SECTION I - RESEARCH PROTOCOL

1. Title : Impact of Vit A intake by children on diarrhoeal and respiratory disease morbidity, nutrition and skin infection and maintenance of blood level following diarrhoea.

2. Principal Investigator : M.U. Khan

   Co-Investigator : D.A. Sack, N. Rahman, A. Ali

3. Starting Date : Within one week of allotment of fund

4. Completion Date : Two years from the date of start

5. Total Direct cost : First Year $20,370 Second Year $7,735

6. Scientific Program Head :

This protocol has been approved by the Disease Transmission Working Group.

(Signature of Program Head)

7. Abstract Summary :

Vit A has been credited to play a key role in child survival through various mechanisms. A prospective study for one year has been planned to assess the level of Vit A in blood upto one year and the impact of Vitamin A supplementation on child's diarrhoeal and respiratory morbidity, nutrition and skin infection (and night blindness). Three groups of children (50 in each group) between three and six months of age will be selected from the treatment centre for followup. They will be systemetically assigned to study, control

and study. Vit A will be given to two groups except the controls. Vit B complex syrup, paracitamol and ORS will be provided to all during the followup if required. The control group will be under strict supervision to detect development of night blindness. In case of development of night blindness the child will be immediately treated. The study group will receive Vit A at 6 month again and all children and control at the close of study. Two ml of blood will be collected from all at hospitalisation, at three months and at six months to estimate the level of Vit A in blood. All children will be followed up for morbidity reports at least for one year. This study will show whether provition of Vit A both to mother and child and to child only maintains safe titre upto three or six months. This will help the clinicians in imparting proper treatment of Bangladeshi children after diarrhoea and advise the parents or authority concerned in the right direction. This study will also show the effect of Vit A on diarrhoeal & respiratory morbidity, nutrition, skin infection (and night blindness).

8. Reviewers : a) Ethical Review Committee

b) Research Review Committee

c) Director

SECTION II - RESEARCH PLAN

A Introduction :

1. Objectives:

1. To study the levels of Vit A in blood after an attack of diarrhoea in children.
2. To see whether safe level of Vit A is maintained for six months after administration of one dose following diarrhoea.
3. To see whether a better Vit A level is maintained when both mother and child receive it, or whether only child receives it.
4. To see whether Vit A reduces morbidity from diarrhoea, respiratory diseases, skin infection and prevents malnutriton.

2. Background :

Disease agents cause disease by their presence in hosts. But Vit A causes disease by its absence in hosts. Opthalmic diseases were the main menifestation of its absence (1). Skin involvement due to its absence has also been known (2). Some of the investigators have associated absence of Vit A with deficient absorption of iron from the gut leading to nutritional consequencies (3). Vit A deficiency has been ascribed to respiratory and diarrhoeal illness (4). In Bangladesh it has not been adequately examined. Child survival has been attributed to adequacy of Vit A (5). Bangladeshi children are said to consume insufficient amount of Vit A (6). In addition, malnutrition and diarrhoea are frequent in Bangladeshi

children (7). It is not adequately known whether diarrhoeal children can sustain normal level after use of a single dose of high potency Vit A upto six month as recommended. Whether administering as single dose to both lacteting mothers and the breastfed children maintains a higher level of Vit A for a longer time is not also known. A study is therefore, planned to assess the Vit A level in children following diarrhoea and follow them for one year observing morbidity from respiratory and diarrhoeal disease, nutritional status, skin disease and night-blindness (if any). Serum Vit A will be estimated during diarrhoeal time and at three and six months interval from all groups.

3. Rationale :

Bangladeshi children are chronically deficient in protein and Vit A. Diarrhoea is also common in Bangladeshi children. Dose and frequency of Vit A have been based on works done mostly in socio-economically better countries. Therefore, it is of utmost importance to know whether prescription of one dose every six month and especially following diarrhoea is enough to prevent deficiency consequencies. Moreover, whether Vit A reduces other morbidities and malnutrition in Bangladeshi children is also not known. This study is likely to answer the above questions which will be beneficial both to the patients, clinicians and nutritionists.

4. Specific Aims :

a) To understand whether diarrhoeal children can maintain a normal Vit A level upto six month following administration of one dose after a diarrhoeal attack.

b) To understand whether Vit A can prevent morbidity from Diarrhoeal disease, respiratory disease, malnutrition, skin infection and (night-blindness).

c) To understand the level of Vit A in control and diarrhoeal children.

d) To understand whether administration to both mother and child is more beneficial.

Methodology :

The study children and mothers will be selected from the treatment Centre of the ICDDR,B. There will be three groups of cases. Group 1 will comprise both mother and child; Group II only child and Group III only control. The age of the children will be between 3-6 months. They should not be recipient of high potency (200,000 units) Vit A already. Children should be moderate to severely purging patients and should not be from well to do families (judged by dress). They should be permanent residents of Dhaka city or from suburban accessible areas. They should be primarily breast fed. Children mainly on formula feeding will not be entered in the study. The mothers will be between the ages of 20-35 and lactating their babies. They should not be pregnant at the time of entry into study. History of LMP will be obtained. In cases of doubt she will be

either rejected or pregnancy test done. Pregnant women should not take Vit A (2000,000). A constant chronological order of selection will be maintained. The first case taken will be both mother and child for study. The second case will be a control child, and the third case a study child. This order should be maintained always. After obtaining consent 2 ml of venus blood will be taken from the cases of each group. When the purging rate comes down to normal one capsule of high potency Vit A will be fed to all except the control child. All of them will be given iron and folic acid tablet for use after the diarrhoea is over. Blood samples will be collected at attendance, at 3 month and at 6 month. If possible blood will be collected at their homes and if not they will be brought to hospital. Attendent would be provided with one meal. At six month a second doze of Vit A will be administered to all except the control. The case and controls will be visited every two weeks for obtaining history of morbidity from diarrhoea, respiratory illness and skin infection. Height, weight and arm circumferences will be obtained from children at discharge and during monthly visits. The controls will be kept under strict visilence for any Vit A deficiency eye sign. A card will be issued to all for attending ICDDR,B and meeting the field teams or surveillance group in cases of diarrhoea or dysentery or night-blindness (XN) between the visits. In case of XN Vit A should be immediately administered and the case dropped from further study and followup. In the morning the field team will attend the treatment centre, interview them and obtain consent and select cases. There will

be 50 cases in each gorup. After selection 2 ml blood would be obtained in a screw capped tube by a technician adopting precaution. If possible blood may be obtained with the blood needed for usual check up and electrolyte testing. The blood will be kept in an ice flask before handing over to biochemistry. All children will be immunised with triple vaccine (DPT) at the hospital before discharge and during one and 2 month's visit to their families. Mothers participating will be given three doses of Tetanus Toxoid. When follow up will be discontinued at the end of one year all children will be given a capsule of high potency Vit A. During the followup they will be obtaining ORS, paracitamol and treatment for scabies in addition to treatment of dysentery when they attend hospital. Vit A will be assayed using the macro and micro method (8). During the visits by field teams consisting of one male and female, history of diarrhoea, respiratory illness, skin infection and night bl[illegible]ll be obtained. Anthropometry for height, weight and arm circumference will be done. The data will [illegible] finally coded and entered into computer. Significance test will be done using X^2 test or Fisher's exact test as required. Field data collection will be continued for one year for each case. If the requisit number of cases are obtained within a short time then they will be followed for completing one year for all study and control cases. If the budget is adequate each will be followed for two years.

D Significance :

Whether administration of one dose of hypotency Vit A is sufficient enough for maintaining normal blood level in mostly malnourished Bangladeshi children is not known. It is also not known whether an

additional dose of Vit A to a lactating mother keeps the Vit A level higher than a single application to a child. In Bangladesh situation whether Vit A prevents children from higher morbidity from diarrhoea, respiratory illness, skin infection and developing night blindness and malnutrition is not also known. This study will provide answer to these questions. This study is therefore of immense value.

E Facilities Required :

No new facilities are needed. No recruitment of staff or acquiring of equipment or office space is needed. We can utilise the existing staff and equipment for this purpose. We have also the transport facilities for field work or we can use cheaper public transport.

References

1. Control of Vit A deficiency and Xeropthalmia. Report of a joint WHO/UNICEF/USAID/HKI/IVACG meeting. WHO Tec Rep Ser No 672, pp 10-13, 1982.
2. Textbook of Medical Physiology by Arthur C Gyton, Fifth Edition, pp 980. WB Saunders Company, London 1976.
3. Mejia LA, Hodges RE & Rucker RB. Clinical signs of anaumia in Vit A deficient rats. Am J Clin Nutr 32:1439-44, 1979.
4. Sommer A, Katz J & Tarwotjo I. Increased risk of respiratory disease and diarrhoea in children with preexisting mild Vit A deficiency. Am J Clin Nutr 40 pp 1090-1095 Nov 1984.
5. Sommer A, Tarwatjo I, Hussaini G, Susanto D. Increased mortality in children with mild Vitamin A deficiency. Lancet V2:585-88, Sept 10, 1983.
6. Institute of Nutrition and Food Science; University of Dhaka, Bangladesh. Nutrition Survey of rural Bangladesh 1975-76, pp 50, 66, 69, 95, 1977.
7. Khan MU & Ahmed K. Withdrawal of food during diarrhoea: Major mechanism of malnutrition following diarrhoea in Bangladesh children. J Trop Padiatr V 32: , 1986.
8. Neild, JB Jr. & Pearson WN. Macro and micro methods for determination of serum Vit A using TFA (modified). J Nutr 79:454-62, 1963.

ICDDR,B
1986 BUDGET PROPOSAL
(In US $)

AREA DESCRIPTION

Program Name: DISEASE TRANSMISSION WORKING GROUP

Project/Protocol/Branch Name: VIT A IN CHILDREN WITH DIARRHOEA

Principal Investigator/Branch Head/Program Head: M.U KHAN

Budget Code: ..... Estimated Beginning Date: .....

Protocol No: ..... Estimated Ending Date: .....

EXPENSE CATEGORY		*Column A	Column B	Column C	Column D
		Total Project Cost	Year 1	Year 2	Proposed Total
A/C No.	Description	Refer Page			
3100	Local Salaries	2	11,035	5,000	16,035
3200	Intl. Salaries	8	0	0	0
3300	Consultants	14	0	0	0
3500	Travel Local	15	0	0	0
3600	Travel Intl.	16	0	0	0
3700	Supplies & Mat.	18	1,235	1,235	2,470
3800	Other Costs	19	4,450	500	4,950
4800	Inter Deptl. Ser.	20	3,650	1,000	4,650
	Total Direct Operating Cost		20,370	7,735	28,105
0300	Capital Expenditure Refer Page 21		** 0	** 0	0
	TOTAL DIRECT COST		20,370	7,735	28,105

* Refers to entire life of project.
** For Finance use only.
Budget86.1-3
AZIZ-5.

PERSONNEL REQUIREMENT-(LOCAL STAFF) 1986

	No.of Positions	No. of Man Months	$ Amount
A. Direct Project/Protocol/Branch Staff at 1.1.1986 Sourced from Page 3	0	0	0
Add:			
B. New Recruitments Sourced from Page 4	0	0	0
C. Staff allocated from other area Sourced from Page 5		60.5	11,035
(i) Sub-Total		60.5	11,035
Less:			
D. Separations Sourced from Page 6	0	0	0
E. Staff allocated to other area Sourced from Page 7	0	0	0
(ii) Sub-Total	0	0	0
(i)-(ii) TOTAL		60.5	* 11,035

*Agrees with Page 1 A/C No.3100 Column D

MANPOWER-ALLOCATED FROM OTHER AREA (LOCAL STAFF)-1986

Job Designation	Level	Budget Code of Other area	No. of Posit.	No.of Man Months	**Rate Per Month	$ Amount
Dr. M.U. Khan (P.I.)	?	010100	1			2,400
Nurur Rahman (FRO)	GS5	061001	1	3	230	690
Health Asst.	GS3	061001	4	48	140	6,720
Programmer	GS5	060901	1	.5	230	115
Secretary Gr.II	GS5	010100	1	3	230	690
Data Entry Techn.	GS3	061001	1	1	140	140
Coding Asst	GS3	061001	1	2	140	280
		TOTAL	* 60.5			* 11,035

** computer printout for average rate per month.

* AGREES WITH PAGE 2 ROW C

Budget/BG.5

SUPPLIES AND MATERIALS-1986

A/C Code	Item Description	$ Amount
3701	Drugs (used for medication in the hospitals and field stations)	500
3702	Glassware (Bottle, beaker, cylinder, petridish, aluminium seal, slides, stopper, tube etc.)	-
3703	Hospital Supplies (bandage, gauze, blade, bowl, catheter, colton, needle, syringe, solution, leukoplast, towel etc.)	100
3704	Stationery and Office Supplies (Battery, book register, binders, files, pencil, fastener, paper, ribbon, stapler etc.)	200
3705	Chemicals and Media (Acid, reagent, dextrose, sodium, bactoagar etc.)	-
3706	Materials for Uniform (Cloth, button etc. required for making uniforms)	-
3707	Fuel, Oil and Lubricants (Diesel, mobil, petrol, Kerosene etc.)	-
3708	Laboratory Supplies (Aluminium foil, bag, blade, brush, cap, container, film X-Ray etc.)	150
3709	Housekeeping Supplies (Aerosol, battery, wiping cloth, duster, lock and key etc.)	-
3710	Janitorial Supplies (Bleaching powder, brush, detol, detergent, insecticide, soap etc.)	-
	(Contd. to Page No. 18)	950

SUPPLIES AND MATERIALS - 1986

(Cont'd. from Page No. 17)

A/C Code	Exp. Description	$ Amount
3711	Tools and Spares (Automobile spares, tyres, tubes, battery, stores required for maintenance services etc.)	-
3712	Non stock Supplies (Materials not normally kept in stock and purchased only against specific requisitions)	-
	Sub-Total	950
3713	Freight and other Charges Add 30% to above sub-total	285
	TOTAL	1,235

AGREES WITH PAGE 1 A/C 3700 COLUMN D

Note: For rates please contact Supply Ext.260 (add 10% to rates for inflation)

Budget86 1%

OTHER COST-1986

A/C Code	Accounts Description	$ Amount
3800	Repairs and Maintenance (Maintenance and repairs of vehicles, equipments, furniture and building)	-
3900	Post, communication and utilities (Postage, telephone, telegram, electricity etc.)	-
4100	Bank charges	-
4200	Legal and professional expenses (Professional membership fee, legal fee, audit fee etc.)	-
300	Printing and Publication (Printing of forms, books, journals, reports etc.)	300
4400	Entertainment, Hospitality & Donations (Guest house accomodation, donations, hospital food, lunch, refreshment etc.)	-
4500	Service Charges (Porter, labour, washing, laundry and other misc. exp.)	4,000(Routine Baby Taxi) 150(Return rickshaw)
4600	Staff Development and Training (Training course fee, training materials, stipend, scholarship, subsistance paid to the staff)	-
	TOTAL	4,450

AGREES WITH PAGE 1 A/C No.3800 COLUMN D

**INTERDEPARTMENTAL SERVICES-1986

A/C Code	Service Area	$ Amount
4801	Computer	500
4802	Transport Dhaka	-
4803	Transport Matlab	-
4804	Water Transport-Matlab	-
4805	Transport Teknaf	-
4806	Xerox and Mimeograph	100
4807	Pathology	-
4808	Microbiology Tests	-
4809	Biochemistry	2,800 (Vit A levels) 175 (Pregnency test)
4810	X Ray	-
4811	I.V. Fluid	-
4812	Medical	-
4813	Patient hospitalisation study	-
4814	Animal Research	-
4815	Medical Illustration	-
4817	Telex	-
4818	Out Patient care	75
4830	Transport Subsidy	-
	TOTAL	* 3,650

** See annexure B for rates.

*AGREES WITH PAGE 1 A/C 4800 COLUMN D

CONSENT FORM

Deficiency of Vit A is associated with increased child mortality, increased morbidity form diarrhoeal and respiratory disease, malnutrition and blindness. ICDDR,B intends to estimate whether Vit A level in Bangladesh infants drops below normal after diarrhoea and how long Vit A level can be kept normal by supplying it to infants. In addition whether Vit A protects infants from diarrhoea, respiratory disease, malnutrition and night blindness will be observed. ICDDR,B will require 2 ml of blood three times: after diarrhoea and after three and six months. Iron, folic acid and DPT injections will be provided free to the infants. Mothers participating will also receive three doses of TT injections. Treatment for diarrhoea, skin infection and fever will be provided. ICDDR,B teams (a male and a female) will visit your family twice a month for one to two years for observation and anthropometry of children. Please sign your name or put LTI if you agree to cooperate with the ICDDR,B's research activity for greater humanaterian benefit. Your disagreement will not affect receiving treatment for diarrhoea from ICDDR,B.

Name: _____ _____

Signature or LTI ____ _____

Date : _____ _____

সম্মতিপত্র

শরীরে ভিটামিন "এ" এর ঘাটতি শিশুমৃত্যুহার, ডাইরিয়া ও শ্বাসতন্ত্রের রোগের প্রকোপ বৃদ্ধি ও অন্ধত্বের সাথে সম্পর্কিত। ডাইরিয়ার পর বাংলাদেশী শিশুদের ভিটামিন "এ" র পরিমান কমে যায় কিনা এবং এটা একবার খাওয়ানোর পর কতদিন শিশুদের শরীরে ভিটামিন "এ" স্বাভাবিক রাখতে পারে আই,সি,ডি,ডি,আর,বি তা জানতে চায়। এর আগে ভিটামিন এ শিশুদেরকে ডাইরিয়া, শ্বাসতন্ত্রের রোগ এবং অন্ধত্ব থেকে রক্ষা করতে পারে কিনা তাও পরীক্ষা করা হবে। এর জন্য ডাইরিয়ার পর, তিনমাস এবং ছয়মাস পর ২(দুই) মিলিলিটার করে ৩(তিন)বার প্রয়োজন হবে। আয়রন, ফলিকএসিড, এবং ডি,পি,টি, ইনজেকশন শিশুদেরকে বিনামূল্যে দেওয়া হবে। অংশগ্রহনকারী মায়েরাও টি,টি ইনজেকশন পাবেন। প্রয়োজনে অনুসারে ডাইরিয়া, হাম রোগ, জ্বর, ইত্যাদি ও চিকিৎসা করা হবে। আই,সি,ডি,ডি,আর,বি টিম (একজন পুরুষ ও একজন মহিলা) মাসে দুইবার করে এক থেকে দুই বৎসর পর্যন্ত আপনার পরিবার পরিদর্শন করবে এবং বাচ্চাদের উচ্চতা, ওজন ইত্যাদি নিবে। বৃহত্তর মানবতার কল্যানে আই,সি,ডি,ডি আর,বির এই গবেষনায় আপনার এই অংশ গ্রহনে রাজী থাকলে নীচে দস্তখত এবং বাম হাতের বৃদ্ধাঙ্গুলীর ছাপ (টিপসহি) দিন। আপনি অংশ গ্রহন না করলেও ডাইরিয়ার চিকিৎসা থেকে বঞ্চিত হবেন না। অংশ গ্রহন করলেও আপনি ইহা প্রত্যাহার করতে পারেন।

নাম _____

দস্তখত এবং
টিপসহি

তারিখ _____

শিশুর নাম _____