

ETHICAL REVIEW COMMITTEE, ICDDR,B.

200

Principal Investigator DR. M.U. KHAN

Trainee Investigator (if any) \_\_\_\_\_

Application No. 80-043

Supporting Agency (if Non-ICDDR,B) \_\_\_\_\_

Title of Study Association of Nutritional  
Corneal disease and night blindness.

Project status:  
( ) New Study ~~Limited 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).

- 1. Source of Population:
  - (a) Ill subjects  Yes  No
  - (b) Non-ill subjects  Yes  No
  - (c) Minors or persons under guardianship  Yes  No
- 2. Does the study involve:
  - (a) Physical risks to the subjects  Yes  No
  - (b) Social Risks  Yes  No
  - (c) Psychological risks to subjects  Yes  No
  - (d) Discomfort to subjects  Yes  No
  - (e) Invasion of privacy  Yes  No
  - (f) Disclosure of information damaging to subject or others  Yes  No
- 3. Does the study involve:
  - (a) Use of records, (hospital, medical, death, birth or other)  Yes  No
  - (b) Use of fetal tissue or abortus  Yes  No
  - (c) Use of organs or body fluids  Yes  No
- 4. Are subjects clearly informed about:
  - (a) Nature and purposes of study  Yes  No
  - (b) Procedures to be followed including alternatives used  Yes  No
  - (c) Physical risks  Yes  No
  - (d) Sensitive questions  Yes  No
  - (e) Benefits to be derived  Yes  No
  - (f) Right to refuse to participate or to withdraw from study  Yes  No
  - (g) Confidential handling of data  Yes  No
  - (h) Compensation &/or treatment where there are risks or privacy is involved in any particular procedure  Yes  No

- 5. Will signed consent form be required:
  - (a) From subjects  Yes  No
  - (b) From parent or guardian (if subjects are minors)  Yes  No
- 6. Will precautions be taken to protect anonymity of subjects  Yes  No
- 7. Check documents being submitted herewith to Committee:
  - Umbrella proposal - Initially submit an overview (all other requirements will be submitted with individual studies).
  - Protocol (Required)
  - 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:

1. 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.
2. Examples of the type of specific questions to be asked in the sensitive areas.
3. 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.

Moslemuddin Khan  
Principal Investigator

Trainee

80-043


Rec'd

28.11.80.

SECTION I - RESEARCH PROTOCOL

1. Title : Association of Nutritional Corneal disease and night-blindness with diarrhoea.
2. Principal Investigator : Dr. M.U. Khan
3. Starting Date : December 1, 1980
4. Completion Date : March 1981.
5. Total Direct Cost : \$ 19,000.00
6. Scientific Program Head :

This protocol has been approved by the Nutrition Working Group

Signature of Scientific Program Head : 

Date : 18/11/80

7. Abstract Summary :

Many Bangladesh population suffers from second and third degree malnutrition. Of the nutrients protein and Vitamin A are very much insufficient specially in rural area. Among the multiple consequences of PCM and Vitamin A malnutrition, it is proposed to study the (1) association of nutritional corneal disease with diarrhoea of the existing blind persons, (2) level of Vitamin A in patients with keratomalacia and nocturnal impairment of vision and (3) level of Vitamin A in acute malnourished diarrhoeal cases hospitalised in Matlab or Dacca.

## SECTION II - RESEARCH PLAN

### A. INTRODUCTION

#### 1. Objective :

- a. To study association of nutritional corneal illness with diarrhoea and Vitamin A level.
- b. To estimate the rates of Keratomalacial Visual defects in the population as compared to injury, infection, small pox etc. among the existing blind people.
- c. To measure blood level of Vitamin A in diarrhoeal patients, with or without nutritional corneal illness, hospitalised in Matlab or Dacca and also in persons with night blindness.
- d. To compare blood level of Vitamin A in keratomalacial and night blind children without diarrhoea.

2. Background : Recent studies in Indonesia has shown that 4 pre-school children per 1000 have corneal nutritional eye disease, while non-corneal Vitamin A deficient disease is 104 per 1000 per year. Accordingly in Bangladesh there is an annual incidence of 48,000 nutritional corneal eye cases and 1,250,000 non-corneal cases(1). They are often seen in association with deficiency of Vitamin A, malnutrition, diarrhoea and

measles. However no epidemiological and clinical study have documented these in Bangladesh. Figures quoted by clinicians are based on selected hospital admitted cases and by the health statistics are mainly unconfirmed figures. Although many of the severely malnourished children are associated with nutritional corneal diseases none of 401 children followed for 3 years in Meheran develop nutritional corneal disease. It is however, likely that many of the severely malnourished children die before developing corneal illness. In a study conducted by the Nutrition and Food Science Institute of Dacca University(2) it has been estimated that nearly 90% of the households are deficient in the intake of Vitamin A and the intake does not exceed 70% of the total requirements. In the same study, it was estimated that nearly 800,000 people of Bangladesh are suffering from night blindness and over 5% of all children under 15 years suffer from impairment of vision at night. Such figures are an indication of the severity of the situation. The incidence of nutritional corneal disease was 24% in admitted PCM deficient cases and 1.2% in OPD cases in a nutritional unit in Dacca(3). Such figures should be interpreted carefully as they concern selected cases and do not reflect over all picture of the country. In a study

from India 1.7% of the children of the age group 0-6 years had keratomalacia(4). Such results are not available for Bangladesh. Though nearly 200 units/Kg. of Vitamin A is needed for infants 0-12 month of age(5) the minimum level which precipitate nutritional corneal lesion has not yet been determined in Bangladesh.

We are proposing to study the nutritional consequences of Vitamin A deficiency in a rural area of Bangladesh (Matlab), and to relate the nutritional corneal illness with diarrhoea and nocturnal visual defect and its extent in the community compared to other famous causes of visual impairment.

3. Rationale : To understand the relation between nutritional corneal illness, night blindness and diarrhoea as no systematic study has been conducted in Bangladesh the extent of nutritional impairment of vision compared to other factors is also not known. Because Vitamin A levels in active nutritional corneal lesion cases have not been studied in our rural areas, such study is needed for nutritional program and for conduction of Vitamin A distribution program in Bangladesh.

In Matlab, there is a defined rural population with known ages upto 16 years; a list of all visual impaired persons in the area; a surveillance report for the 2 following years; a diarrhoea treating centre where all severe diarrhoea cases, some of whom having nutritional corneal ailments, are admitted for treatment; and finally, we have the unique facility to assay Vitamin A in our laboratory. These conditions create a unique position to conduct a study on the subject. The result will be helpful for vitamin distribution and nutritional programs in Bangladesh and in other LDC where vitamin A deficiency prevails.

**B. SPECIFIC AIMS**

1. To study the relation between nutritional corneal illness, nocturnal visual defect and diarrhoea.
2. To compare nutritional visual impairment to visual defects due to other causes in rural population.
3. To measure blood level of Vitamin A in hospitalised diarrhoea cases with and without corneal nutritional lesion.
4. To study whether impairment of vision at night appears before development of keratomalacia and whether the former can be taken as a warning signal of the development of nutritional corneal lesion.

C. METHODS OF PROCEDURE

One Physician and a Field Assistant will be trained in Ispahani Eye Hospital outdoor department in diagnosing nutritional corneal diseases for about a week. Prof. S.A. Wadood has permitted them to undergo training in order to understand the disease in its acute and chronic forms and also to look for association of PCM and diarrhoeal illness with corneal nutritional disease. Otherwise, a physician with training in ophthalmology will be hired for 3 months.

In Matlab a team will be formed with these staff and an additional Field Assistant to help them. Lists of the persons with visual defects have already been prepared along with surveillance data of 2 years. The Field Assistants of a nearby group of villages will be given the lists of those persons and they will be instructed to assemble the people at prominent places, or schools or markets nearest to the villages. The team will visit the place on prefixed dates. The Field Assistants (trained) will fill the detailed history on printed forms. The Physician will examine the eyes and establish the cause of visual impairment. Attempts will be made to elicit the presence of diarrhoeal diseases at the time of development of the malady. Whether

there was any discontinuation of breast feeding due to death, divorce or separation of mothers or due to an immediate birth of another issue to the mothers will be questioned. Similar questions will be put to another identical control with visual defect from other causes. In case of children mothers will be asked. In some cases nearest neighbours can also help. The physician will also confirm the history and examine the corneas and lenses. The cornea will develop special features like anterior staphyloma with opacity, keratoconus with opacity, bilateral scars, uniform round dense or light opacity, specially on the lower part, thin central opacity perforation and adhesion, perforation with iris prolaps, phthisis bulbi etc. In all cases, the presence of conjunctival xerosis, rusty discoloured hair, night blindness, toad skin and PCM malnutrition will be assessed. History of injury and infection of eye, at the time of development of the visual impairment, will also be obtained.

For the cases, within the health services area, the subcentres may be used as places for examination, and their country boats which are kept waiting after bring the usual cases, may be used. The cases which are



curable will be referred to the Dacca hospitals. If possible they may be assisted in coming to Dacca. When needed eye drops, eye ointment and Vitamin A will be distributed.

Two ml. of blood(not exceeding 50 samples) will be collected from the night blind children(0-10) and controls(50) of the same SES group and areas. From patients of Matlab hospital 2 ml. of blood will be collected for estimation of Vitamin A level from diarrhoea with(50) cases and without (50) corneal nutritional diseases(0-10). Along with this, the nutritional status of all 4 groups of children such as weight, hight, arm circumference and skinfold thickness will be obtained for comparison. If sufficient diarrhoeal cases(100 cases) are not available they can be had from Dacca hospital or from children nutritional unit Maghbazar, Dacca. Vitamin A assay will be done in ICDDR,B laboratory. The data will be coded, punched and then transferred to computer tapes for analysis. Association with degree of malnutrition and diarrhoeal diseases will be looked for. Prevalence in the population will be calculated to compare its incidence with other factors affecting eye sight. An estimation of its rate in the rural area will be available to compare the incidence of nutritional keratomolacia with other countries. Analysis will be made to see if there is any strong association between night blindness, Vitamin A level, .....continued P.8.

diarrhoea, malnutritional status and interruption of breast-feeding. The usual Chisquare tests or Fisher's Exact test will be applied to test for significance. The data will be then presented to the appropriate group for consideration of publication.

D. SIGNIFICANCE

The study will be of particular interest as there is no data available on the corneal nutritional disease and the rate of annual incidence of visual impairment of the rural people of Bangladesh. The study will document the relative role of Vitamin A deficiency in causing corneal lesion, its association with night blindness, diarrhoea and interrupted breast feeding. The possible significance of night blindness and or low Vitamin A blood level as a marker for later development of corneal lesion will be assessed.

E. FACILITIES REQUIRED

1. Office Space : No additional office space will be needed. The subcentres, village school premises or the marketing areas will be used for examination of patients.

2. Laboratory Space : Assay of Vitamin A will be done in the biochemistry laboratory of ICDDR,B-Dacca. No additional space is needed for this purpose.
3. Logistic Support : The ICDDR,B existing logistic support will be needed. Weekly one trip from Dacca to Matlab combined with other travellers to Matlab will be used. One speed boat will be needed for the study period in Matlab. In addition some country boats will be needed during the monsoon period for transporting the people from their houses to the place of examination. Some people may need to be transported to Dacca for treatment.

F. COLLABORATIVE ARRANGEMENT

No collaborative arrangement for this study is required.

SECTION III - BUDGET

A. DETAILED BUDGET

1. PERSONNEL SERVICES

<u>N A M E</u>	<u>POSITION</u>	<u>% TIME USED</u>	<u>PERIOD</u>	<u>PROJECT REQUIREMENT</u>	
				<u>TAKA</u>	<u>DOLLAR</u>
Dr. M.U. Khan	Scientist	20%	1 year		4,800
Dr. (to be named)	Physician	100%	6 month		1,200
Supervisor	1	20%	6 month		350
Health Assistant	2	100%	6 month		1,200
Statistical Asstt.	1	100%	1 month		150
Biochemist	1	100%	7 days		100
Sub total				Tk.- \$	7,800

2. SUPPLIES AND MATERIALS

<u>I T E M</u>	<u>AMOUNT</u>	<u>TAKA</u>	<u>DOLLAR</u>
Vitamin A Injection	100	-	50.00
Vitamin A capsule	2000	-	100.00
Iron tablet	2000	-	50.00
Vitamin A drop	100 vial	-	50.00
Eye drop(chloromy.)	100 vial	-	150.00
Eye ointment(tetracycline)	100 tubes	-	50.00
Eye testing chart	2 ps	-	10.00
Ophthalmoscope	1 ps	-	250.00
Torch light	1 ps	-	5.00
Magnifying glass	1 ps	-	10.00
Batteries	2 dozon	-	15.00
One 20 + feet tape	1 ps	-	10.00
Paper-stencils etc.		-	150.00
Candy + Baloon		-	50.00
Sub total		Tk.- \$	950.00

3.	<u>EQUIPMENT</u>		
	Reagent for Vitamin A assay		\$ 100.00
4.	<u>PATIENT HOSPITALISATION</u>		
	Physicians food for 70 days @ Tk. 45 daily		\$ 200.00
5.	<u>OUTPATIENT CARE</u>		
	Some patients may need referring to hospital		\$ 200.00
6.	<u>ICDDR, TRANSPORT</u>		
	Dacca Matlab Trip - 20(including food)		\$ 360.00
	Matlab speed boat hour 2 daily for 90 days		\$ 1200.00
	Country boat 20% time 1 daily for 70 days		\$ 100.00
		Sub total	\$ 1660.00
7.	<u>TRAVEL AND TRANSPORTATION OF PERSONS</u>		
	Nil	Presentation	\$ 3000.00
8.	<u>TRANSPORTATION OF THINGS</u>		
	Nil		
9.	<u>RENT, COMMUNICATION &amp; UTILITIES</u>		
	Nil		
10.	<u>PRINTING AND PUBLICATION</u>		\$ 300.00
11.	<u>OTHER CONTRACTUAL SERVICE</u>		
	Programmer & Electoral service		\$ 250.00
12.	<u>CONSTRUCTION, RENOVATION, ALTERATION</u>		
	Nil		

B. BUDGET SUMMARY

<u>C A T E G O R Y</u>	<u>TAKA</u>	<u>DOLLAR</u>
1. Personnel	-	7,800.00
2. Supplies	-	950.00
3. Equipment	-	100.00
4. Hospitalisation	-	200.00
5. Outpatient care	-	200.00
6. ICDDR,B Transport	-	1,660.00
7. Travel of persons	-	3,000.00
8. Transportation of things	-	-
9. Rent-Communication	-	-
10. Printing and reproduction	-	300.00
11. Other contractual services computer time(with transportation)	-	250.00
12. Construction, renovation, alteration	-	-
		<hr/>
Total	-	\$14,460.00
overhead charge@30%		\$ 4,340.00
		<hr/>
Grand total		<u><u>\$18,800.00</u></u>
say		\$ 19,000.00

## REFERENCES

1. Sommer, A., Segana, T., Hussaini, G., Emran, N., and Tarotjo, Tg: Xerophthalmia : Determinants and Control. Report to 23rd International Congress of Ophthalmology, May 1978, Kyoto, Japan.
2. Nutrition Survey of Rural Bangladesh 1975-76. Institute of Nutrition and Food Science, University of Dacca.
3. Brown, K., Gaffar, A., Alamgir, S.M., Vitamin A deficiency, Protein Calorie Malnutrition and Infection in Children(submitted for publication).
4. Shwaminathan, M.C., Susheela, T.P., Thimmayamma, B.V.S. Am. J. Cl. Nutr. V: 23 # 1, Jan. 1970, P. 119-122.
5. WHO Technical Report Series # 590.

## ABSTRACT SUMMARY

In Matlab study area there are 1500 people with impairment of vision. There may be many factors causing visual impairment. As few food items containing Vitamin A is consumed in rural area and as a good number of children suffer from 3rd degree malnutrition we expect that many of the visual defective persons have developed nutritional corneal illness. We want to study the rates of such cases in rural areas, association of development of illness with diarrhoea, breast-feeding and night blindness. Further, we want to study the blood level of Vitamin A in patient admitted with diarrhoea having both corneal lesion or without lesion. This study may offer specific indication for treatment and intervention of nutritional corneal visual impairing illness.

The visual defective persons will be examined in their village areas for confirmation of diagnosis and for



be able to give consent except in cases of infants and children where the parents will give consent on behalf of the children.

2. There is no risk involved in examining the people in respect of physical, psychological, social, legal or other. There will be however, slight physical pain while obtaining blood. But we will collect 1 ml blood from the hospitalised cases under proper care and precaution. It may help some of the patients in prescribing adequate amount of Vitamin A. Infact, there is no risk involved in obtaining this little amount of blood.
3. There is no potential risk. Adequate sterility will be maintained. Mild analgesics may be given only in selected cases.
4. There is no confidentiality about impairment of eye sight of these people. Every one in the locality are aware of it. However, the history will be kept confidential and the people will not be identified by names; Census number will be used for reporting the cases. The records will be used only by the Investigator and the Statisticians

in Dacca and as such there is no possibility in disclosing their history.

5. There is no potential risk. However, informed consent will be obtained from them. The consent for the minors will be obtained from the legal guardians.
  - a. Consent will be obtained
  - b. No information will be withheld
  - c. No privacy will be encroached upon. In suitable cases people will be helped to obtain treatment from Dacca. For active cases treatment will be provided right in the village or hospital.
6. The study will involve interview. This will be in the villages of the people or at the nearest ICDDR, subcentres. The interview will be absolutely on matters related to their impairment of vision only. Time taken will be about 10 minutes for each.
7. For active cases treatment will be provided without cost. Curable old cases will be helped to go Dacca for treatment. Other cases of visual impairment (as cataract) will be referred to eye hospital and

they may be helped by offerring transportation to Dacca. They will be getting the advice which is not available to them right in their areas and many of the visual impaired persons may get back their vision. Some other suitable cases may get treatment for infection or glaucoma etc. These certainly outweigh all risks if at all in giving history and 1 ml of blood.

8. The activity require use of CRL census record, and birth record for all cases. Only about 100 samples of blood is needed and it may help prescribing proper treatment.

CONSENT FORM

The ICDDR,B is conducting a study to explore the causes of visual ailment. History of your healthy child and died and or history of development of your or your ward's illness and examination of your or your child's eyes will be needed. Two ml. of blood will be required to be tested from you or your child. This may help in prevention of visual impairment you or your ward will be treated for anaemia. In addition, if your eye disease is active and curable it will be treated. If it needs operation you may be sent to a suitable Hospital if you desire. You will receive treatment for diarrhoea from ICDDR,B hospital irrespective of your participation in our study. If you agree to participate and cooperate with our study please sign your name or give left thumb impression below.

NAME \_\_\_\_\_

or LTI \_\_\_\_\_

VTS/HOSP.NO. \_\_\_\_\_

HOSPITAL \_\_\_\_\_

DATE \_\_\_\_\_

## সম্মতি পত্র

অন্তর্জাতিক উদ্বোধন ব্যক্তি গবেষণা কেন্দ্র চক্রবর্তীর কারন সম্মতের অনুসন্ধান করাছেন। এই অনুসন্ধানের জন্য আপনাকে বা আপনার ছোলেমেয়েদের আচরণ ও চক্রবর্তীর ইতিহাস এবং চক্রবর্তীর প্রয়জন হয়ে। আপনার বা আপনার ছোলেমেয়েদের ২০৩ থেকে ২ মিলিলিটার বকু নেওয়া হবে। এই বকু গবেষণা এবং চিকিৎসা দুই কাজের লক্ষ্য। আপনার বকুশূন্যতা থাকলে তার চিকিৎসা করা হবে। যদি চিকিৎসার প্রয়জন হয় তাহলে এই কেন্দ্রে খতমের সহযোগিতায় চিকিৎসা করা হবে। যদি অপারেশনের প্রয়জন হয় তাহলে চরম সমাধা সহযোগিতায় পাঠানো হবে। আপনি এ গবেষণায় অংশগ্রহণ করেন বা না করেন আপনার উদ্বোধনের চিকিৎসা চলবে। যদি আপনি এই গবেষণায় অংশগ্রহণ এবং সহযোগিতা করতে চান তাহলে নীচে আপনার নাম সন্নিবেশিত করে অথবা চিঠি সন্নিবেশিত দিন।

স্বাক্ষর