

Date 11.5.87

ETHICAL REVIEW COMMITTEE, ICDDR,B.

22

Principal Investigator Dr Nigar S. Shahid Trainee Investigator (if any) _____

Application No. 81-021EP Supporting Agency (if Non-ICDDR,B) _____

Title of Study Measles Antibody Project status:
in Serum and Saliva
() New Study
() Continuation with change
() No change (do not fill out rest of form)

- Circle the appropriate answer to each of the following (If Not Applicable write NA).
- Source of Population:
 - Ill subjects Yes No
 - Non-ill subjects Yes No
 - Minors or persons under guardianship Yes No
 - Does the study involve:
 - Physical risks to the subjects Yes No
 - Social Risks Yes No
 - Psychological risks to subjects Yes No
 - Discomfort to subjects Yes No
 - Invasion of privacy Yes No
 - Disclosure of information damaging to subject or others Yes No
 - Does the study involve:
 - Use of records, (hospital, medical, death, birth or other) Yes No
 - Use of fetal tissue or abortus Yes No
 - Use of organs or body fluids Yes No
 - Are subjects clearly informed about:
 - Nature and purposes of study Yes No
 - Procedures to be followed including alternatives used Yes No
 - Physical risks Yes No
 - Sensitive questions Yes No
 - Benefits to be derived Yes No
 - Right to refuse to participate or to withdraw from study Yes No
 - Confidential handling of data Yes No
 - Compensation &/or treatment where there are risks or privacy is involved in any particular procedure Yes No
 - Will signed consent form be required:
 - From subjects Yes No
 - From parent or guardian (if subjects are minors) Yes No
 - Will precautions be taken to protect anonymity of subjects Yes No
 - Check documents being submitted herewith to Committee:
 - Umbrella proposal - Initially submit an overview (all other requirements will be submitted with individual studies).
 - Protocol (Required) Limited
 - Abstract Summary (Required)
 - Statement given or read to subjects on nature of study, risks, types of questions to be asked, and right to refuse to participate or withdraw (Required)
 - Informed consent form for subjects
 - Informed consent form for parent or guardian
 - Procedure for maintaining confidentiality
 - Questionnaire or interview schedule *
- * If the final instrument is not completed prior to review, the following information should be included in the abstract summary:
- A description of the areas to be covered in the questionnaire or interview which could be considered either sensitive or which would constitute an invasion of privacy.
 - Examples of the type of specific questions to be asked in the sensitive areas.
 - An indication as to when the questionnaire will be presented to the Cttee. for review.

We agree to obtain approval of the Ethical Review Committee for any changes involving the rights and welfare of subjects before making such change.

Nigar Sayem Shahid
Principal Investigator

Trainee

81-021(P)
rec'd 11/5/81

SECTION I - RESEARCH PROTOCOL

- 1. Title: Measles Antibody in Serum and Saliva
- 2. Principal Investigator: Dr. Nigar Shahid
Co-Investigator: Dr. Lief Gothefors
- 3. Starting Date: 15th May 1981
- 4. Completion Date: 25th May 1981
- 5. Total Direct Cost: US\$450
- 6. Scientific Program Head:

This protocol has been approved by the combined Disease Transmission and Host Defense Working Groups.

Signature of Scientific Program Head: W.B. [Signature]

Date: 15/5/81

7. Abstract Summary: A limited protocol is proposed to determine the presence of measles antibody in saliva as well as in serum in twenty-five post-measles hospitalized cases under two years of age. Haemagglutination inhibition test in both these body fluids will be used.

- 8. Review:
 - a. Ethical Review Committee: 13/5/81
 - b. Research Review Committee _____
 - c. Director: _____
 - d. BMRC: _____
 - e. Controller/Administrator _____

SECTION II - PLAN OF LIMITED STUDY

A. INTRODUCTION

1. Objectives.

To compare measles antibody level in serum and saliva.

2. Background Information

The knowledge of measles built up during the last century suggests that densely populated countries can expect a measles epidemic every year, and only a few of the non-immunized will escape measles in childhood. It is a killing disease during infancy in the LDC's^{1,2} 1963. The child is protected by maternal immunity for the first few months of life and the level of immunity falls steadily after 5 months.

The vaccination schedule of the extended programme of immunization in Bangladesh suggest measles vaccine to be given after 9 months age. Data from Matlab suggest however that very young children develop measles³. The DSS measles surveillance picked up cases of children less than 1 month of age (unpublished data). The identification of these cases was done by Medical assistance field workers. It has been shown that measles locally known as "Lunti" is easily recognizable within the community and antibodies checked for the virus found to be present in 98% of the reported cases⁴.

Thus the clinical findings by the field workers must be seriously considered. One of the objectives of the next full protocol will be to find out how long the maternal antibodies last in a child. For that we are planning to

do a cohort study on children under 2 years of age starting right from birth. We intend taking blood of the mother (.5 ml) and the child (.5 ml) at birth + cord blood. From the immunological point of view it thereafter would be enough with samples every two months, but as our experience shows we may have gaps in the follow up, and thus advocate monthly samples for the first 6 months. This may not be very practicable and we may lose a lot of subjects on follow-up. If the presence of the antibody in some other body fluid is established we do not have to do the fingerprick so often but depend on the titre in the other body secretion which will be more easily obtained.

Literature shows that antibodies are present in other body secretion e.g., lacrimal, nasal, salivary, intestinal, colostrum and urine although at different variety titres, i.e., the titre level of different fluids may be different but a standard could be obtained.

Antibodies are found at an appreciable titre in the saliva to polio and influenza viruses⁵. Since measles virus also invades the gastrointestinal tract there is a possibility that its presence will stimulate local antibody synthesis in the saliva. Usually ELISA is the method for measuring IgA but since we are not aware of any one measuring measles antibodies by ELISA we shall try conventional haemagglutination inhibition in saliva as well as in serum.

Convalescent serum and saliva will be used as the titre is highest from 1-4 days of on-set of rash and gradually declines⁶.

B. SPECIFIC AIMS

1. To see whether measles antibody is present in saliva and reflects the antibody levels in the serum.
2. To relate the presence of antibody serum/saliva to the level of nutrition.
3. Clinical picture of post measles diarrhoea in relation to the microscopic picture of stool and c/s.

C. METHODS OF PROCEDURES

Study Methods

In this limited study blood (lcc) from 25 post measles cases under 2 years of age will be obtained at the same time as femoral blood is being drawn for clinical indications (electrolytes. c/s). No additional prick will be made for the purpose.

Saliva will be collected by cotton swabs placed under the tongue for a few minutes. All specimens will be kept at -20°C for laboratory testing. HI test will be done in microtitre method. Monkey blood will be necessary and measles antigen will have to be obtained from a standard laboratory.

At the moment we are having a measles epidemic and it is necessary that we take the advantage of collecting the samples. Requests have already been sent for the measles antigen and 2 rhesus monkeys.

D. SIGNIFICANCE

So far we know of no studies where the presence of measles antibody in the saliva is compared with titres in the serum. This will enable us to write up a full protocol looking into age at which maternal antibody for measles tend to disappear in our population. A relation between the level of nutrition and antibody titres will be looked for. This is especially important in relation to reorganizing the EPI schedule.

E. FACILITIES REQUIRED

1. Office space : The present office space of Dr. NIGAR S. SHAHID will be used.
2. Laboratory space : Storage space in Freezer for 50 glass tubes.
3. Hospital resources : yes.
4. Animal resources : 2 rhesus monkeys
5. Equipment : Weighing scales, measuring board and measuring tape currently available in the hospital. Measles antigen with control sera request sent to National Bacteriological Laboratory, Sweden.

F. COLLABORATIVE ARRANGEMENT

Dr. Farida Haq, Chief Microbiologist, I.P.H. Mohakhali

REFERENCES

1. Morley D.C. - Severe measles in the tropics.
BMJ 297-300, 363-65, 1969
2. Schimshaw S.N., Joas B., Salomon, Bruch A., Hans and Gordon J.E.
(1966) - Studies in diarrhoeal diseases in central America.
American J. Trop. Med. Hyg 15:4, 625-630
3. Shahid N.S., Claquin P., Sheikh K., Zimicki S. - Complications of
measles in rural Bangladesh - Submitted for publication - to
Lancet
4. Koster F.T., Aziz K.M.A., Haque A. & Curlin G.C. (1976-77) -
Annual Report, JHU Centre for Medical Research and Training
p.29-32
5. Stiehm and Fulginiti (1973) - Immunological disorders in infants
and children, W.B. Saunders p.118, Table 8-2
6. Jawetz, Melnick J.L., Adelberg E.A. - Review of Medical Microbiology,
Lange 1974 p.410-412

Abstract Summary

1. The study population is sampled from among children < 2 years of age who are admitted to the ICDDR,B hospital for post measles complications. This age cut-off is used because it is seen that 60% of children have had an attack of measles by the time they are two years old.

We do not know of any study reporting the presence of measles antibody in saliva as has been done in polio and influenza viruses. Since measles also involves the gastrointestinal tract there is a possibility that its presence will stimulate local antibody synthesis in the saliva. The results of this limited study will enable us to write up a full protocol looking into the age at which maternal antibody for measles tends to disappear in our population.

2. There will be no potential risk to the subject. One ml of blood will be taken from 25 post measles cases at the time femoral blood is being drawn for clinical indications.

3. Not relevant.

- 4-5 All efforts will be made to maintain complete confidentiality and protection of anonymities. Written consent of parents and guardians will be taken on the spot before taking the subject into the study.

6. Material will be used as a base for future research work.

7. The exact time may be ascertained in future at which measles immunization should be done in Bangladesh. At present EPI suggests measles immunization at 9 months although research in rural Bangladesh has shown that cases occur much earlier.
8. Hospital records on clinical assessment of the patients will be used. Saliva will be obtained by cotton swabs put in the mouth for a few minutes.

1. Patient No.
2. Name :
3. Father's Name :
4. Address :
5. Age in months :
6. Sex
7. Date when measles occurred (in wks) :
8. Cl. Features on hospitalization :
9. Days hospitalized :
10. Diarrhoea : Present or Absent
11. If present :
 - a. ME picture
 - b. C / S
12. Amount of Diarrhoea during hospitalization in Litres :
13. Antibiotic used : Dose _____
 - A. Serum
 - B. Saliva
 - C. Cotton Swabs

SECTION III - BUDGETA. DETAILED BUDGET1. PERSONNEL SERVICES

<u>Name</u>	<u>Position</u>	<u>Time & % effort</u>	<u>Annual Salary</u>	<u>Taka</u>	<u>Dollar</u>
Nigar S. Shahid	Investigator	1 month 25%	55392	1154	-
Lief Gothefors	Co- Investigator	-	-	-	-
Lab Staff (one) Immunology		½ month		1000	-

2. SUPPLIES AND MATERIALS

2 Rhesus Monkeys				1000	
Antigen, antisera					200
Glass-ware					7

3. EQUIPMENT - Nil4. HOSPITALIZATION COST: Nil5. OUTPATIENT CARE: Nil6. ICDDR, B TRANSPORT: Nil7. TRAVEL: Nil8. TRANSPORT: Nil9. RENT, COMMUNICATION: Nil0. PRINTING: Nil1. CONTRACTUAL SERVICES: Nil

Grand Total:

3154

207

(or US\$ 450)

PERMISSION FORM - WITHDRAWING 1 ml OF BLOOD AND $\frac{1}{2}$ ml OF SALIVA
FROM POST MEASLES CASES

Post measles complications such as dysentery, broncho pneumonia is very common amongst our children. Very effective vaccination for this infectious disease is available but a lot of doses are wasted due to its delayed administration. The International Centre for Diarrhoeal Disease Research, Bangladesh is carrying out research to determine at what age maternal antibody for measles disappears in Bangladeshi children.

1. If you decide to let your child join the study we will draw 1ml of blood from him at the same time blood is being drawn for clinical indications. No additional prick will be made for the purpose. We shall also require some amount of saliva (0.5ml) from the child.
2. If you decide that you do not want your child to join the study you will still be eligible to care at ICDDR,B. You may also decide to withdraw your child after entering the study and this will not affect any medical care you might require now or later on.
3. Your medical records will be kept confidential.

If you decide that your child may join the study please sign here.

অনুমতি করুন -- হাম উত্তর কেস হইতে এক মিঃ গ্রাঃ রক্ত

ও $\frac{1}{2}$ মিঃ গ্রাম লানা গ্রহণ

আমাদের বাচ্চাদের মধ্যে হাম পরবর্তী জটিলতা খুবই লক করা যায়, যেমন আশাশয়, ত্রুক্ষো নিউমোনিয়া ইত্যাদি। এই সমস্তু সংক্রমক রোগের জন্য খুবই কার্যকরী টিকা পাওয়া গেলেও ইহার যথাযত ব্যবহারের অভাবে বা বিলম্বের জন্য অনেক ঔষধ নষ্ট হইয়া যায়। আই, সি, ডি, ডি, আর, বি গবেষণা চালাচ্ছে যে কোন বয়সে বাংলাদেশী শিশুদের মধ্যে হামের রোগ প্রতিরোধ শক্তি বিলুপ্ত হয়।

১। আপনি কি আপনার শিশুকে এই পরীক্ষায় অংশ করাতে চান তবে তার চিকিৎসা চলাকালীন যখন রক্ত পরীক্ষা করা হবে সেই সমস্তু একবার মাত্র ১ সি সি রক্ত আমরা হামের প্রতিরোধ টিকার গবেষণার জন্য সংগ্রহ করবো। শিশুর কাছ থেকে কিছু লানাও আঘাদের দরকার হবে।

২। আপনি যদি আপনার শিশুর এই পরীক্ষায় অংশগ্রহণ না করাতে চান তথাপিও আপনি আই, সি, ডি, ডি, আর, বি-তে চিকিৎসা পেতে থাকবেন। এই পরীক্ষায় অংশগ্রহণের পরেও আপনি আপনার শিশুকে এই পরীক্ষা হতে প্রজ্ঞাহার করে নিতে পারবেন তাতে বর্তমানে বা পরবর্তী সময়ে আপনার প্রয়োজনীয় চিকিৎসার কোন ব্যাঘাত হবে না।

৩। আপনার রেকর্ড পত্রের গোপনীয়তা বজায় রাখা হবে।

৪। আপনি যদি শিহর করেন যে, আপনার শিশু এই পরীক্ষায় অংশ নিক তাহলে বিষয়ে দসুখত করুন।
