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CSD
2001

Memorandum

10 July 2002

To : Dr. KMA Jamil
Senior Medical Officer, Clinical Sciences Division

From: Professor Mahmudur Rahman
Chairman, Ethical Review Committee (ERC)

Sub : Approval of the modified version of the protocol # 2001-028

Thank you for your memo of 3rd July 2002 with the modified version of your protocol # 2001-028 entitled "A pilot study to assess antioxidant status in health and malnourished Bangladeshi children". The modified version of the protocol is hereby approved.

You shall conduct the study according to the ERC-approved protocol; and shall be responsible for protecting the rights and welfare of the subjects and compliance with the applicable provisions of the ERC Guidelines. You shall also submit report(s) as required under the ERC Guidelines. Relevant excerpt of the ERC Guidelines is attached for your information and guidance.

I wish you all the success in running the above-mentioned study.

Thank you.

Copy: Head, Clinical Sciences Division



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MEMORANDUM

Date: July 3, 2002

To: David A Sack, MD
Chairman, Research Review Committee (RRC)

From: Dr. K.M.A. Jamil
Senior Medical Officer
Clinical Sciences Division *A. Jamil*

Subject : Request to approve the modified version of the Protocol # 2001-028
after incorporation of the addendum approved by RRC and ERC

Please find enclosed a modified version of our Protocol # 2001-028 entitled "A pilot study to assess antioxidant status in healthy and malnourished Bangladeshi children". An addendum to the protocol was approved earlier by RRC and ERC to change the age of the study subjects to a range of six months to three years. This is the final version of the protocol which incorporates the changes mentioned above.

Thank you.

*I have gone through the
protocol (modified version) (inclusion
of children
6 months to 3 years)
it is okay and
may be approved
Dr. Kabir*

RESEARCH PROTOCOL

Protocol No.:

FOR OFFICE USE ONLY

RRC Approval: Yes/ No Date: _____

ERC Approval: Yes/No Date: _____

AEEC Approval: Yes/No Date: _____

Project Title: A pilot study to assess antioxidant status in healthy and malnourished Bangladeshi children

Theme: (Check all that apply)

- | | |
|---|--|
| <input checked="" type="checkbox"/> Nutrition | <input type="checkbox"/> Environmental Health |
| <input type="checkbox"/> Emerging and Re-emerging Infectious Diseases | <input type="checkbox"/> Health Services |
| <input type="checkbox"/> Population Dynamics | <input type="checkbox"/> Child Health |
| <input type="checkbox"/> Reproductive Health | <input type="checkbox"/> Clinical Case Management |
| <input type="checkbox"/> Vaccine evaluation | <input type="checkbox"/> Social and Behavioural Sciences |

Key words: Antioxidant status, malnutrition, kwashiorkor

Principal Investigator: K.M.A. Jamil, M.B.B.S., Ph.D., Clinical Sciences Division, ICDDR,B, Mohakhali, Dhaka 1212, Bangladesh. Tel. 880-2-8811751 Ext 2333 Fax: 880-2-8823116, E-mail: jamil@icddr.org

Co-Investigator(s):
 1. Tahmeed Ahmed, M.B.B.S., Ph.D. ICDDR,B
 2. Kenneth H. Brown, M.D., UC Davis, U.S.A.
 3. Carl Keen, Ph.D., UC Davis, U.S.A.

Collaborating Institute(s): University of California Davis, U.S.A.

Population: Inclusion of special groups (Check all that apply):

- | | |
|---|--|
| Gender | <input type="checkbox"/> Pregnant Women |
| <input checked="" type="checkbox"/> Male | <input type="checkbox"/> Fetuses |
| <input checked="" type="checkbox"/> Females | <input type="checkbox"/> Prisoners |
| Age | <input type="checkbox"/> Destitutes |
| <input type="checkbox"/> 0 – 5 years | <input type="checkbox"/> Service providers |
| <input type="checkbox"/> 5 – 9 years | <input type="checkbox"/> Cognitively Impaired |
| <input type="checkbox"/> 10 – 19 years | <input type="checkbox"/> CSW |
| <input type="checkbox"/> 20 + | <input checked="" type="checkbox"/> Others: 6 mo – 3 years |
| <input type="checkbox"/> > 65 | <input type="checkbox"/> Animal |

Project / study Site (Check all the apply):

- | | |
|--|--|
| <input checked="" type="checkbox"/> Dhaka Hospital | <input type="checkbox"/> Mirsarai |
| <input type="checkbox"/> Matlab Hospital | <input type="checkbox"/> Patyia |
| <input type="checkbox"/> Matlab DSS area | <input type="checkbox"/> Other areas in Bangladesh _____ |
| <input type="checkbox"/> Matlab non-DSS area | <input type="checkbox"/> Outside Bangladesh |
| <input type="checkbox"/> Mirzapur | name of country: _____ |
| <input type="checkbox"/> Dhaka Community | <input type="checkbox"/> Multi centre trial |
| <input type="checkbox"/> Chakaria | (Name other countries involved) |
| <input type="checkbox"/> Abhoynagar | _____ |

Revised on: July3, 2002

Type of Study (Check all that apply):

- | | |
|---|---|
| <input type="checkbox"/> Case Control study | <input type="checkbox"/> Cross sectional survey |
| <input type="checkbox"/> Community based trial / intervention | <input type="checkbox"/> Longitudinal Study (cohort or follow-up) |
| <input type="checkbox"/> Program Project (Umbrella) | <input type="checkbox"/> Record Review |
| <input type="checkbox"/> Secondary Data Analysis | <input type="checkbox"/> Prophylactic trial |
| <input type="checkbox"/> Clinical Trial (Hospital/Clinic) | <input type="checkbox"/> Surveillance / monitoring |
| <input type="checkbox"/> Family follow-up study | <input checked="" type="checkbox"/> Others: Pilot |

Targeted Population (Check all that apply):

- | | |
|---|--------------------------------------|
| <input checked="" type="checkbox"/> No ethnic selection (Bangladeshi) | <input type="checkbox"/> Expatriates |
| <input type="checkbox"/> Bangalee | <input type="checkbox"/> Immigrants |
| <input type="checkbox"/> Tribal groups | <input type="checkbox"/> Refugee |

Consent Process (Check all that apply):

- | | |
|---|--|
| <input checked="" type="checkbox"/> Written | <input checked="" type="checkbox"/> Bengali language |
| <input checked="" type="checkbox"/> Oral | <input type="checkbox"/> English language |
| <input type="checkbox"/> None | |

Proposed Sample size:

Total sample size: 40

Sub-group Kwashiorkor=20 Marasmus=10

Age- and sex-matched/healthy controls=10 _____

Determination of Risk: Does the Research Involve (Check all that apply):

- | | |
|---|---|
| <input type="checkbox"/> Human exposure to radioactive agents? | <input type="checkbox"/> Human exposure to infectious agents? |
| <input type="checkbox"/> Fetal tissue or abortus? | <input type="checkbox"/> Investigational new drug |
| <input type="checkbox"/> Investigational new device?
(specify _____) | <input type="checkbox"/> Existing data available via public archives/source |
| <input type="checkbox"/> Existing data available from Co-investigator | <input checked="" type="checkbox"/> Pathological or diagnostic clinical specimen only |
| | <input type="checkbox"/> Observation of public behaviour |
| | <input type="checkbox"/> New treatment regime |

Yes/No

Is the information recorded in such a manner that subjects can be identified from information provided directly or through identifiers linked to the subjects?

Does the research deal with sensitive aspects of the subject's behaviour; sexual behaviour, alcohol use or illegal conduct such as drug use?

Could the information recorded about the individual if it became known outside of the research:

a. place the subject at risk of criminal or civil liability?

b. damage the subject's financial standing, reputation or employability; social rejection, lead to stigma, divorce etc.

Do you consider this research (Check one):

- | | |
|--|---|
| <input type="checkbox"/> greater than minimal risk | <input checked="" type="checkbox"/> no more than minimal risk |
| <input type="checkbox"/> no risk | <input type="checkbox"/> only part of the diagnostic test |

Minimal Risk is "a risk where the probability and magnitude of harm or discomfort anticipated in the proposed research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical, psychological examinations or tests. For example, the risk of drawing a small amount of blood from a healthy individual for research purposes is no greater than the risk of doing so as a part of routine physical examination".

Yes/No

Is the proposal funded?

If yes, sponsor Name: NIH-Fogarty International Center

No

Is the proposal being submitted for funding ?

If yes, name of funding agency: (1) _____

(2) _____

Do any of the participating investigators and/or their immediate families have an equity relationship (e.g. stockholder) with the sponsor of the project or manufacturer and/or owner of the test product or device to be studied or serve as a consultant to any of the above? No

IF YES, submit a written statement of disclosure to the Director.

Dates of Proposed Period of Support

(Day, Month, Year - DD/MM/YY)

Beginning date 01/03/2002

End date 31/08/2002

Cost Required for the Budget Period (\$)

a. *1st Year 2nd Year 3rd Year Other years*

\$3,000 _____

b. *Direct Cost : \$3,000 Total Cost : \$3,000*

Approval of the Project by the Division Director of the Applicant

The above-mentioned project has been discussed and reviewed at the Division level as well by the external reviewers. The protocol has been revised according to the reviewer's comments and is approved.

Name of the Division Director

Signature

Date of Approval

Certification by the Principal Investigator

I certify that the statements herein are true, complete and accurate to the best of my knowledge. I am aware that any false, fictitious, or fraudulent statements or claims may subject me to criminal, civil, or administrative penalties. I agree to accept responsibility for the scientific conduct of the project and to provide the required progress reports if a grant is awarded as a result of this application.

Signature of PI

Date:

Name of Contact Person (if applicable)

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Check here if appendix is included

PROJECT SUMMARY: Describe in concise terms, the hypothesis, objectives, and the relevant background of the project. Describe concisely the experimental design and research methods for achieving the objectives. This description will serve as a succinct and precise and accurate description of the proposed research is required. This summary must be understandable and interpretable when removed from the main application. (TYPE TEXT WITHIN THE SPACE PROVIDED).

Principal Investigator: Kazi Mohammad Asif Jamil

Project Name: A pilot study to assess antioxidant status in healthy and malnourished Bangladeshi children

Total Budget : US\$ 3,000

Beginning Date: March 1, 2002

Ending Date: Aug 31, 2002

Protein-energy malnutrition (PEM) remains one of the major health problems of children in developing countries. Edematous malnutrition or kwashiorkor is one of the most severe forms of malnutrition with a high risk of mortality and morbidity. Although kwashiorkor is classically described as a form of protein-energy malnutrition, there is much controversy as to the mechanism of edema formation in kwashiorkor. Recently conducted studies suggest that hypoproteinemia alone may not be sufficient to cause kwashiorkor. It has been proposed that generation of toxic free radicals inside the body during infections causes injury to the cell membranes and makes them leaky leading to the development of edema (the 'free radical theory'). The hypothesis has important clinical implications as it suggests a possible role of antioxidants in the management of kwashiorkor. Supplementation with a high protein diet during acute phase illness has reportedly caused an increase in mortality in severely malnourished children. Thus a careful approach is warranted to assess the need for any additional supplementation in this vulnerable group to improve the management of this condition. The proposed pilot study is designed to gather information on three different indicators of oxidative stress/antioxidant status of children with edematous malnutrition. The subjects will consist of twenty children with kwashiorkor, ten with marasmus, and ten age- and sex-matched healthy controls. Antioxidant status of the subjects will be assessed by measuring total plasma antioxidant capacity, concentration of lipid peroxides in plasma, and erythrocyte superoxide dismutase (SOD). The data obtained from this study will be analyzed to assess any need for antioxidant supplementation and also to estimate the sample size if intervention with antioxidants is warranted.

KEY PERSONNEL (List names of all investigators including PI and their respective specialties)

Name	Professional Discipline/ Specialty	Role in the Project
1. K.M.A. Jamil	Senior Medical Officer, ICDDR,B/Nephrology; nutrition	PI
2. Tahmeed Ahmed	Associate Scientist, ICDDR,B/Nutrition; child health	Co-investigator
3. Kenneth H. Brown	Professor, UC Davis/Nutrition	Co-investigator
4. Carl Keen	Professor, UC Davis/Nutrition	Co-investigator

DESCRIPTION OF THE RESEARCH PROJECT

Hypothesis to be tested:

Concisely list in order, in the space provided, the hypothesis to be tested and the Specific Aims of the proposed study. Provide the scientific basis of the hypothesis, critically examining the observations leading to the formulation of the hypothesis.

The antioxidant status in children with edematous malnutrition is significantly poorer than in marasmic and healthy children of similar age and sex.

Specific Aims:

Describe the specific aims of the proposed study. State the specific parameters, biological functions/ rates/ processes that will be assessed by specific methods (TYPE WITHIN LIMITS).

In order to assess antioxidant status in edematous malnutrition, the following will be measured in and compared between children with edematous malnutrition, non-edematous malnutrition (marasmus), and healthy children:

1. Total antioxidant capacity of plasma
2. Lipid peroxidation in plasma
3. Erythrocyte superoxide dismutase

Background of the Project including Preliminary Observations

Describe the relevant background of the proposed study. Discuss the previous related works on the subject by citing specific references. Describe logically how the present hypothesis is supported by the relevant background observations including any preliminary results that may be available. Critically analyze available knowledge in the field of the proposed study and discuss the questions and gaps in the knowledge that need to be fulfilled to achieve the proposed goals. Provide scientific validity of the hypothesis on the basis of background information. If there is no sufficient information on the subject, indicate the need to develop new knowledge. Also include the **significance and rationale** of the proposed work by specifically discussing how these accomplishments will bring benefit to human health in relation to biomedical, social, and environmental perspectives. (DO NOT EXCEED 5 PAGES, USE CONTINUATION SHEETS).

Protein-energy malnutrition (PEM) is one of the major health problems of children in developing countries. The case-fatality rate for severely malnourished children remains unacceptably high despite all the recent advancements in medicine (Ahmed, 1999). Faulty case management including a high protein diet during acute phase illness has reportedly caused an increase in mortality in severely malnourished children (Schofield et al, 1996). Classically, PEM was described to be of two types, edematous (kwashiorkor) and non-edematous (marasmus) although the two types can overlap (marasmic-kwashiorkor). There is much controversy regarding the pathogenesis of edematous malnutrition. The classical 'protein deficiency theory' describes hypoalbuminemia as the major cause of kwashiorkor (Waterlow, 1984; Jackson, 1990), while the more recent 'free radical theory' claims that kwashiorkor results from an imbalance between the production of free radicals and their safe disposal (Golden, 1998).

Hypoalbuminemia and PEM

Prospective studies on children in Uganda showed that a fall in plasma albumin preceded the development of edema (Frood et al., 1971; Whitehead et al., 1973). These observations were fairly consistent with Starling's classical theory that linked edema to hypoalbuminemia through a reduction in colloid osmotic pressure of plasma (COP). Coward (1975) showed that children in Uganda with low serum albumin concentrations did indeed have a decrease in serum COP, which was roughly, but not linearly, related to the degree of edema. Hypoalbuminemia, on the other hand, may occur without edema, as in congenital analbuminemia (Bearn and Litwin, 1978; Joles et al, 1989). A very strong argument against the 'protein

deficiency theory' is based on the lack of correlation between edema and albumin level in response to treatment. Hansen (1956) found that the edema of kwashiorkor could disappear completely on a protein-free diet containing only glucose and a salt mixture that included potassium. Gopalan (1968) reported a prospective study on diets of some 2000 village children in India, of whom about 1.5 per cent developed kwashiorkor and a somewhat higher proportion marasmus. No quantitative or qualitative differences were found in the diets of these two groups of children. Golden et al (1980) observed that on treatment edema disappeared without any increase in plasma albumin concentration. In another study they examined the rate of disappearance of edema in children fed a number of different diets and found that the rate of loss of edema was significantly related to the energy intake and not at all to protein intake (Golden, 1982).

Endogenous antioxidants and plasma iron in PEM

Vitamin E and β -carotene are two important dietary antioxidants, and deficiency of these has been documented in PEM (McLaren and Shirajian, 1969; Mathias, 1983). Children with kwashiorkor had lower plasma carotene levels than those with marasmus, which could be due to a greater destruction of carotene by free radicals rather than a difference in intake (Golden and Ramdath, 1987). A very recent study showed that the plasma levels of vitamins C, A, and E were all significantly lower in severely malnourished children than in controls (Ashour, 1999)

In malnourished children, especially in kwashiorkor, plasma iron concentrations were reported to be either normal or elevated (Golden and Ramdath, 1987). A significant concentration of free or loosely bound iron has been observed in severely edematous children using the bleomycin-detectable iron (BDI) technique (Dempster et al, 1995; Ashour MN et al, 1999). This free iron can act as a redox catalyst and add to the oxidative stress already present in these severely malnourished children, especially in those with kwashiorkor.

The 'free radical theory'

According to Golden's hypothesis, the cell membrane in kwashiorkor becomes 'leaky' as a result of a variety of environmental insults, termed by Golden as 'noxae', which increase the production of free radicals. The most important noxae are infections, which are well known to precipitate the onset of kwashiorkor, and particular emphasis is laid on bacterial overgrowth in the bowel producing numerous toxic products. Jackson (1986) demonstrated that the glutathione content of red cells was greatly reduced in kwashiorkor but not in marasmus. These observations were confirmed and extended by Golden and Ramdath (1987). Free radicals and their products react with reduced GSH to produce oxidized glutathione (GSSG) by the catalytic action of glutathione peroxidase (GPX). The activity of GPX in erythrocytes is often reduced in severe PEM, to a greater extent in edematous than in non-edematous cases. Reduced glutathione is regenerated from its oxidized form by a reaction coupled with oxidation of NADPH. Erythrocyte NADPH was found to be very low in kwashiorkor and marasmic kwashiorkor but not in marasmus (Golden and Ramdath, 1987; Golden et al, 1991).

The free radical theory has received much attention not only because it provides new clue to the pathogenesis of severe PEM, especially edematous malnutrition, but also because it may have important implications for treatment. The present study has therefore been designed to assess the antioxidant status of Bangladeshi children with edematous malnutrition; the study may provide guidelines for a role of antioxidant supplementation in the treatment of this condition. Antioxidant status will also be determined in healthy control children of similar age and sex.

Research Design and Methods

Describe in detail the methods and procedures that will be used to accomplish the objectives and specific aims of the project. Discuss the alternative methods that are available and justify the use of the method proposed in the study. Justify the scientific validity of the methodological approach (biomedical, social, or environmental) as an investigation tool to achieve the specific aims. Discuss the limitations and difficulties of the proposed procedures and sufficiently justify the use of them. Discuss the ethical issues related to biomedical and social research for employing special procedures, such as invasive procedures in sick children, use of isotopes or any other hazardous materials, or social questionnaires relating to individual privacy. Point out safety procedures to be observed for protection of individuals during any situations or materials that may be injurious to human health. The methodology section should be sufficiently descriptive to allow the reviewers to make valid and unambiguous assessment of the project. (DO NOT EXCEED TEN PAGES, USE CONTINUATION SHEETS).

Study design: Descriptive study

Methods:

Patient selection

A total of twenty patients with edematous malnutrition attending the ICDDR,B Dhaka Hospital for treatment of diarrhea and other associated illnesses will be selected for the study. Since most children admitted in ICDDR,B hospital receive complementary feeding in addition to breast milk, subjects who are partially-breastfed will be selected for the study. In addition, ten children with marasmus and ten healthy children will also be studied. Healthy controls will be selected from children attending the immunization or nutrition follow-up clinic. The inclusion criteria of the subjects will be as follows:

1. All subjects should be within the age range of six months to three years. *6 months to 36 mo?*
2. All subjects should be partially breast-fed. *< how many children from 24-36 month will cont. BM*
3. Cases with edematous malnutrition should have bilateral pedal edema without any evidence of renal insufficiency.
4. Cases with marasmus should have a Z-score of -3 or less on the basis of weight-for-height.

The exclusion criteria will be as follows:

1. Children with major congenital anomalies like Down's syndrome, etc.
2. Critically ill patients with irreversible shock, uncontrollable seizure, or coma.

An informed consent will be obtained from the parent/legal guardian of the subjects before enrollment into the study.

The present study has been designed to obtain baseline data on antioxidant status of the population under investigation. The sample of forty subjects including cases and controls is expected to provide valuable data needed for a subsequent intervention trial with antioxidants. The required sample size for the intervention trial will be calculated from data obtained from this pilot study.

Blood collection

5 ml of blood will be drawn from each subject just before feeding ensuring at least two hours of interval between the previous feed and the time of blood collection. The sample will then be prepared and stored for the measurement of total antioxidant capacity (TAC), RBC superoxide dismutase (SOD), and lipid peroxidation products (TBARS). The blood samples will be carried to the Department of Nutrition of the University of California Davis where the tests will be carried out.

Measurement of total antioxidant capacity of plasma

The total radical trapping potential (TRAP) in the samples will be determined by using a method developed by Wayner et al (1985). It is based on the measurements of induction times in the oxidation of a lipid dispersion exposed to a free radical source with a constant rate of free radical production in aerobic

conditions. 2,2-azo-bis (2-amidinopropane) (ABAP) is used as the free radical source, and the decrease in oxygen concentration is used to measure the oxidation rate.

Measurement of erythrocyte superoxide dismutase (SOD)

Whole blood will be centrifuged at 1800 g and plasma removed and frozen for other use. RBC in precipitate will be used for the measurement of SOD following the procedure of Marklund (1974). This assay relies on the auto-oxidation of pyrogallol under basic conditions. Briefly, pyrogallol is added to a basic buffer solution with the hemolysate sample containing RBC SOD. The pyrogallol auto-oxidizes forming a yellow product with an absorbance maximum at 420 nm. Depending on how much RBC SOD is contained in the sample and the amount of sample added, the auto-oxidation of pyrogallol will be inhibited to different degrees. One unit of SOD activity is defined as the amount of sample needed to inhibit the pyrogallol auto-oxidation by 50% and is expressed per mg hemoglobin. Therefore, hemoglobin concentration must also be determined on the hemolysate.

Assessment of lipid peroxidation

Peroxidation of lipids will be assessed by the analysis of malonaldehyde-thiobarbituric acid adduct following reaction of sample with thiobarbituric acid (Yagi et al, 1989).

Facilities Available

Describe the availability of physical facilities at the place where the study will be carried out. For clinical and laboratory-based studies, indicate the provision of hospital and other types of patient's care facilities and adequate laboratory support. Point out the laboratory facilities and major equipments that will be required for the study. For field studies, describe the field area including its size, population, and means of communications. (TYPE WITHIN THE PROVIDED SPACE).

ICDDR,B Dhaka Hospital is located in a busy urban area and provides medical care to patients of all ages who present with diarrhea and its complications. A large number of malnourished children visit the hospital every day and they are treated not only for diarrhea but are also provided treatment and rehabilitation services for the management of malnutrition as well. ICDDR,B is thus an ideal place for conducting the present study for which children with edematous malnutrition will need to be recruited. In addition to its clinical service facility, ICDDR,B also has standard laboratory facilities where basic clinical tests and procedures can be carried out by trained staff who are available round the clock. The laboratory staff can ensure proper processing and storage of clinical specimens until they are used for experiments.

The University of California Davis is a part of the University of California System which is globally recognized for its excellence in education and research. The Nutrition Department of UC Davis has a collaborative arrangement with ICDDR,B and provides training to its staff at various levels. A number of research projects on vitamin A have been successfully completed as a joint venture between the two institutions in the recent years. The blood samples of the study subjects will be sent to UC Davis for the assessment of total antioxidant capacity, lipid peroxides and erythrocyte SOD which will be carried out by the PI who is now working at UC Davis as a postdoctoral fellow. The laboratory of UC Davis has all technical facility for conducting the experiments.

Data Analysis

Describe plans for data analysis. Indicate whether data will be analyzed by the investigators themselves or by other professionals. Specify what statistical softwares packages will be used and if the study is blinded, when the code will be opened. For clinical trials, indicate if interim data analysis will be required to monitor further progress of the study. (TYPE WITHIN THE PROVIDED SPACE).

Group means will be compared by the investigators using analysis of variance to determine whether the antioxidant status in the cases and the controls vary significantly in respect of their total antioxidant capacity, lipid peroxides and erythrocyte SOD levels. Variables will be assessed for conformance to the normal distribution and transformed as necessary; if no suitable transformation works, then non-parametric procedures will be used. SPSS for Windows will be used for data analysis. Level of significance will be 0.05.

Ethical Assurance for Protection of Human Rights

Describe in the space provided the justifications for conducting this research in human subjects. If the study needs observations on sick individuals, provide sufficient reasons for using them. Indicate how subject's rights are protected and if there is any benefit or risk to each subject of the study.

This study is aimed at elucidating the role of oxidative stress in the pathogenesis and progression of edematous malnutrition. Experimental and observational data suggest a causative role of oxidant injury in the pathogenesis of kwashiorkor. It is therefore extremely important to determine the baseline antioxidant status in children with edematous malnutrition and in healthy controls. The results of this study will provide important information as to the need for antioxidant supplementation in this vulnerable group. Only 5 ml of blood will be drawn from each child which is not expected to cause any harm other than pain inflicted by any venepuncture during clinical assessment of the patient. An informed consent will be obtained from the parent/guardian of the subjects before blood collection and standard aseptic precaution will be followed during the procedure. Blood will not be drawn from any child whose parent/guardian refuses to give consent; treatment, immunization, or nutritional counseling, however, will be provided to all children.

Use of Animals

Describe in the space provided the type and species of animal that will be used in the study. Justify with reasons the use of particular animal species in the experiment and the compliance of the animal ethical guidelines for conducting the proposed procedures.

No animals will be used for this study.

Literature Cited

Identify all cited references to published literature in the text by number in parentheses. List all cited references sequentially as they appear in the text. For unpublished references, provide complete information in the text and do not include them in the list of Literature Cited. There is no page limit for this section, however exercise judgment in assessing the "standard" length.

1. Ahmed, T., Fuchs, G. J. et al. (1999). Mortality in severely malnourished children with diarrhoea and use of a standardised management protocol. *Lancet* 353: 1919 – 22.
2. Ashour MN, Salem SI, El-Gadban HM, Elwan NM, and Basu TK. (1999). Antioxidant status in children with protein-energy malnutrition (PEM) living in Cairo, Egypt. *Eur J Clin Nutr* 52: 669 – 673.
3. Beam, A. G., Litwin, S. G. (1978). Deficiencies of circulating enzymes and plasma proteins. In Stanbury, J. B., Wyngaarden, J. B., Frederickson, D. S. (eds) *The metabolic basis of inherited disease*. McGraw Hill, New York, pp. 1712 - 1725.
4. Coward, W. A. (1975). Serum colloidal osmotic pressure in the development of kwashiorkor and in recovery: its relationship to albumin and globulin concentrations and oedema. *Brit J Nutr* 34: 459 - 467.
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6. Frood, J. D. L., Whitehead, R. G., Coward, W. A. (1971). Relationship between pattern of infection and development of hypoalbuminaemia and hypo- β -lipoproteinaemia in rural Ugandan children. *Lancet* 2: 1047 - 1049.
7. Golden, M H N, Golden B E, Jackson A A. (1980). Albumin and nutritional edema. *Lancet* 1: 114 - 116.
8. Golden MH. (1982). Protein deficiency, energy deficiency, and the oedema of malnutrition. *Lancet* 1: 1261 –1265.
9. Golden, M. H. N., Ramdath, D. (1987). Free radicals in the pathogenesis of kwashiorkor. *Proc Nutr Soc* 46: 53 - 68.
10. Golden, M. H. N., Ramdath, D. D., Golden, B. E. (1991). Free radicals and malnutrition. In Dreosti, I. E. (ed) *Trace elements, micronutrients and free radicals*. Humana Press, Clifton, New Jersey.
11. Golden, M H N. (1998). Oedematous Malnutrition. *Brit Med Bul* 54: 433 - 444.
12. Gopalan, C. (1968). Kwashiorkor and marasmus. Evolution and distinguishing features. In McCanne RA, Widdowson EM (eds) *Calorie deficiencies and protein deficiencies*. Churchill, London, pp. 49 – 58.
13. Hansen, J. D. L. (1956). Electrolyte and nitrogen metabolism in kwashiorkor. *S Afr J Lab Clin Med* 2: 206 - 231.
14. Jackson AA. (1986). Blood glutathione in severe malnutrition in childhood. *Trans R Soc Trop Med Hyg* 80: 911 - 913.

15. Jackson AA. (1990). The aetiology of kwashiorkor. *In* Harrison GA, Waterlow JC (eds) *Diet and disease in traditional and developing societies*. Cambridge University Press, pp. 76.- 113.
16. Joles, J. A., Jansen, E. H.J. M. et al. (1989). Plasma proteins in growing analbuminemic rats fed on a diet of low protein content. *Brit J Nutr* 61: 485 - 495.
17. McLaren, D.S., Shirajian, E. (1969). Short-term prognosis in protein-calorie malnutrition. *Am J Clin Nutr* 22: 863 - 870.
18. Marklund and Marklund. (1974). Involvement of the superoxide anion radical in the autooxidation of pyrogallol and a convenient assay for superoxide dismutase. *Eur J Biochem* 47: 469 - 479.
19. Mathias, P. M. (1983). Vitamin status of children during recovery from severe malnutrition. *Proc Nutr Soc* 41: 143A.
20. Schofield, C., Ashworth, A. (1996). Why have mortality for severe malnutrition remained so high? *Bull World Health Organ* 74: 223 - 229.
21. Waterlow, J. C. (1984). Kwashiorkor revisited: the pathogenesis of oedema in kwashiorkor and its significance. *Trans R Soc Trop Med Hyg* 78: 436 - 441.
22. Wayner, D.D.M., Burton, G.W., Ingold, K.U., Locke, S. (1985). Quantitative measurement of the total peroxy-radical trapping antioxidant capability of human blood plasma by controlled lipid peroxidation. *FEBS Letters* 187: 33 - 37.
23. Whitehead, R. G., Coward, W. A., Lunn, P. G. (1973). Serum albumin concentration and the onset of kwashiorkor. *Lancet* 1: 63 - 66.
24. Yagi K. (1989). A simple fluorometric assay for lipid peroxides in blood serum or plasma. *In* Miguel J, Quintnilha AT and Weber H (eds) *CRC Handbook of Free Radicals and Antioxidants in Biomedicine*, vol.3, pp. 215 -218. Boca Raton, FL: CRC Press.

Dissemination and Use of Findings

Describe explicitly the plans for disseminating the accomplished results. Describe what type of publication is anticipated: working papers, internal (institutional) publication, international publications, international conferences and agencies, workshops etc. Mention if the project is linked to the Government of Bangladesh through a training programme.

The results of this study will be reported in relevant scientific seminars and meetings and published in regional and international journals. The results of the study will prove or refute the causal association between oxidative stress and edematous malnutrition. If the association is proved, then the data from this pilot study will be used to design an anti-oxidant intervention trial for the management of edematous malnutrition in children.

Collaborative Arrangements

Describe briefly if this study involves any scientific, administrative, fiscal, or programmatic arrangements with other national or international organizations or individuals. Indicate the nature and extent of collaboration and include a letter of agreement between the applicant or his/her organization and the collaborating organization. (DO NOT EXCEED ONE PAGE)

This is a collaborative proposal with the University of California at Davis. The PI is currently doing postdoctoral training at Davis. The PI will perform the assays at Davis. If in any case time is not sufficient enough for performing the assays, the co-investigators from Davis will make efforts for arranging an assay set-up in the Centre. The expense for this pilot study will be borne from a Fogarty grant.

Biography of the Investigators

Give biographical data in the following table for key personnel including the Principal Investigator. Use a photocopy of this page for each investigator.

Present Address: Clinical Sciences Division, ICDDR,B
Mohakhali, Dhaka-1212, Bangladesh
Tel. 880-2-8811751 Ext 2333
E-mail: jamil@icddr.org

- 1 Name : Kazi Mohammad Asif Jamil
- 2 Present position : Senior Medical Officer Grade II
- 3 Educational background :
(last degree and diploma & training relevant to the present research proposal)
 - March 1988 : Passed M.B.B.S. (Bachelor of Medicine and Surgery; equivalent of M.D.) from Chittagong Medical College, Chittagong, Bangladesh.
 - April 1988 – April 1989 : One-year *internship* was completed in Chittagong Medical College Hospital, Chittagong, Bangladesh.
 - May 1989 – Dec 1989 : Served as *Lecturer of Physiology and Biochemistry* at the University of Science and Technology Chittagong (USTC), Pahartoli, Chittagong, Bangladesh.
 - Jan 1990 – Mar 1991 : Enrolled as *Research student* at the University of Tokyo School of Medicine and conducted research related to *renal physiology*.
 - April 1991 – Mar 1995 : Attended *Ph.D. course in Medical Sciences* at the University of Tokyo School of Medicine. The title of doctoral dissertation was “*Mechanisms of Vasopressin VI receptor antagonism*”.
 - June 1995 – May 1997 : Served as Assistant Professor of Medicine and Physiology *at the* University of Science and Technology Chittagong (USTC), Bangladesh.
 - April – July 1997 : Trained as *Clinical fellow in Nephrology* at Toranomon Hospital Kidney Center, Tokyo, Japan.
 - Sep 1997 – Till date : Serving as Senior Medical Officer/Assistant Scientist at Clinical Sciences Division, ICDDR,B, Dhaka, Bangladesh. About half of the working hours are spent for clinical service and the rest for research.

AWARDS:

- 1982 – 1988 : Scholarship in *Talent Pool* during the study of medicine at Chittagong Medical College, Bangladesh
- 1990 – 1995 : Scholarship from the *Ministry of Education, Japan* during graduate study at the University of Tokyo School of Medicine.
- April 1997 – July 1997 : Scholarship from *Japanese Council for Medical Training* for advanced training in nephrology in Toranomon Hospital Kidney Center, Japan.
- 2001 : *NIH-Fogarty Fellowship* for postdoctoral research at University of California, Davis, USA.

4. List of ongoing research protocols
(start and end dates; and percentage of time)

4.1. As Principal Investigator

Protocol Number	Starting date	End date	Percentage of time
99-044	01.01.2000	31.12.2001	20

4.2. As Co-Principal Investigator

Protocol Number	Starting date	End date	Percentage of time

4.3. As Co-Investigator

Protocol Number	Starting date	Ending date	Percentage of time

5 Publications

Types of publications	Numbers
a) Original scientific papers in peer-review journals	3
b) Peer reviewed articles and book chapters	
c) Papers in conference proceedings	2
d) Letters, editorials, annotations, and abstracts in peer-reviewed journals	2
e) Working papers	
f) Monographs	

6 Five recent publications including publications relevant to the present research protocol

1. Expression of platelet activating factor receptor in renal tubular cell line (LLC-PK1). K.M.A.Jamil, T.Takano, A.Nakao, Z.Honda, T. Shimizu, T.Watanabe and K.Kurokawa. *Biochem. Biophys. Res. Commun.* 1992; 187: 767-772.
2. Distinct mechanisms of action of V1 antagonists OPC-21268 and [d(CH₂)₅Tyr(Me)AVP] in mesangial cells. K.M.A.Jamil, T.Watanabe, A.Nakao, T. Okuda and K. Kurokawa. *Biochem. Biophys. Res. Commun.* 1993; 193: 738-743.
3. Low temperature hemodialysis prevents hypotensive episodes by reducing nitric oxide synthesis. *Nephron.* 2000 Mar;84(3):284-6.
4. Response of estimated total body vitamin A stores to daily supplementation with green leafy vegetables or sweet potatoes in healthy Bangladeshi men. Haskell MJ, Jamil KM, Peerson J, Wahed MA, Fuchs GJ, Brown KH. (2001) *FASEB Journal* 15: 228.6 (Abstract)

Biography of the Investigators

1. Name : Dr. Tahmeed Ahmed
2. Present position : Associate Scientist and Coordinator
Child Health Programme
Clinical Sciences Division, ICDDR
3. Educational background : PhD, 1996, University of Tsukuba, Japan
Training in Pediatrics, 1990-92, Department of Pediatrics, University of Tsukuba Hospital, Japan
Training in Pediatrics, 1989-90, Dhaka Shishu (Children's) Hospital, Dhaka
4. List of ongoing research protocols

4.1 As Principal Investigator

Protocol number	Starting date	End date	Percentage of time
99-040	January 2000	December 2001	20
2000-12	January 2001	December 2002	10

4.2 As Co-Principal Investigator

Protocol number	Starting date	End date	Percentage of time
99-042	January 2000	December 2001	20

5. Publications

Type of publication	Number
a) Original scientific papers in peer-reviewed journals	12
b) Peer-reviewed articles and book chapters	2
c) Papers in conference proceedings	15
d) Letters, editorials, annotations, and abstracts in peer-reviewed journals	3
e) Working papers	
f) Monographs	

6. Five recent publications

- 1) Mortality in severely malnourished children with diarrhoea and use of a standardised management protocol. Ahmed T, Ali M, Ullah M, Choudhury I, Haque E, Salam A, Rabbani G, Suskind R, Fuchs G. *Lancet* 1999;353:1919-22.
- 2) Management of severe malnutrition and diarrhea. Ahmed T, Begum B, Badiuzzaman, Ali M, Fuchs G. *Indian J Pediatr* 2001;68(1):45-51.
- 3) Production of safe therapeutic feeds from contaminated water supplies. Roy SK, Seal AJ, Tomkins AM, Shameem T, Islam MS, Ahmed T, Fuchs GJ, Asma A, Parvin N, Begum R. *Lancet* 2001;357:1587-88.
- 4) Gastrointestinal allergy to food: a review. Ahmed T and Fuchs G. *J Diarrhoeal Dis Res* 1997;15:211-223.
- 5) Humoral immune and clinical responses to food antigens following acute diarrhea in children. Ahmed T, Sumazaki R, Shibasaki M, Nagai Y, Shin K, Fuchs GJ, Takita H. *J Paediatr Child Health* 1998;34:229-232.

Biography of the Investigators

Kenneth H. Brown, M.D.

Department of Nutrition, University of California, Davis, California 95616-8669
Telephone No. (916) 752-1992 FAX No. (916) 752-3406 E-Mail: KHBrown@UCDavis.edu (Internet)

Current Appointments

Professor, Department of Nutrition University of California, Davis, California
Director, Program in International Nutrition, University of California, Davis, California

Education

1964-1968 Columbia University, New York, New York - B.A.
1968-1973 University of Pennsylvania, School of Medicine, Philadelphia, Pennsylvania - M.D.

Training and Professional Experience

1973-1975 Internship & Assistant Residency in Pediatrics, Boston Children's Hospital Medical Center, Boston, MA
(Clinical Fellow in Pediatrics, Harvard University School of Medicine)
1975-1977 Research Associate, Departments of Medicine and Pathology, Johns Hopkins University School of Medicine
and Sch. of Hygiene and Public Health, Baltimore, MD (Visiting Scientist, Internatl Center for Medical
Research, and the Cholera Research Laboratory, Dhaka, Bangladesh)
1978-1984 Assistant Professor, Department of Pediatrics, Johns Hopkins University School of Medicine
1980-1985 Visiting Scientist, Instituto de Investigación Nutricional, Lima, Perú
1984-1989 Associate Professor, Dept. of Pediatrics and Dept. of Internal Health School of Hygiene & Pub Hlth, Johns
Hopkins University School of Medicine
1985-1989 Director, Division of Human Nutrition, Department of International Health, Johns Hopkins University School
of Hygiene and Public Health, Baltimore, MD
1989- Professor, Department of Nutrition, University of California, Davis, California
1989- Director, Program in International Nutrition, University of California, Davis, California

PUBLICATIONS: (recent papers selected from a total of more than 180 publications)

1. Brown KH, Peerson JM, Allen LH. Effect of zinc supplementation on childrens growth: A meta-analysis of intervention trials. *Bibliotheca Nutritio et Dieta* 54:76-83, 1998.
2. Rivera JA, Ruel MT, Santizo M-C, Brown KH, Lönnerdal B. Zinc supplementation improves the growth of stunted rural Guatemalan infants. *J Nutr* 128:556-562, 1998.
3. Haskell MJ, Islam MA, Handelman GJ, Peerson JM, Jones AD, Wahed MA, Mahalanabis D, Brown KH. Plasma kinetics of an oral dose of $^2\text{H}_4$ -retinyl acetate in human subjects with low or high total body stores of vitamin A. *Am J Clin Nutr* 68:90-95, 1998.
4. Brown KH, Dewey KG, Allen LH. Complementary feeding of young children in developing countries: A review of current scientific knowledge. World Health Organization (WHO/NUT/98.1), Geneva, Switzerland, 1998.
5. Brown KH. Effect of infections on plasma zinc concentration and implications for zinc status assessment in low-income countries. *Am J Clin Nutr* 68:425S-429S, 1998.
6. Mendoza C, Viteri FE, Lonnerdal B, Young KA, Raboy V, Brown KH. Effect of genetically modified, low-phytate maize on absorption of iron from tortilla. *Am J Clin Nutr* 68:1123-1127, 1998.
7. Goto K, Chew F, Torun B, Peerson JM, Brown KH. Epidemiology of altered intestinal permeability to lactulose and mannitol in Guatemalan infants. *J Pediatr Gastroenterol Nutr* 28:282-290, 1999.
8. Bennett VA, Morales E, Gonzalez J, Peerson JM, Lopez de Romana G, Brown KH. Effects of dietary viscosity and energy density on total daily energy consumption by young Peruvian children. *Am J Clin Nutr* 70:285-291, 1999.
9. Penny ME, Peerson JM, Marin RM, Duran A, Lanata CF, Lönnerdal B, Black RE, Brown KH. Randomized, community-based trial of the effect of zinc supplementation, with and without other micronutrients, on the duration of persistent childhood diarrhea in Lima, Peru. *J Pediatr* 135:208-217, 1999.
10. Lartey A, Manu A, Brown KH, Peerson JM, Dewey KG. A randomized, community-based trial of the effects of improved, centrally processed complementary foods on growth and micronutrient status of Ghanaian infants from 6 to 12 mo of age. *Am J Clin Nutr* 70:391-404, 1999.

Biography of the Investigators

CARL L. KEEN

Department of Nutrition, University of California, Davis, CA 95616
Telephone: (530) 752-6331, Fax: (530) 752-8966
E-mail: clkeen@ucdavis.edu

Education:

Pasadena City College, Pasadena, CA, 1970-1972
University of California, Davis, CA, B.S., 1974 (Nutrition)
University of California, Davis, CA, Ph.D., 1979 (Nutrition; minor in Physiological Biochemistry)

Professional Experience:

Chair, Department of Nutrition, University of California, Davis, July 1993-present
Acting Chair, Department of Nutrition, University of California, Davis, July 1991-July 1992
Professor of Nutrition, Department of Nutrition; Department of Internal Medicine, University of California, Davis, July 1988-present
Associate Professor of Nutrition, Department of Nutrition, July 1985-June 1988
Associate Professor of Internal Medicine, Department of Internal Medicine, University of California, Davis, 1986-1988
Assistant Professor of Nutrition, Department of Nutrition, University of California, Davis, 1984-1985
Assistant Research Nutritionist, Department of Nutrition, University of California, Davis, 1981-1983
National Institute of Dental Research Postdoctoral Fellow, Department of Nutrition, University of California, Davis, 1979-1981
Procter and Gamble Predoctoral Fellow, Department of Nutrition, University of California, Davis, 1978-1979
National Institute of Dental Research Predoctoral Fellow, Department of Nutrition, University of California, Davis, 1975-1978

Selected Recent Presentations

- 2000 "Micronutrients, Cytokines and Teratogenesis," American Society of Reproductive Immunology, June 10-12, 2000, Jacksonville, FL
- 2000 "Dietary supplementation of antioxidants and phytochemicals," 7th Annual Meeting of the Oxygen Society, November 16-20, 2000, San Diego, CA
- 2001 "Cytokine responses to cocoa in humans," Oxidants and Antioxidants in Biology Conference, Society for Free Radical Research International/Linus Pauling Institute, March 7-10, Santa Barbara, CA
- 2001 "Diets, Antioxidants and Environmental Influences on Health and Disease," March 13-14, Raleigh, NC
- 2001 "What Are the Relevant Antioxidants and Phytonutrients?," The Antioxidant Initiative – Phytonutrients complete the good health puzzle, Oldways Preservation & Exchange Trust, April 22-24, 2001, Lake Tahoe, CA.
- 2001 "Flavonoid Rich Foods: A Current Perspective on their Ability to Enhance Cardiovascular Health," The First International Conference on Food Synergy, May 11, Washington, DC
- 2001 "The Latest Facts on Antioxidants: Chocolate and More," Diet Technology Update 2001, June 7, Santa Rosa Junior College, Santa Rosa, CA

Detailed Budget for New Proposal

Project Title: A pilot study to assess antioxidant status in healthy and malnourished Bangladeshi children

Name of PI: Kazi Mohammad Asif Jamil

Protocol Number: #2001-028

Name of Division: Clinical Sciences

Funding Source: NIH-Fogarty International Center

Amount Funded (direct): US\$ 3,000.00
Total: US\$ 3,000.00

Starting Date: March 1, 2002

Closing Date: Aug 31, 2002

Strategic Plan Priority Code(s):

Sl. No	Account Description	Salary Support			US \$ Amount Requested		
		Position	Effort%	Salary	1st Yr	2 nd Yr	3 rd Yr
	Personnel						
	Kazi Mohammad Asif Jamil			0			
	Tahmeed Ahmed			0			
	Research Assistant (1)—3 months		50	450			
	Sub Total				450		
	Local Travel	For recruiting patients			50		
	International Travel						
	Sub Total				50		
	Supplies and Materials (Description of Items)						
	UC Davis:						
	a. Chemicals and supplies				1,950		
	b. Communications and transport of materials				200		
	ICDDR,B:						
	a. Chemicals and supplies				50		
	b. Communications and transport of materials				300		
	Sub Totals				2,500		

TOTAL DIRECT COST: US\$ 3,000.00

Budget Justifications

Please provide one page statement justifying the budgeted amount for each major item. Justify use of man power, major equipment, and laboratory services.

The services of the research assistant (on a 50% effort basis) will be required for identification, screening and enrolment of children. The tests specified in the proposal are specialized in nature and require special reagents. These reagents are expensive and not available in Bangladesh.

Check List

After completing the protocol, please check that the following selected items have been included.

1. Face Sheet Included
2. Approval of the Division Director on Face Sheet
3. Certification and Signature of PI on Face Sheet, #9 and #10
4. Table on Contents
5. Project Summary
6. Literature Cited
7. Biography of Investigators
8. Ethical Assurance
9. Consent Forms
10. Detailed Budget

Consent Form for Cases

Page 1 of 3

Informed Consent to Participate in a Research Study

**INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH,
BANGLADESH
AND UNIVERSITY OF CALIFORNIA, DAVIS**

Title of Study: A pilot study to assess antioxidant status in healthy and malnourished Bangladeshi children

Investigators:

K.M.A. Jamil, M.B.B.S., Ph.D., Dhaka, Bangladesh Tel. 880-2-8811751 Ext 2333
Tahmeed Ahmed, M.B.B.S., Ph.D. ICDDR,B, Dhaka, Bangladesh Tel. 880-2-8811751
Ext 2304
Kenneth H. Brown, M.D., Department of Nutrition, UC Davis, Tel. (530) 752-1992
Carl Keen, Ph.D., Department of Nutrition, UC Davis, Tel (530) 752-6331

Purpose

You are being asked to allow your child to participate in a research study. Investigators at the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) in Dhaka and at the University of California, Davis (UC Davis) are conducting a study to learn more about the antioxidant status in normal and severely malnourished children in Bangladesh. Antioxidants are very important constituents of blood which are believed to protect the body against damage caused by some toxic substances (known as 'free radicals') that are produced during infection. In this study we will be able to assess the antioxidant status of healthy and malnourished children in Bangladesh. This will help us to determine if additional supplementation of antioxidants is necessary for the health and well being of these children.

Procedures

If you decide to let your child volunteer, we will ask a set of questions about the child's medical history and diet. We will then obtain a blood sample of 5 ml from the vein of his/her arm. We will finally collect another blood sample of 5 ml from your child before he/she is discharged from the hospital.

Initial of the child's parent/guardian _____

Risks:

There are no major risks associated with participation in this study. Risks of venipuncture include some discomfort, bruising and rarely infection. The amount of blood that will be taken will not affect the health of your child in any way.

Benefits

Your child may not benefit personally from participating in this study. However, your child's participation in the study will help us to understand the antioxidant status of healthy and malnourished children of Bangladesh. This information will benefit society in general.

Confidentiality

The results from the tests will be analyzed by the investigators listed above, and will be available to these investigators only. Any information obtained in connection with the study will be used in a manner that does not publicly disclose the identity of your child and will be kept confidential. Absolute confidentiality cannot be guaranteed, since research documents are not protected from subpoena.

Costs/Compensation

You will incur no financial costs as the result of your child's participation in this study. In the unlikely event that your child is physically injured as a direct result of research procedures, he/she will receive reasonable medical treatment at no cost. The International Centre for Diarrhoeal Disease Research, Bangladesh and the University of California do not provide any other form of compensation for injury.

Right to Refuse or Withdraw

You may refuse to allow your child to participate in the study without any consequences. You may change your mind about his/her continuation of participation in the study and quit after the study has started.

Questions

If you have any questions, please ask us. If you have additional questions later, either Dr. Jamil, or Dr. Tahmeed, or Dr. Brown, or one of their assistants will answer them. Dr. Jamil and Dr. Tahmeed can be reached at the International Centre for Diarrhoeal Disease, Mohakhali, Dhaka, Bangladesh, tel.8811751. Dr. Brown can be reached at Meyer Hall, UC Davis, Davis, CA 95616, Tel. (530) 752-1992.

Initial of the child's parent/guardian _____

Consent:

YOUR SIGNATURE BELOW, WILL INDICATE THAT YOU HAVE DECIDED TO VOLUNTEER AS A RESEARCH SUBJECT AND THAT YOU HAVE READ AND UNDERSTOOD THE INFORMATION PROVIDED ABOVE AND THE BILL OF RIGHTS.

Date

Signature of the child's parent/guardian

Date

Signature of the witness

Date

Signature of the investigator

You will be given a signed and dated copy of this form to keep. You will also be given a copy of the Experimental Subject's Bill of Rights.

Consent Form for Controls

Page 1 of 3

Informed Consent to Participate in a Research Study

**INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH,
BANGLADESH
AND UNIVERSITY OF CALIFORNIA, DAVIS**

Title of Study: A pilot study to assess antioxidant status in healthy and malnourished Bangladeshi children

Investigators:

K.M.A. Jamil, M.B.B.S., Ph.D., Dhaka, Bangladesh Tel. 880-2-8811751 Ext 2333
Tahmeed Ahmed, M.B.B.S., Ph.D. ICDDR,B, Dhaka, Bangladesh Tel. 880-2-8811751
Ext 2304
Kenneth H. Brown, M.D., Department of Nutrition, UC Davis, Tel. (530) 752-1992
Carl Keen, Ph.D., Department of Nutrition, UC Davis, Tel (530) 752-6331

Purpose

You are being asked to allow your child to participate in a research study. Investigators at the International Centre for Diarrhoeal Disease Research, Bangladesh (ICDDR,B) in Dhaka and at the University of California, Davis (UC Davis) are conducting a study to learn more about the antioxidant status in normal and severely malnourished children in Bangladesh. Antioxidants are very important constituents of blood which are believed to protect the body against damage caused by some toxic substances (known as 'free radicals') that are produced during infection. In this study we will be able to assess the antioxidant status of healthy and malnourished children in Bangladesh. This will help us to determine if additional supplementation of antioxidants is necessary for the health and well being of these children.

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Initial of the child's parent/guardian _____

Risks:

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Benefits

Your child may not benefit personally from participating in this study. However, your child's participation in the study will help us to understand the antioxidant status of healthy and malnourished children of Bangladesh. This information will benefit society in general.

Confidentiality

The results from the tests will be analyzed by the investigators listed above, and will be available to these investigators only. Any information obtained in connection with the study will be used in a manner that does not publicly disclose the identity of your child and will be kept confidential. Absolute confidentiality cannot be guaranteed, since research documents are not protected from subpoena.

Costs/Compensation

You will incur no financial costs as the result of your child's participation in this study. In the unlikely event that your child is physically injured as a direct result of research procedures, he/she will receive reasonable medical treatment at no cost. The International Centre for Diarrhoeal Disease Research, Bangladesh and the University of California do not provide any other form of compensation for injury.

Right to Refuse or Withdraw

You may refuse to allow your child to participate in the study without any consequences. You may change your mind about his/her continuation of participation in the study and quit after the study has started.

Questions

If you have any questions, please ask us. If you have additional questions later, either Dr. Jamil, or Dr. Tahmeed, or Dr. Brown, or one of their assistants will answer them. Dr. Jamil and Dr. Tahmeed can be reached at the International Centre for Diarrhoeal Disease, Mohakhali, Dhaka, Bangladesh, tel.8811751. Dr. Brown can be reached at Meyer Hall, UC Davis, Davis, CA 95616, Tel. (530) 752-1992.

Initial of the child's parent/guardian _____

Consent:

YOUR SIGNATURE BELOW, WILL INDICATE THAT YOU HAVE DECIDED TO VOLUNTEER AS A RESEARCH SUBJECT AND THAT YOU HAVE READ AND UNDERSTOOD THE INFORMATION PROVIDED ABOVE AND THE BILL OF RIGHTS.

Date

Signature of the child's parent/guardian

Date

Signature of the witness

Date

Signature of the investigator

You will be given a signed and dated copy of this form to keep. You will also be given a copy of the Experimental Subject's Bill of Rights.

রোগীর জন্য “সম্মতি পত্র”

আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র, বাংলাদেশ ও ক্যালিফোর্নিয়া বিশ্ববিদ্যালয় ডেভিস, ইউ.এস.এ

গবেষণার নাম : সুস্থ ও তীব্র অপুষ্টিতে আক্রান্ত বাংলাদেশী শিশুদের শরীরে এন্টিঅক্সিডেন্ট বা ‘জারন-প্রতিরোধক’-এর মাত্রা নির্ণয়ের জন্য পরীক্ষামূলক (পাইলট) গবেষণা।

গবেষকদের নাম :

- ১। কাজী মোহাম্মদ আসিফ জামিল, আই, সি, ডি, ডি, আর, বি (ফোন- ৮৮১১৭৫১ এক্স-২৩৩৩)
- ২। তাহমীদ আহমেদ, আই, সি, ডি, ডি, আর, বি (ফোন - ৮৮১১৭৫১ এক্স-২৩০৪)
- ৩। কেনেথ এইচ ব্রাউন, ক্যালিফোর্নিয়া বিশ্ববিদ্যালয় ডেভিস (ফোন-১(৫৩০) ৭৫২-১৯৯২)
- ৪। কার্ল কীন, ক্যালিফোর্নিয়া বিশ্ববিদ্যালয় ডেভিস (ফোন-১(৫৩০) ৭৫২-৬৩৩১)

উদ্দেশ্য :

আপনার শিশুকে একটি গবেষণায় অংশগ্রহণ করার অনুমতি দেয়ার জন্য আপনাকে অনুরোধ জানানো হচ্ছে। আই, সি, ডি, ডি, আর, বি ও ক্যালিফোর্নিয়া বিশ্ববিদ্যালয়ের গবেষকরা সুস্থ ও তীব্র অপুষ্টিতে আক্রান্ত, বাংলাদেশী শিশুদের শরীরে এন্টিঅক্সিডেন্টের মাত্রা নির্ণয় করার জন্য এই গবেষণা চালাবেন। এন্টিঅক্সিডেন্টগুলি রক্তের অত্যন্ত গুরুত্বপূর্ণ উপাদান বা শরীরকে জীবাণুর আক্রমণ বা ইনফেকশনজনিত ক্ষতিকর “ফ্রী র্যাডিকেল” থেকে রক্ষা করে। এই গবেষণার মাধ্যমে আমরা সুস্থ ও তীব্র অপুষ্টিতে আক্রান্ত বাংলাদেশী শিশুদের শরীরে এন্টিঅক্সিডেন্টের মাত্রা নির্ণয় করতে পারবো। এর মাধ্যমে আমরা জানতে পারবো এইসব শিশুদের স্বাস্থ্য রক্ষার জন্য খাদ্যের সঙ্গে অতিরিক্ত এন্টিঅক্সিডেন্ট যোগ করার প্রয়োজন আছে কিনা।

শিশুর পিতা/মাতা/অভিভাবকের স্বাক্ষর : _____

পদ্ধতি :

আপনি যদি আপনার শিশুর এই গবেষণায় অংশ গ্রহনে রাজী হন, তাহলে আপনাকে প্রথমে শিশুটির স্বাস্থ্যগত অবস্থা ও খাদ্যাভ্যাস সম্পর্কে কিছু প্রশ্ন করা হবে। তারপর শিশুর শিরাতে সূঁচ ঢুকিয়ে এক চামচ (পাঁচ মিঃ লিঃ) পরিমান রক্ত সংগ্রহ করা হবে। পরবর্তী পর্যায়ে আপনার শিশু হাসপাতাল ত্যাগ করার আগে আর একবার তার শিরা থেকে ৫ মিঃ লিঃ রক্ত নেয়া হবে।

ঝুঁকি :

এই গবেষণায় অংশগ্রহনে কোন বড় ধরনের ঝুঁকি নেই। শিরা থেকে রক্ত নেবার ঝুঁকি হচ্ছে ক্ষতস্থানে সামান্য ব্যথা ও কোন কোন সময় জীবানুর সংক্রমণ (ইনফেকশন)। আপনার শিশুর শরীর থেকে যে পরিমান রক্ত নেয়া হবে তাতে শিশুর স্বাস্থ্যের কোন ক্ষতি হবে না।

উপকারিতা :

এই গবেষণা থেকে আপনার শিশু হয়তো ব্যক্তিগতভাবে উপকৃত হবে না। তবে এই গবেষণায় আপনার শিশুর অংশ গ্রহনের ফলে আমরা সুস্থ ও তীব্র অপুষ্টিতে আক্রান্ত শিশুদের শরীরে এন্টিঅক্সিডেন্টের মাত্রা সম্পর্কে জানতে পারবো। এই তথ্য সমাজের সবার উপকারে আসবে।

গোপনীয়তা :

এই গবেষণার ফলাফল শুধুমাত্র উপরোক্ত গবেষকরা জানতে পারবেন। এই গবেষণায় যা কিছু তথ্য পাওয়া যাবে তা এমনভাবে ব্যবহৃত হবে যাতে আপনার শিশুর পরিচয় প্রকাশ না পায় এবং গোপনীয়তা বজায় থাকে। পরিপূর্ণভাবে গোপনীয়তা রক্ষা করার নিশ্চয়তা অবশ্য দেয়া যায় না, কারণ গবেষণা কাজে প্রাপ্ত তথ্য আদারতের সাক্ষ্য-প্রমানের জন্য প্রয়োজনবোধে ব্যবহৃত হতে পারে।

মূল্য/ক্ষতিপূরণ :

আপনার শিশু এই গবেষণায় অংশগ্রহন করায় আপনাকে কোন খরচ বহন করতে হবে না। এই গবেষণার ফলে যদি শিশুটির শারীরিক কোন ক্ষতি হয়- যার সম্ভাবনা নেই বললেই চলে - তবে তাকে বিনামূল্যে চিকিৎসা করা হবে। আই, সি, ডি, ডি, আর, বি, বা ক্যালিফোর্নিয়া বিশ্ববিদ্যালয় এছাড়া অন্য কোন ধরনের ক্ষতিপূরণ দিতে অপারগ।

শিশুর পিতা/মাতা/অভিভাবকের স্বাক্ষর : _____

গবেষণায় অংশগ্রহন প্রত্যাহার করার অধিকার :-

আপনি যেকোন সময় আপনার শিশুর নাম গবেষণা থেকে প্রত্যাহার করে নিতে পারেন। গবেষণায় আপনার শিশুর অংশগ্রহন করার ব্যাপারে আপনার মত পরিবর্তন করলেও এই হাসপাতালে চিকিৎসা সুবিধা থেকে আপনার শিশু বঞ্চিত হবে না।

প্রশ্নোত্তর :-

আপনার কোন প্রশ্ন থাকলে অনুগ্রহ করে জিজ্ঞাসা করুন। আপনার মনে যদি পরেও কোন প্রশ্ন জাগে সেক্ষেত্রে আপনার প্রশ্নের উত্তর ডাঃ জামিল, ডাঃ তাহমীদ, ডাঃ কীন, ডাঃ ব্রাউন বা তাদের অধঃস্তন কোন ডাক্তার দিবেন। ডাঃ জামিলের ঠিকানা :- আই, সি, ডি, ডি, আর, বি, মহাখালী, ঢাকা; ফোন নাম্বার ৮৮১১৭৫১-৬০/২৩৩৩, ডাঃ ব্রাউন ও ডাঃ কীনের সঙ্গে নিম্নের ঠিকানায় যোগাযোগ করা যাবে : Department of Nutrition, University of California Davis, One Shields Avenue, Davis, CA 95616. Tel: (530) 752-1992

আপনার নীচের স্বাক্ষরটি এই অর্থ বহন করবে যে, আপনি স্বেচ্ছায় আপনার শিশুর এই গবেষণায় অংশগ্রহনে সম্মত হয়েছেন এবং আপনি উপরে বর্ণিত তথ্যসমূহ এবং আপনার অধিকার সম্পর্কে পড়েছেন এবং বুঝতে পেরেছেন।

তারিখ

অংশগ্রহনকারী শিশুর পিতা/মাতা
অভিভাবকের স্বাক্ষর

তারিখ

অভিভাবকের স্বাক্ষর

তারিখ

গবেষকের স্বাক্ষর

সুস্থ শিশুর জন্য “সম্মতি পত্র”

আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র, বাংলাদেশ ও
ক্যালিফোর্নিয়া বিশ্ববিদ্যালয় ডেভিস, ইউ.এস.এ

গবেষণার নাম : সুস্থ ও তীব্র অপুষ্টিতে আক্রান্ত বাংলাদেশী শিশুদের শরীরে এন্টিঅক্সিডেন্ট বা ‘জারন-প্রতিরোধক’-এর মাত্রা নির্ণয়ের জন্য পরীক্ষামূলক (পাইলট) গবেষণা।

গবেষকদের নাম :

- ১। কাজী মোহাম্মদ আসিফ জামিল, আই, সি, ডি, ডি, আর, বি (ফোন - ৮৮১১৭৫১ এক্স-২৩৩৩)
- ২। তাহমীদ আহমেদ, আই, সি, ডি, ডি, আর, বি (ফোন - ৮৮১১৭৫১ এক্স-২৩০৪)
- ৩। কেনেথ এইচ ব্রাউন, ক্যালিফোর্নিয়া বিশ্ববিদ্যালয় ডেভিস (ফোন-১(৫৩০) ৭৫২-১৯৯২)
- ৪। কার্ল কীন, ক্যালিফোর্নিয়া বিশ্ববিদ্যালয় ডেভিস (ফোন-১(৫৩০) ৭৫২-৬৩৩১)

উদ্দেশ্য :

আপনার শিশুকে একটি গবেষণায় অংশগ্রহণ করার অনুমতি দেয়ার জন্য আপনাকে অনুরোধ জানানো হচ্ছে। আই, সি, ডি, ডি, আর, বি ও ক্যালিফোর্নিয়া বিশ্ববিদ্যালয়ের গবেষকরা সুস্থ ও তীব্র অপুষ্টিতে আক্রান্ত, বাংলাদেশী শিশুদের শরীরে এন্টিঅক্সিডেন্টের মাত্রা নির্ণয় করার জন্য এই গবেষণা চালাবেন। এন্টিঅক্সিডেন্টগুলি রক্তের অত্যন্ত গুরুত্বপূর্ণ উপাদান বা শরীরকে জীবাণুর আক্রমণ বা ইনফেকশনজনিত ক্ষতিকর “ফ্রী র্যাডিকেল” থেকে রক্ষা করে। এই গবেষণার মাধ্যমে আমরা সুস্থ ও তীব্র অপুষ্টিতে আক্রান্ত বাংলাদেশী শিশুদের শরীরে এন্টিঅক্সিডেন্টের মাত্রা নির্ণয় করতে পারবো। এর মাধ্যমে আমরা জানতে পারবো এইসব শিশুদের স্বাস্থ্য রক্ষার জন্য খাদ্যের সঙ্গে অতিরিক্ত এন্টিঅক্সিডেন্ট যোগ করার প্রয়োজন আছে কিনা।

শিশুর পিতা/মাতা/অভিভাবকের স্বাক্ষর : _____

পদ্ধতি :

আপনি যদি আপনার শিশুর এই গবেষণায় অংশ গ্রহনে রাজী হন, তাহলে আপনাকে প্রথমে শিশুটির স্বাস্থ্যগত অবস্থা ও খাদ্যাভ্যাস সম্পর্কে কিছু প্রশ্ন করা হবে। তারপর শিশুর শিরাতে সূঁচ ঢুকিয়ে এক চামচ (পাঁচ মিঃ লিঃ) পরিমান রক্ত সংগ্রহ করা হবে। আপনার শিশুর কাছ থেকে শুধু একবারই রক্ত নেয়া হবে - পরবর্তী সময়ে আবার রক্ত দেয়ার কোন প্রয়োজন হবে না।

ঝুঁকি :

এই গবেষণায় অংশগ্রহনে কোন বড় ধরনের ঝুঁকি নেই। শিরা থেকে রক্ত নেবার ঝুঁকি হচ্ছে ক্ষতস্থানে সামান্য ব্যথা ও কোন কোন সময় জীবানুর সংক্রমণ (ইনফেকশন)। আপনার শিশুর শরীর থেকে যে পরিমান রক্ত নেয়া হবে তাতে শিশুর স্বাস্থ্যের কোন ক্ষতি হবে না।

উপকারিতা :

এই গবেষণা থেকে আপনার শিশু হয়তো ব্যক্তিগতভাবে উপকৃত হবে না। তবে এই গবেষণায় আপনার শিশুর অংশ গ্রহনের ফলে আমরা সুস্থ ও তীব্র অপুষ্টিতে আক্রান্ত শিশুদের শরীরে এন্টিঅক্সিডেন্টের মাত্রা সম্পর্কে জানতে পারবো। এই তথ্য সমাজের সবার উপকারে আসবে।

গোপনীয়তা :

এই গবেষণার ফলাফল শুধুমাত্র উপরোক্ত গবেষকরা জানতে পারবেন। এই গবেষণায় যা কিছু তথ্য পাওয়া যাবে তা এমনভাবে ব্যবহৃত হবে যাতে আপনার শিশুর পরিচয় প্রকাশ না পায় এবং গোপনীয়তা বজায় থাকে। পরিপূর্ণভাবে গোপনীয়তা রক্ষা করার নিশ্চয়তা অবশ্য দেয়া যায় না, কারন গবেষণা কাজে প্রাপ্ত তথ্য আদারতের সাক্ষ্য-প্রমানের জন্য প্রয়োজনবোধে ব্যবহৃত হতে পারে।

মূল্য/ক্ষতিপূরণ :

আপনার শিশু এই গবেষণায় অংশগ্রহন করায় আপনাকে কোন খরচ বহন করতে হবে না। এই গবেষণার ফলে যদি শিশুটির শারীরিক কোন ক্ষতি হয়- যার সম্ভাবনা নেই বললেই চলে - তবে তাকে বিনামূল্যে চিকিৎসা করা হবে। আই, সি, ডি, ডি, আর, বি, বা ক্যালিফোর্নিয়া বিশ্ববিদ্যালয় এছাড়া অন্য কোন ধরনের ক্ষতিপূরণ দিতে অপারগ।

শিশুর পিতা/মাতা/অভিভাবকের স্বাক্ষর : _____

গবেষণায় অংশগ্রহন প্রত্যাহার করার অধিকার :-

আপনি যেকোন সময় আপনার শিশুর নাম গবেষণা থেকে প্রত্যাহার করে নিতে পারেন। গবেষণায় আপনার শিশুর অংশগ্রহন করার ব্যাপারে আপনার মত পরিবর্তন করলেও এই হাসপাতালে চিকিৎসা সুবিধা থেকে আপনার শিশু বঞ্চিত হবে না।

প্রশ্নোত্তর :-

আপনার কোন প্রশ্ন থাকলে অনুগ্রহ করে জিজ্ঞাসা করুন। আপনার মনে যদি পরেও কোন প্রশ্ন জাগে সেক্ষেত্রে আপনার প্রশ্নের উত্তর ডাঃ জামিল, ডাঃ তাহমীদ, ডাঃ কীন, ডাঃ ব্রাউন বা তাদের অধঃস্তন কোন ডাক্তার দিবেন। ডাঃ জামিলের ঠিকানা :- আই, সি, ডি, ডি, আর, বি, মহাখালী, ঢাকা; ফোন নাম্বার ৮৮১১৭৫১-৬০/২৩৩৩, ডাঃ ব্রাউন ও ডাঃ কীনের সঙ্গে নিম্নের ঠিকানায় যোগাযোগ করা যাবে : Department of Nutrition, University of California Davis, One Shields Avenue, Davis, CA 95616. Tel: (530) 752-1992

আপনার নীচের স্বাক্ষরটি এই অর্থ বহন করবে যে, আপনি স্বেচ্ছায় আপনার শিশুর এই গবেষণায় অংশগ্রহনে সম্মত হয়েছেন এবং আপনি উপরে বর্ণিত তথ্যসমূহ এবং আপনার অধিকার সম্পর্কে পড়েছেন এবং বুঝতে পেরেছেন।

তারিখ

অংশগ্রহনকারী শিশুর পিতা/মাতা
অভিভাবকের স্বাক্ষর

তারিখ

অভিভাবকের স্বাক্ষর

তারিখ

গবেষকের স্বাক্ষর

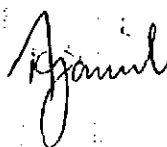


International Centre for Diarrhoeal Disease Research, Bangladesh
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Cable : Cholera Dhaka

MEMORANDUM

Date: April 16, 2002

To: Professor Mahmudur Rahman
Chairman, Ethical Review Committee (ERC)

From: Dr. K.M.A. Jamil
Senior Medical Officer
Clinical Sciences Division 

Subject: Request to approve minor modification of the Protocol # 2001-028

I would like to inform you that we have started recruitment of subjects for the pilot study mentioned above as soon as we obtained approval from the ERC. We originally planned to enroll all subjects within the age range of one to three years because it was believed by most authorities that kwashiorkor is prevalent mainly among children of this age group. Interestingly, we have been observing a trend of admission of patients with kwashiorkor who are less than one year of age.

Considering the above fact, I would request you to allow us to enroll subjects between 6 months to three years of age. A copy of the protocol is also enclosed herewith.

Thank you.



CENTRE FOR HEALTH AND POPULATION RESEARCH

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Memorandum

12 March 2002

To : Dr. K M A Jamil
Clinical Sciences Division

From: Professor Mahmudur Rahman
Chairman, Ethical Review Committee (ERC)

Sub : Approval of the protocol # 2001-028

Thank you for your memo of 11th March 2002 with the modified version of your protocol # 2001-028 entitled "A pilot study to assess antioxidant status in healthy and malnourished Bangladeshi children". The modified version of the protocol is hereby approved upon your satisfactory addressing of the issues raised by the ERC in its meeting held on 6th March 2002.

You shall conduct the study according to the ERC-approved protocol; and shall be responsible for protecting the rights and welfare of the subjects and compliance with the applicable provisions of the ERC Guidelines. You shall also submit report(s) as required under the ERC Guidelines. Relevant excerpt of the ERC Guidelines is attached for your information and guidance.

I wish you all the success in running the above mentioned study.

Copy: Acting Associate Director
Clinical Sciences Division



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MEMORANDUM

March 11, 2002

To: Professor Mahmudur Rahman
Chairman, Ethical Review Committee (ERC)

From: Dr. K.M.A. Jamil *K.M.A. Jamil*
Senior Medical Officer
Clinical Sciences Division

Sub : Protocol # 2001-028

This is to respond to your queries regarding the protocol # 2001-028 entitled "A pilot study to assess antioxidant status in healthy and malnourished Bangladeshi children", which the ERC considered in its meeting held on March 6, 2002. The queries of ERC ('a' through 'd') have been addressed below for your kind consideration:

- a) The severely malnourished children (cases) who will be recruited for the study will receive multiple micronutrients as part of the current management protocol of ICDDR,B. It is thus expected that their antioxidant status will change at discharge. We therefore need to evaluate the antioxidant status both during admission and at discharge from the hospital in order to evaluate the need for antioxidant supplementation in this group.
- b) This is exactly why we should measure antioxidant status of the subjects during discharge.
- c) The item #1 (c) has been corrected.
- d) The Bangla consent form has been modified as suggested.

I would, therefore, request you to kindly approve the modified version of the protocol.

Thank you.

*okay!
Protocol may be
approved
KAM*

cc: Acting Associate Director, CSD



INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH
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Memorandum

10 March 2002

To : Dr. K M A Jamil
Clinical Sciences Division

From: Professor Mahmudur Rahman
Chairman, Ethical Review Committee (ERC)

Sub : Protocol # 2001-028

Thank you for your protocol # 2001-028 entitled "A pilot study to assess antioxidant status in healthy and malnourished Bangladeshi children", which the ERC considered in its meeting held on 6th March 2002. After review and discussion, the Committee made the following observations on the protocol:

- a) The rationale for taking a second blood sample, which was not mentioned in the body of the protocol, should be provided.
- b) Almost all the children will get multiple micronutrients supplementation as a routine management. That is definitely going to alter the antioxidant status at discharge.
- c) On the ERC Face Sheet, item # 1 (c) should be marked YES instead of no.
- d) The Bangla consent form needed modification since some of the words were not properly translated (for example the word 'চীজ' should be replaced by the word "মাবাজর")

You are, therefore, advised to modify the protocol incorporating the above observations and submit the modified version of the protocol for consideration of the Chair.

Copy: Acting Associate Director
Clinical Sciences Division



International Centre for Diarrhoeal Disease Research, Bangladesh
CENTRE FOR HEALTH AND POPULATION RESEARCH

Memorandum

Date: March 6, 2002

To: Prof. Mahmudur Rahman
Chairman, ERC

From: Dr. Iqbal Kabir 
Scientist, ICDDR,B & Member, ERC

Subject: Review of the protocol entitled "A pilot study to assess antioxidant status in healthy and malnourished Bangladeshi children" Protocol # 2001-028

Thank you so much for giving me the opportunity to review this protocol. This is basically a pilot study to assess the antioxidant status of severely malnourished (kwashiorkor and marasmus) children admitted to ICDDR,B Dhaka Hospital. 5 ml of blood will be collected from 30 severely malnourished children and will be compared with control children.

This is an important study and will help to understand the mechanism of development of severe malnutrition particularly kwashiorkor. This pilot study will help to develop large study to evaluate the role of supplementing antioxidant to improve the management of severely malnourished children and thereby improve child survival.

This study does not have any major ethical problem. I do have some scientific question though;

1. What is the rationale for having a second blood sample. Is not this true, almost all these children will get multiple micronutrients supplementation as a routine management. That definitely going to alter the antioxidant status at discharge.
2. Is this sample size (10 kwash, 20 marasmus) is adequate to make an inference/conclusion?

The face sheet, consent form look okay. The protocol may be approved.



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Cable : Cholera Dhaka

6 July 2002

Dear Participant

You are welcome to Bangladesh and ICDDR,B! I hope your trip was pleasant and we hope to make your stay at ICDDR,B as useful as well.

Your accommodation (single) while in Dhaka has been booked at the Royal Garden Guest House (House #24/A, Road # 1, Baridhara, Dhaka 1212; Tel: 9887698 or 9883730). It may please be noted that breakfast is included with the room charge.

While in Dhaka, you will take breakfast and dinner at the Royal Garden and you will have lunch at the Centre.

Transport will pick you up from the Royal Garden at 8:10 am. on Sunday. You may accordingly advise the guesthouse of the time for serving breakfast. Drop will be provided at the end of the workshop.

If you need any assistance you may call me (Tel: Off: 8826318 and Res: 8117073)

Please bring your passport and ticket with you for confirmation of your return trip.

Please do not hesitate to contact us if you require any further information about your participation in the training workshop.

Look forward to having you at the workshop.

Best regards,

Yours sincerely,

Dr. A. N. Alam
Head
Training and Education Unit