, experience or capabilities in mycoplasma isolation, capabilities for chlamydia isolation including virology, experience in sero diagnostics, current facilities and staffing.
3. Field - Longevity of work in community/access to hospital and community populations, village projects; organization, accomplishments, and goals of community projects; field staff and facilities; center-based project staff; and relationships apparent on site visit.
4. Clinical - background and potential time demands among obstetrical and pediatric professionals; thinking about the issues of proposed study.
5. Interest/commitment - collective response to idea of study, willingness to be part of collaborative effort, control of resources and environment.