INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH
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CENTRE
FOR HEALTH AND
POPULATION RESEARCH

Memorandum

31 October 1999

To : Dr. Jena D. Hamadani
Clinical Sciences Division

From : Professor Mahmudur Rahman
Chairman, Ethical Review Committee

Subject: Approval of protocol # 99-021

This has reference to your memo of 24th October 1999 along with a modified copy of your protocol # 99-021 entitled "The effect of psychosocial stimulation on the development of malnourished children in BINP Centres". I am pleased to inform you that the protocol is hereby approved upon your appropriate addressing of the issues raised by the Committee in its meeting held on 25th August 1999.

Thanking you and wishing you success in running the said study.

copy: -Division Director
Clinical Sciences Division

International Centre for Diarrhoeal Disease Research, Bangladesh

Memorandum

To: The Chairman, Ethical Review Committee

Thru: Division Director, CSD

From: Dr. Jena D. Hamadani
PI, Protocol #99-021

Date: October 30, 1999

Sub: Revised copy of the protocol entitled "The effect of psychosocial stimulation on the development of malnourished children in BINP Centres"

With reference to your memo of 08 September 1999 this is to inform you that since I was away from the Centre I could not reply to your above-mentioned memo. earlier.

I have taken into account the observations made in the memo and revised the protocol accordingly. Please find enclosed a copy of the revised protocol for your record.

Thank you,

Encl: a/a

Attachment 1.

(FACE SHEET) ETHICAL REVIEW COMMITTEE, **APPROVED COPY**

Date 17.8.99

Principal Investigator Dr. Jena D. Hamadani Trainee Investigator (if any) x

Application No. 99 - 021 Supporting Agency (if Non-ICDDR,B) NCOE

Title of Study The effect of psycho-social stimulation on the development of malnourished children in BINF Centers

Project status:
(✓) New Study
( ) Continuation with change
( ) No change (do not fill out rest of form)

Circle the appropriate answer to each of the following (If Not Applicable write NA).

1. Source of Population:
   (a) Ill subjects — Yes No
   (b) Non-ill subjects — (Yes) No
   (c) Minors or persons under guardianship — (Yes) No
2. Does the study involve:
   (a) Physical risks to the subjects — Yes (No)
   (b) Social Risks — Yes (No)
   (c) Psychological risks to subjects — Yes (No)
   (d) Discomfort to subjects — Yes (No)
   (e) Invasion of privacy — (Yes) No
   (f) Disclosure of information damaging to subject or others — Yes (No)
3. Does the study involve:
   (a) Use of records, (hospital, medical, death, birth or other). — Yes (No)
   (b) Use of fetal tissue or abortus — Yes (No)
   (c) Use of organs or body fluids — Yes (No)
4. Are subjects clearly informed about:
   (a) Nature and purposes of study — (Yes) No
   (b) Procedures to be followed including alternatives used — (Yes) No
   (c) Physical risks — (Yes) No
   (d) Sensitive questions — (Yes) No
   (e) Benefits to be derived — (Yes) No
   (f) Right to refuse to participate or to withdraw from study — (Yes) No
   (g) Confidential handling of data — (Yes) No
   (h) Compensation &/or treatment where there are risks or privacy is involved in any particular procedure — (Yes) No
5. Will signed consent form be required:
   (a) From subjects — Yes (No)
   (b) From parent or guardian (if subjects are minors) — (Yes) No
6. Will precautions be taken to protect anonymity of subjects — (Yes) No
7. Check documents being submitted herewith to Committee:
   ____ Umbrella proposal - Initially submit an overview (all other requirements will be submitted with individual studies).
   ____ Protocol (Required)
   ____ Abstract Summary (Required)
   ____ Statement given or read to subjects on nature of study, risks, types of questions to be asked, and right to refuse to participate or withdraw (Required)
   ____ Informed consent form for subjects
   ____ Informed consent form for parent or guardian
   ____ Procedure for maintaining confidentiality
   ____ Questionnaire or interview schedule *

* If the final instrument is not completed prior to review, the following information should be included in the abstract summary:
1. A description of the areas to be covered in the questionnaire or interview which could be considered either sensitive or which would constitute an invasion of privacy.
2. Examples of the type of specific questions to be asked in the sensitive areas.
3. An indication as to when the questionnaire will be presented to the Cttee. for review.

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

Principal Investigator

Trainee

Principal Investigator: Last, first, middle Hamadani, Jena, Derakhshani

International Centre for Diarrhoeal Disease Research, Bangladesh

RESEARCH PROTOCOL

99-021

FOR OFFICE USE ONLY

Protocol No: Date:

RRCApproval: Yes/ No Date:

ERC Approval: Yes/No Date:

1. Title of Project (Do not exceed 60 characters including spaces and punctuations) The effect of psychosocial stimulation on the development of malnourished children in BINP Centers

2a. Name of the Principal Investigator(s) (Last, Middle, First).	2b. Position / Title	2c. Qualifications
Hamadani, Derakhshani, Jena	Sr. Medical Officer	MBBS, DCH

3. Name of the Division/ Branch / Programme of ICDDR,B under which the study will be carried out.
Clinical Sciences Division

4. Contact Address of the Principal Investigator

4a. Office Location: Dhaka Hospital, ICDDR,B
Mohakhali
Dhaka
Bangladesh

4b. Fax No: 880 2 883116, 880 2 886050
4c. E-mail: jena@icddrb.org
4d. Phone / Ext: 880 2 871751-60 Ext, 2331

5. Use of Human Subjects	5a. Use of Live Animal	5b. If Yes, Specify Animal Species
Yes ☑	Yes ☐	
No ☐	No ☐	

6. Dates of Proposed Period of Support
(Day, Month, Year - DD/MM/YY)
01/10/999 to 01/02/2002

7. Cost Required for the Budget Period
7a. Ist Year ($): 65,381/= 2nd Year ($): 41,481/= 3rd Year: 13,387/=

7b. Direct Cost ($) 120,249/= Total Cost ($) 138,286/=

8. 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.

Dr. M.A. Salam
Name of the Division Director

Signature

3/8/99
Date of Approval

9. 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.

10. Signature of PI

Jena

Date: 3.8.99

আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র
মহাখালী, ঢাকা-১২১২

বিনিপ সেন্টারে অপুষ্টিতে আক্রান্ত শিশুদের বুদ্ধিবিকাশে বিভিন্ন উৎসাহব্যাঞ্জক কার্যক্রমের মাধ্যমে মায়েদের পরিচর্যা ও যত্নের ভূমিকা

ইন্টারভেনশন গ্রুপ

সম্মতি পত্র

কলেরা হাসপাতালের ক্লিনিক্যাল সায়েন্স ডিভিশন শিশুদের বুদ্ধি বিকাশে মায়েদের যত্ন এবং লালন পালনের ভূমিকার উপর একটি গবেষণা কাজ হাতে নিয়েছে।

আপনি অবগত আছেন যে, বাংলাদেশে অপুষ্টি একটি মারাত্মক স্বাস্থ্য-সমস্যা। অপুষ্টির কারণে শিশুদের দৈহিক বৃদ্ধি যেমন বাধাপ্রাপ্ত হয়, তেমনি মানসিক বুদ্ধি বিকাশেও সমস্যা দেখা দিতে পারে। আপনার বাচ্চার পূর্ণ মানসিক বিকাশের জন্য আপনাকে আরো যত্নবান হতে হবে। বিনিপ ফিডিং সেন্টরে প্রতিদিন আপনার বাচ্চাকে পুষ্টিকর খাবার খাওয়ানো হয়। এ ছাড়াও আমরা প্রতি সপ্তাহে একদিন আপনাকে ট্রেনিং দেব - কিভাবে শিশুকে সুষ্ঠু ও পরিপূর্ণ যত্ন নিতে হয়, আপনার বাড়ীতেই পরে থাকা বিভিন্ন জিনিষ দিয়ে খেলনা তৈরী করে কিভাবে আপনি আপনার বাচ্চার সাথে খেলবেন - এ সমস্ত বিভিন্ন বিষয়ে আমরা আপনাকে প্রশিক্ষণ দেব।

আমরা এ কাজের শুরুতে এবং শেষে মোট ২ বার আপনার বাচ্চাকে পরীক্ষা করে দেখব - বাচ্চার মানসিক বুদ্ধিবৃত্তি কতটুকু বৃদ্ধি পেয়েছে। এ কাজে অংশগ্রহণ করলে আপনার বাচ্চার কোনভাবেই কোন সমস্যা দেখা দেবে না। এছাড়া আপনার বাড়ীতে গিয়ে আর্থ-সামাজিক অবস্থা এবং বাচ্চার বুদ্ধিবিকাশের উপযোগী পরিবেশের উপর বেশ কিছু প্রশ্ন করব। যে সমস্ত তথ্য আপনি দেবেন তার একান্ত গোপনীয়তা রক্ষা করা হবে।

আপনার যদি আমাদের সাথে সহযোগিতায় কোন প্রকার আপত্তি থাকে, আপনার সম্পূর্ণ স্বাধীনতা আছে এ কাজে যোগদান না করার। আপনি বরাবর যেমন খাবার পাচ্ছিলেন, তা চলতে থাকবে। এ কাজ চলাকালে কখনোও আপনি যদি মনে করেন যে আমাদের সাথে আর কাজ করবেন না আপনি আপনার অসম্মতি সরাসরি জানাতে কোন প্রকার সংকোচ করবেন না।

আপনি যদি আমাদের এ কাজে সহযোগিতা করতে রাজী থাকেন, তবে নিম্নে অনুগ্রহ করে আপনার স্বাক্ষর/ বাম হাতের বৃদ্ধাঙ্গুলির টিপ সহি দিবেন।

আমাদের এ কাজে সহযোগিতা করার জন্য আপনাকে অশেষ ধন্যবাদ।

প্রধান গবেষকের স্বাক্ষর	সাক্ষীর স্বাক্ষর	পিতামাতা বা অভিভাবকের স্বাক্ষর/বাম হাতের বৃদ্ধাঙ্গুলির ছাপ
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আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র
মহাখালী, ঢাকা-১২১২

বিনিপ সেন্টারে অপুষ্টিতে আক্রান্ত শিশুদের বুদ্ধিবিকাশে বিভিন্ন উৎসাহব্যাঞ্জক কার্যক্রমের মাধ্যমে মায়েদের পরিচর্যা ও যত্নের ভূমিকা

কন্ট্রোল গ্রুপ

সম্মতি পত্র

কলেরা হাসপাতালের ক্লিনিক্যাল সায়েন্স ডিভিশন শিশুদের বুদ্ধি বিকাশে মায়েদের যত্ন এবং লালন পালনের ভূমিকার উপর একটি গবেষণা কাজ হাতে নিয়েছে।

আপনি অবগত আছেন যে, বাংলাদেশে অপুষ্টি একটি মারাত্মক স্বাস্থ্য-সমস্যা। অপুষ্টির কারণে শিশুদের দৈহিক বৃদ্ধি যেমন বাধাপ্রাপ্ত হয়, তেমনি মানসিক বুদ্ধি বিকাশেও সমস্যা দেখা দিতে পারে। বিনিপ ফিডিং সেন্টারে কিছুকিছু মায়েদের আমরা ট্রেনিং দেব কিভাবে বাচ্চাকে পরিপূর্ণ যত্ন নিতে হয় এবং ঘরে তৈরী বিভিন্ন খেলনা দিয়ে বাচ্চাদের সাথে কিভাবে খেলতে হয়, সে বিষয়ে আমরা আপনার বাচ্চার সাথে সে সব বাচ্চাদের তুলনা করে দেখব বুদ্ধিবৃত্তিতে কোন পার্থক্য আছে কিনা। এ কাজের শেষে আমরা আপনাকেও পূর্ণ প্রশিক্ষণ দেব এ সমস্ত বিষয়ে।

আমরা এ কাজের শুরুতে এবং শেষে মোট ২ বার আপনার বাচ্চাকে পরীক্ষা করে দেখব - বাচ্চার মানসিক বুদ্ধিবৃত্তি কতটুকু বৃদ্ধি পেয়েছে। এ কাজে অংশগ্রহণ করলে আপনার বাচ্চার কোনভাবেই কোন সমস্যা দেখা দেবে না। এছাড়া আপনার বাড়ীতে গিয়ে আর্থ-সামাজিক অবস্থা এবং বাচ্চার বুদ্ধিবিকাশের উপযোগী পরিবেশের উপর বেশ কিছু প্রশ্ন করব। যে সমস্ত তথ্য আপনি দেবেন তার একান্ত গোপনীয়তা রক্ষা করা হবে।

আপনার যদি আমাদের সাথে সহযোগিতায় কোন প্রকার আপত্তি থাকে, আপনার সম্পূর্ণ স্বাধীনতা আছে এ কাজে যোগদান না করার। আপনি বরাবর যেমন খাবার পাচ্ছিলেন, তা চলতে থাকবে। এ কাজ চলাকালে কখনোও আপনি যদি মনে করেন যে আমাদের সাথে আর কাজ করবেন না আপনি আপনার অসম্মতি সরাসরি জানাতে কোন প্রকার সংকোচ করবেন না।

আপনি যদি আমাদের এ কাজে সহযোগিতা করতে রাজী থাকেন, তবে নিম্নে অনুগ্রহ করে আপনার স্বাক্ষর/ বাম হাতের বৃদ্ধাঙ্গুলির টিপ সহি দিবেন।

আমাদের এ কাজে সহযোগিতা করার জন্য আপনাকে অশেষ ধন্যবাদ।

প্রধান গবেষকের স্বাক্ষর	সাক্ষীর স্বাক্ষর	পিতামাতা বা অভিভাবকের স্বাক্ষর/বাম হাতের বৃদ্ধাঙ্গুলির ছাপ
তারিখ ঃ	তারিখ ঃ	তারিখ ঃ

পরিচর্যা ও যত্নের ভূমিকা

কম্পারিজন গ্রুপ

সম্মতি পত্র

কলেরা হাসপাতালের ক্লিনিক্যাল সায়েন্স ডিভিশন শিশুদের বুদ্ধি বিকাশে মায়েদের যত্ন এবং লালন পালনের ভূমিকার উপর একটি গবেষণা কাজ হাতে নিয়েছে।

আপনি অবগত আছেন যে, বাংলাদেশে অপুষ্টি একটি মারাত্মক স্বাস্থ্য-সমস্যা। অপুষ্টির কারণে শিশুদের দৈহিক বৃদ্ধি যেমন বাধাপ্রাপ্ত হয়, তেমনি মানসিক বুদ্ধি বিকাশেও সমস্যা দেখা দিতে পারে। আপনি নিশ্চয় জানেন, আপনার এলাকায় বিনিপ সেন্টোরে অপুষ্টিতে আক্রান্ত বাচ্চাদের পুষ্টিকর খাবার দেয়া হচ্ছে। এ সমস্ত ফিডিং সেন্টারে কিছুকিছু মায়েদের আমরা ট্রেনিং দেব কিভাবে বাচ্চাকে পরিপূর্ণ যত্ন নিতে হয় এবং ঘরে তৈরী বিভিন্ন খেলনা দিয়ে বাচ্চাদের সাথে কিভাবে খেলতে হয়, সে বিষয়ে আমরা এ কাজের শুরুতে আপনার বাচ্চাকে পরীক্ষা করে দেখব আপনার বাচ্চার মানসিক বুদ্ধিবৃত্তি অপুষ্টিতে আক্রান্ত বাচ্চার তুলনায় কতটুকু এগিয়ে আছে। এ কাজে অংশগ্রহণ করলে আপনার বাচ্চার কোনভাবেই কোন সমস্যা দেখা দেবে না। এছাড়া আপনার বাড়ীতে গিয়ে আর্থ-সামাজিক অবস্থা এবং বাচ্চার বুদ্ধিবিকাশের উপযোগী পরিবেশের উপর বেশ কিছু প্রশ্ন করব। যে সমস্ত তথ্য আপনি দেবেন তার একান্ত গোপনীয়তা রক্ষা করা হবে।

আপনার যদি আমাদের সাথে সহযোগিতায় কোন প্রকার আপত্তি থাকে, আপনার সম্পূর্ণ স্বাধীনতা আছে এ কাজে যোগদান না করার।

আপনি যদি আমাদের এ কাজে সহযোগিতা করতে রাজী থাকেন, তবে নিম্নে অনুগ্রহ করে আপনার স্বাক্ষর/ বাম হাতের বৃদ্ধাঙ্গুলির টিপ সহি দিবেন।

আমাদের এ কাজে সহযোগিতা করার জন্য আপনাকে অশেষ ধন্যবাদ।

প্রধান গবেষকের স্বাক্ষর	সাক্ষীর স্বাক্ষর	পিতামাতা বা অভিভাবকের স্বাক্ষর/বাম হাতের বৃদ্ধাঙ্গুলির ছাপ
তারিখ ঃ	তারিখ ঃ	তারিখ ঃ

INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH
Mail : ICDDR,B, GPO Box 128, Dhaka-1000, Bangladesh
Phone : 871751-60, Telex: 675612 ICDD BJ
Fax : 880-2-883116, 886050, 871568, 871686, Cable : Cholera Dhaka

ICDDR,B
CENTRE
FOR HEALTH AND
POPULATION RESEARCH

Memorandum

08 September 1999

To : Dr Jena D. Hamadani
Clinical Sciences Division

From: Professor Mahmudur Rahman
Chairman, Ethical Review Committee

Sub : Protocol # 99-021

The Ethical Review Committee met on 25th August 1999 and considered your Protocol # 99-021 entitled "The effect of phychosocial stimulation on the development of malnourished children in BINP Centres in Bangladesh". After thorough discussion in the meeting, the Committee made the following observations:

a) the words 'in Bangladesh' in the title are considered redundant. Therefore, these may be deleted.

b) in the Bangla consent the words 'কিন্তু সে জন্য আপনাকে কোনভাবেই ক্ষতিগ্রস্থ করা হবে না' should be deleted.

You are requested to modify the protocol incorporating the above observations and **resubmit** a copy of it to the Chair of the Committee for necessary action.

Thank you.

copy:- Interim Head
Clinical Sciences Division

ICDDR,B
CENTRE
FOR HEALTH AND
POPULATION RESEARCH

INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH
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Thank you.

copy:- Interim Head
Clinical Sciences Division

Attachment 1.

Date 17.8.99

(FACE SHEET) ETHICAL REVIEW COMMITTEE, ICDDR,B.

Principal Investigator Dr. Jena D. Hamadani Trainee Investigator (if any) x

Application No. 99 - 021 Supporting Agency (if Non-ICDDR,B) NCOE

Title of Study The effect of psycho-social stimulation on the development of malnourished children in BINP Centers in Bangladesh

Project status:
(✓) New Study
( ) Continuation with change
( ) No change (do not fill out rest of form)

Circle the appropriate answer to each of the following (If Not Applicable write NA).

1. Source of Population:
   (a) Ill subjects — Yes No
   (b) Non-ill subjects — (Yes) No
   (c) Minors or persons under guardianship — (Yes) No
2. Does the study involve:
   (a) Physical risks to the subjects — Yes (No)
   (b) Social Risks — Yes (No)
   (c) Psychological risks to subjects — Yes (No)
   (d) Discomfort to subjects — Yes (No)
   (e) Invasion of privacy — (Yes) No
   (f) Disclosure of information damaging to subject or others — Yes (No)
3. Does the study involve:
   (a) Use of records, (hospital, medical, death, birth or other) — Yes (No)
   (b) Use of fetal tissue or abortus — Yes (No)
   (c) Use of organs or body fluids — Yes (No)
4. Are subjects clearly informed about:
   (a) Nature and purposes of study — (Yes) No
   (b) Procedures to be followed including alternatives used — (Yes) No
   (c) Physical risks — (Yes) No
   (d) Sensitive questions — (Yes) No
   (e) Benefits to be derived — (Yes) No
   (f) Right to refuse to participate or to withdraw from study — (Yes) No
   (g) Confidential handling of data * — (Yes) No
   (h) Compensation &/or treatment where there are risks or privacy is involved in any particular procedure — (Yes) No
5. Will signed consent form be required:
   (a) From subjects — Yes (No)
   (b) From parent or guardian (if subjects are minors) — (Yes) No
6. Will precautions be taken to protect anonymity of subjects — (Yes) No
7. Check documents being submitted herewith to Committee:
   ___ Umbrella proposal - Initially submit an overview (all other requirements will be submitted with individual studies).
   ___ Protocol (Required)
   ___ Abstract Summary (Required)
   ___ Statement given or read to subjects on nature of study, risks, types of questions to be asked, and right to refuse to participate or withdraw (Required)
   ___ Informed consent form for subjects
   ___ Informed consent form for parent or guardian
   ___ Procedure for maintaining confidentiality
   ___ Questionnaire or interview schedule *

* If the final instrument is not completed prior to review, the following information should be included in the abstract summary:
1. A description of the areas to be covered in the questionnaire or interview which could be considered either sensitive or which would constitute an invasion of privacy.
2. Examples of the type of specific questions to be asked in the sensitive areas.
3. An indication as to when the questionnaire will be presented to the Cttee. for review.

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

Jena

Principal Investigator

Trainee

Principal Investigator: Last, first, middle Hamadani, Jena, Derakhshani

International Centre for Diarrhoeal Disease Research, Bangladesh

RESEARCH PROTOCOL

99-021

FOR OFFICE USE ONLY
Protocol No: Date:
RRCApproval: Yes/ No Date:
ERC Approval: Yes/No Date:

1. Title of Project (Do not exceed 60 characters including spaces and punctuations) The effect of psychosocial stimulation on the development of malnourished children in BINP Centers in Bangladesh.

2a. Name of the Principal Investigator(s) (Last, Middle, First).	2b. Position / Title	2c. Qualifications
Hamadani, Derakhshani, Jena	Sr. Medical Officer	MBBS, DCH

3. Name of the Division/ Branch / Programme of ICDDR,B under which the study will be carried out.
Clinical Sciences Division

4. Contact Address of the Principal Investigator
4a. Office Location: Dhaka Hospital, ICDDR,B
Mohakhali
Dhaka
Bangladesh

4b. Fax No: 880 2 883116, 880 2 886050
4c. E-mail: jena@icddrb.org
4d. Phone / Ext: 880 2 871751-60 Ext. 2331

5. Use of Human Subjects Yes [✓] No [ ]
5a. Use of Live Animal Yes [ ] No [ ]
5b. If Yes, Specify Animal Species

6. Dates of Proposed Period of Support
(Day, Month, Year - DD/MM/YY)
01/10/999 to 01/02/2002

7. Cost Required for the Budget Period
7a. Ist Year (S): 65,381/= 2nd Year (S): 41,481/= 3rd Year: 13,387/=
7b. Direct Cost (S) 120,249/= Total Cost (S) 138,286/=

8. 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.

Dr. M.A. Salam
Name of the Division Director

Signature

3/8/99
Date of Approval

9. 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.

10. Signature of PI

Date: 3.8.99

Table of Contents

☐ Check here if appendix is included

Principal Investigator: Last, first, middle Hamadani, Jena, Derakhshani

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

Dr. Jena Derakhshani Hamadani

Project Name: The effect of psychosocial stimulation on the development of malnourished children in BINP Centers in Bangladesh.

Total Budget US $ 138,286/= Beginning Date 01/10/1999 Ending Date 01/02/2002

Recently, there has been increasing concern among international agencies and national governments over the loss of human potential in children growing up with poverty and malnutrition and possible ways of improving the situation are being explored. Bangladesh Integrated Nutrition Program (BINP) is a major governmental effort to improve malnourished children's nutritional status. This program should reduce mortality and morbidity in children but it is unlikely to also improve their general cognitive, social and emotional development. This proposal concerns incorporating a low cost, feasible, and culturally appropriate program of child development activities into BINP feeding centers with the aim of improving the social and cognitive development of malnourished children and the child rearing skills of their mothers. It is a randomized controlled trial involving the BINP feeding centers, where a group of malnourished children and their mothers will participate in an intervention on child development activities and will be compared with a control group of malnourished children attending other feeding centers. They will also be compared with a group of wellnourished children living in the intervention areas and matched for age, sex, maternal education, and standard of housing. Intervention will include teaching mothers how to play with their children in a way to promote good development, and how to make toys from waste materials. Attention will also be paid to improving maternal child verbal interaction and to improving mothers' self esteem. The intervention program will last for one year. Stimulation at home and the socio-economic status of the family will be measured during a home visit. Before and after the study, the children's developmental levels, behavior, temperament and anthropometry and the mothers' knowledge of child development and child rearing practices will be assessed.

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

Name	Professional Discipline/ Specialty	Role in the Project
1. Dr. Jena Derakhshani Hamadani	SMO./Paediatrics	Principal Investigator
2. Dr. Syed Nazmul Huda	Associate Professor/Nutrition	Co-PI
3. Dr. Rukhsana Haider	Associate Scientist/Nutrition	Co-Investigator
4. Prof. G. Fuchs	Interim Director/Gastroenterology	Co-Investigator
5. Prof. S.G. McGregor	Professor/Child Development	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.

Mental development of the malnourished children can be improved through psychosocial stimulation added to nutritional supplementation in the BINP community nutrition centers. The child rearing practices of their mothers can also be improved through such a program.

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).

To establish and evaluate a child development program in BINP nutrition centers to improve the development of moderately and severely malnourished children and their mothers' child rearing practices. The long-term aim is to spread the program to all centers. An additional aim is to determine the deficit in children's development and behavior attributed to protein energy malnutrition.

OBJECTIVES

1. Using a randomised controlled design, to establish a child development intervention in 10 feeding centers serving moderately and severely malnourished children aged 6-24 months and their mothers.
2. To compare the intervention group with a control group who also suffer from moderate or severe malnutrition and attend 10 other centers on the following: growth in height and weight for height, behavior, temperament and developmental levels of the children, the mothers' child rearing practices and knowledge of child development, health and nutrition.
3. On the above variables to compare the malnourished groups with a group of adequately nourished children matched for area of residence, maternal education and standard of housing.
4. To determine the logistical problems with implementation of the program.
5. At the end of the study to train existing staff from the control feeding centers in the conduct of the program.

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).**

Introduction: This proposal concerns incorporating a low cost, feasible, and culturally appropriate program of child development activities into the Bangladeshi Integrated Nutrition Project (BINP) feeding centers with the aim of improving the social and cognitive development of severely malnourished children and the child rearing skills of their mothers. The study will be based at the International Center for Diarrheal Diseases Research in Bangladesh (ICDDRB) and is a collaboration between ICDDRB, the Institute of Nutrition and Food Science, Dhaka University, and the Center for International Child Health, Institute of Child Health, University College London.

In recent years, there has been a marked decline in infant mortality rates in nearly all developing countries. In Bangladesh, rates have fallen from 151 per 1,000 in 1960 to 83 in 1996. Although increasing numbers of children are surviving, the quality of many children's lives remains extremely poor. An enormous number of children under five years are malnourished, as many as 56% are moderately or severely underweight and 18% are moderately or severely wasted[i]. Many studies have shown that malnutrition of this degree is highly likely to detrimentally affect children's cognitive, motor and social development[ii]. They are likely to fail in school and subsequently have poor employment opportunities. Compared with better-educated parents, poorly educated parents tend to have larger numbers of children[iii], who have poorer health, nutrition[iv] and cognitive development[v]. Thus the poverty cycle is continued.

The Bangladesh government, like many other developing countries, has made great strides in increasing places in primary schools, however much of this investment will be wasted if the children are unable to benefit fully. The enormous number of malnourished children who almost certainly have poor mental development has implications not only for the individuals but also for national development. There is an urgent need to begin programs to address this problem.

Adoption studies of severely malnourished children have shown that marked improvements in cognitive development are possible if the children are exposed to vastly improved environments[v,vi]. However malnourished children usually come from extremely poor environments; not only is the housing and sanitation inadequate but the 'microenvironment' is also poor with few toys and little opportunity for play[vii]. The mothers usually have low levels of education and lack awareness of the importance of play for children's development.

Recently, there has been increasing concern among international agencies and national governments over the loss of human potential in children growing up with poverty and malnutrition and possible ways of improving the situation are being explored[viii,ix,x].

Interventions in developed countries: Research into early childhood education programs in the USA shows that deprived children generally improve in cognitive development while the programs are running and many show sustained benefits in school performance and social development [8,9]. However the more successful programs have tended to be center based, intensive and high cost, and the children have not usually been undernourished. Therefore the model is probably not useful for developing countries. The challenge is to find low cost and culturally appropriate ways of improving these children's development.

Intervention studies in developing countries: Although interventions have been run with deprived children in several developing countries, extremely few have been rigorously evaluated[xi]. Two early interventions with severely malnourished children used highly trained staff but restricted the duration to the time the children spent in hospital[xii] or rehabilitation center[xiii]. The children showed immediate cognitive benefits but the gains were transient and no longer present 12 months later. In Jamaica, investigators took a different approach, in which paraprofessionals (aides), with relatively little training, visited the homes over a much longer period. The aides demonstrated play techniques using toys made from discarded materials and focused on the mothers as well as the children. The aims were to improve maternal child interactions, the mothers' knowledge of child development and their teaching techniques[xiv,xv,xvi]. The intention was to use the mothers as the intervention agent and it was expected that other children in the family would also benefit. The first study involved severely malnourished children who were in hospital at the beginning of the intervention[13]. They were played with daily in hospital then visited at home for three years following leaving hospital. The children showed marked benefits that were sustained at least up to the age of 16 years. A second study[14] involved moderately growth retarded (stunted) children who were identified in the community and visited for two years. The children were randomly assigned into four groups: supplemented, stimulated, both interventions and control. By the end of the intervention, the children showed independent benefits to their psychomotor development from both stimulation and supplementation, and the group receiving both treatments showed the greatest gains. At 12 years of age, the children still showed benefits to their IQ from stimulation. Interestingly, benefits were more enduring from stimulation than from supplementation. However supplementation is likely to have a greater impact where malnutrition is more severe. Another Jamaican study with deprived but adequately nourished children, showed that weekly contacts produced greater benefits than two weekly or monthly contacts [xvii].

Although the Jamaican approach used paraprofessionals and home made play materials, and was thus low cost compared with North American programs, it may still be too expensive to implement on a large scale in low-income countries. The studies involved frequent individual home visits which are relatively costly and a group approach might reach more children for the same expenditures. The Jamaican government is currently piloting a program working with groups of mothers in order to reduce the costs. Groups may have other benefits to the mothers themselves who will be able to share their problems and make new social contacts.

Treatment of malnourished children in Bangladesh: The present BINP program is a major governmental effort to improve malnourished children's nutritional status. It comprises a total of 972 community nutrition centers where malnourished children are referred for supplementary feeding. Children with weights for age below -3 z scores or with growth faltering (<600g per 2 months in under one year of age, <300g in 2 months in under two years) are referred and they are given supplementary feeding. They are discharged when they reach >-2 z scores but monitoring is continued until the children

are 24 months old. This program should reduce mortality and morbidity in children but it is unlikely to also improve their general cognitive, social and emotional development.

Justification of proposed study: The BINP nutrition centers present an opportunity to introduce child development activities into the treatment of malnourished children in order to promote their all round development. We propose to design an intervention that can be added to the present treatment of malnourished children. The intervention will be piloted and evaluated in feeding centers in a randomized controlled trial. Only one small, non-randomized study elsewhere[13] has shown that severely malnourished children gain long-term benefits from psychosocial stimulation and there is a need to replicate the finding.

There is also a need to develop models for promoting child development that are innovative, low cost and feasible and in this study we will pilot such a program. It is intended to work with groups of mothers and children in the feeding centers. The program will last for as long as one year because short-term interventions have had only transient benefits[13, 14]. We will also meet with the mothers every week as this frequency has been shown to be most effective[18].

It is important that the intervention is culturally appropriate. We recently assessed the stimulation in the home in a study in Dhaka and obtained some useful data. However, more qualitative information would be helpful to enable us to design a suitable intervention, which builds onto the strengths of the culture. We will therefore conduct a rapid survey of child rearing practices in the study villages preceding the study.

In the past researchers have tended to focus on the cognitive effects of malnutrition[xviii]. There is relatively little information on their social behavior and temperament. We will therefore ask new questions about the temperament of malnourished children.

The effects of malnutrition and intervention may be modified by the children's home environment. For example, malnutrition usually causes smaller deficits in children from middle class homes than in poor homes[xix], and intervention is more likely to benefit children in the poorer homes[xx]. The effect of malnutrition in the extremely poor situations found in Bangladesh may therefore be more devastating than that found in better off countries. There is little information on the development of malnourished Bangladeshi children and this study should increase our understanding of their developmental problems and assist in the design of future interventions. In the present study we will measure the socio-economic background of the families and stimulation in the home in detail and determine how they relate to both the effects of malnutrition and treatment.

Finally, the ICDDRB in collaboration with Dhaka University intends to develop a group of academics with skills to conduct essential research linking child development to health and nutrition and to design interventions. There is now a small group of researchers with the necessary skills to run and evaluate an intervention. The proposed study will offer an opportunity to strengthen this group and allow them to get further experience and acquire new skills.

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

A rapid survey comprising holding focus group discussions with women in the villages and interviewing key informants will precede the main study. The main study will be a randomized controlled trial of the effect of adding stimulation to the treatment of malnourished children in feeding centers. Narsingdi thana which is close to Dhaka was recently visited by the investigators and was selected for the study. There are on average 8-10 moderately and severely malnourished children in each feeding center at any time. Twenty selected centers will be randomly assigned to treatment or control groups. (It is not considered ethical to randomize individually within each center). The intervention will run for one year and the outcome measures will be assessed in mothers and children both before and after the study

In addition to the treatment trial, a cohort of matched adequately nourished children will be studied to compare with the malnourished groups. They will come from the same villages served by the intervened centers and will fulfil the same criteria for age, area of residence, and socio-economic background to the intervened children. This comparison will enable us to determine the initial behavioral and psychomotor deficits in the malnourished groups and assess whether the children return to levels normal for their community following intervention.

Recognizing that the children are clustered into feeding centers or villages we will use multilevel modelling in the analyses to enable us to analyze data at the individual child level as well as examine the variance by feeding center and treatment group.

Survey of Child Rearing Practices

Two focus groups with approximately six mothers of children under 5 years of age will be held in 3 control villages and 3 intervention villages. Mothers of malnourished children attending the feeding centers will not be involved.

Each focus group will have a leader and a recorder. The leaders will be Dr. Jena, Dr. Huda and the senior psychologist. Information will be sought on all activities mothers do with their babies, their attitude towards play and child development, knowledge of child development and any games, songs and nursery rhymes, their aspirations for their children and who makes decisions in the family about child care and education.

Treatment Trial

Samples

The study will be conducted in BINP nutrition centers in the Narsingdi Thana. Narsingdi which is situated near Dhaka and has a total population of 353,275 out of whom, there are 21,090 children below the age of 2 years. About 2229 of these children require nutritional supplementation and are enrolled in the BINP community nutrition centers. Narsingdi thana comprises 14 unions with 17-29 feeding centers in each union making a total of 326 feeding centers. Only six of these unions are accessible to Dhaka. For ethical reasons randomization into intervention and control will be by centers and not within each center. Twenty feeding centers from the two unions most accessible to Dhaka, will be selected to participate in the study. Only centers expected to enrol at least 10 children in the five month enrolment period will be selected. The sampling will be in two steps. In the first step, centers that are so close to each other that there is a high probability of the mothers or staff mixing socially, will be formed into clusters. One center from each cluster will then be randomly selected for further sampling. The first stage should prevent any spill over between treatment groups. In the second step 10 centers will be randomly selected for the intervention group and 10 for the control group, from the two unions.

A sample of 84 in each group will be sufficient to detect a difference of 6 developmental quotient (DQ) points between the groups with a power of 90% at the 5% level of significance. Assuming a loss of 16% we need 100 children in each group.

The study will have 3 groups making a total of 300 children who will have all measurements. However, because we want to assess the feasibility of incorporating this programme into a service model we will enrol into the intervention all children who present at the centers and fit the enrolment criteria during the enrolment period. The extra children will not have the measurements but enrolling all available children into the intervention will enable us to determine any problem with implementation at a service level.

Treatment group: The first 10 children referred to each intervention feeding center after the beginning of the study, and fulfil the selection criteria will be enrolled making a total of 100. However, all the children attending the intervention centers will have play opportunities.

Control group: The first 10 children referred to each control feeding center after the beginning of the study and fulfil the selection criteria will be enrolled making a total of 100.

Inclusion criteria: weights for age <-2sd, aged between 6 and 24 months, mothers agree to participate in the study and intend to stay in the area for the next year.

Exclusion criteria: twins and disabled children will be included in the intervention for ethical and demonstration purposes but will not be part of the evaluated sample.

Comparison group: The child living nearest to every treated malnourished child with weight for age >-1sd, of the same age (+/- one month) and sex, maternal education and standard of housing will be enrolled making a total of 100.

Measurements

The Drs Hamadani and Huda will do the piloting and quality control of all measurements.

Developmental level: The infants will be assessed on the Bayley Scales of Mental Development at the beginning and end of the study. We have used these scales before in Bangladesh and good interobserver reliability was attained. The assessments will be done by one of two trained female psychologists who are unaware of the children's group assignment. Care will be taken to keep the testers blind to the child's group and the testing will not be done in the feeding centers.

Behavior: The children's behavior during the tests will be rated by the testers on five 9 point scales: the amount of vocalisation, co-operation with the test procedure, activity level, emotional tone and response to examiner. These scales have also been used before in Bangladesh and are modified from those of Bayley and Wolke et al[xxi].

Temperament: At the end of the study the mothers will be given a questionnaire by the psychologists concerning their child's temperament. There is no standardised test for Bangladeshi children. We will therefore pilot an instrument developed by Mary Rothbart[xxii] and one being developed by Theodore Wachs from Purdue University for use in Jamaica and Peru and combine and modify the instruments where necessary. The following behaviors will be investigated: activity level, positive emotionality (smiling/laughing), negative emotionality (fussing/crying), social approach (response to strange adults), object fear (fear of new objects), attention/orientation, manageability (response to frustration/ co-operativeness), soothability (reduction of distress in response to soothing). These behaviors are well recognised components of temperament[xxiii].

Anthropometry: All children will have their weights, lengths, head and mid upper arm circumferences measured using standard techniques on enrolment and every 3 months by the research assistant.

Socio-economic background and stimulation in the home: All homes will be visited at the beginning of the study and information will be sought on the families' wealth, standard of housing, family structure and parental characteristics. The stimulation in the home will be assessed using a modified version of the Betty Caldwell home inventory[xxiv], which was modified for Bangladesh in a previous study by this research group.

Child rearing practices: The mothers' knowledge of child development and child rearing practices will be assessed at the beginning and end of the study by the psychologist.

Hb Measurement: As suggested by one of the reviewers, we will consider testing the children for their Hb level provided funds are available.

Quality Control of Measurements: Before the study begins, and after training the measurers, inter-observer reliabilities will be assessed for all measures. Values of over $r>0.9$ are expected for all measures and training will continue until this standard is attained. Five to 10 percent of all tests throughout the study will be observed and independently scored by an observer. Test-re-test reliabilities

will also be assessed at the beginning of the study for the temperament scales and Bayley test in 20 subjects and values >0.7 are expected.

Intervention

The intervention will be based on one used previously in Jamaica[15]. It will be modified for Bangladesh following an initial rapid survey of child rearing practices. The mothers will meet in groups at the feeding center for one hour every week for a year. During the initial days, when mothers come daily to the centers, the play leaders will take the opportunity to work individually with mothers and children whenever possible. If the children are judged to be recovered and discharged from the usual services before the end of the year, they will still be included in the stimulation intervention. Those who do not attend will be visited at home and encouraged to come. At the meetings the mothers will be helped to make home made toys and they will be shown how to interact with their children and teach them simple concepts in such a way to improve their development. Only participatory methods or demonstrations will be used. Attention will be paid to improving the maternal child verbal interaction and to improving the mother's self esteem, child rearing and feeding practices. Records will be kept for each child of all contacts with the program staff.

Training: A short training workshop will be held to inform and motivate senior staff concerning the program. A two-week workshop will be held for the play leaders who will be running the program

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).

The feeding centers that we will use are organized by CARE and supervised by ICDDRB. The facilities at the centers will be used for training mothers and observing their children. In addition, we will rent a house in the Narsingdi town where we will conduct the developmental tests. Training of the staff will also be conducted at this house as well as the feeding centers. Data entry and subsequent analysis will be carried out at ICDDRB offices.

To investigate any illness in the study subjects, we will use ICDDRB laboratory. Thana health complexes near the feeding centers will be used for referring the ill subjects. In case of severe diarrhea they will be referred to ICDDRB hospital, while for other serious illnesses requiring tertiary care, Dhaka Shishu Hospital will be contacted.

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).

The qualitative data will be analysed using the framework procedures identified by Ritchie and Spencer[xxv] including indexing, charting, mapping and interpretation.

For the quantitative data, all test records will be checked by a second person and double entered into the computer. All continuous variables will be examined for normality and transformed if necessary. Initial differences between the randomized malnourished groups will be examined using t-tests or analysis of variance for normally distributed data and chi-squared or Mann-Whitney for non-normal data. To compare initial differences between the adequately nourished and malnourished groups the enrolment data for the two malnourished groups will first be combined. When analyzing behavioral data, age and sex will be controlled if they are significantly related to the outcome variable.

As the sample is clustered into feeding centers, multi-level modelling will be used to examine the treatment effect on the children's development, behavior, and temperament and on the maternal outcomes. For this analysis, we will use the computer package designed by the Institute of Education, London[xxvi]. The model used will have 3 levels, the individual child, the feeding centers and the treatment group. With this model we will be able to control for random variance at each of these levels and to examine whether treatment has different effects in different centers.

TIME SCHEDULE

Rapid survey of child rearing practices	2 months
Analyses of findings from survey/ visits to all feeding centers, orientation of staff / piloting of questionnaires/ development of local curriculum/ training of play leaders	4 months
Enrolling of subjects and base line measurements	5 months
Running intervention/home visits (overlap with above 5 months)	7 months
Post-test measurements	5 months
Analyses/reporting/training staff in control centers	5 months
Total time	**28 months**

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.

Signed informed consent of the parents will be obtained after thorough explanation of the purpose of the study, requirements of participation, and the benefits to the child. Another person will be acting as witness.

The study does not include any invasive procedure. However since the study subjects are malnourished children and are always at risk of acquiring illnesses, they will be examined by the study physicians upon enrolment. During the study minor illnesses will be treated and for any major illness, they will be referred to health centers. Liaison with the nearby health centers will be established and maintained to facilitate the referral.

Some of the information collected may be considered sensitive in nature. Therefore, measures will be taken to ensure strict confidentiality of the information obtained.

Approval will be sought from the Ethical Review Committee of ICDDR,B.

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.

Not Applicable

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.

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16. McDonald K., Grantham-McGregor S., Chang S. (1989) *Social stimulation of the severely malnourished child. A home training program.* Indian Journal of Paediatrics 56: 97-103.

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18. Grantham-McGregor S. (1995) A Review of Studies of the Effect of Severe Malnutrition on Mental Development. In: Journal of Nutrition 125 (8S): 2223S-2244S. Supplement on Undernutrition and Behavioral Development in Children.

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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 main purpose of this study is to establish a child development program in BNIP feeding centers to improve the development of moderately and severely malnourished children and their mothers' child rearing practices. However, the long-term aim is to spread the program to all centers. For this purpose a link will be set up with the government of Bangladesh to disseminate the program to all the community nutrition centers in the country. We will publish the results in international journals and present the findings at local meetings.

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)

There will be a scientific collaboration between ICDDR,B, Dhaka University and the Institute of Child Health in London. Associate Professor Dr. Syed Nazmul Huda from Dhaka University is selected as the Co-PI of the project with 35% of his time. Prof. Sally Grantham McGregor of the Institute of Child Health is another Co-Investigator.

Principal Investigator: Last. first. middle Hamadani, Jena, Derakhshani

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.

Name	Position	Date of Birth
Dr. Jena Derakhshani Hamadani 1958	Sr. Medical Officer. CSD ICDDR,B.; Dhaka. Bangladesh	February 18.

Academic Qualifications (Begin with baccalaureate or other initial professional education)

Institution and Location	Degree	Year	Field of Study
University of Dhaka	Diploma in Child Health	1996	Paediatric
Rajshahi Medical College. Rajshahi	M.B.B.S	1984	Medicine
Research and Professional Experience			

Concluding with the present position. list. in chronological order. previous positions held. experience. and honours. Indicate current membership on any professional societies or public committees. List. in. chronological order. the titles. all authors. and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. (DO NOT EXCEED TWO PAGES. USE CONTINUATION SHEETS).

1. One year residential trainig (Inservice training) at Rajshahi Medical College Hospital: Feb'84 - Feb'85

2. Worked as Medical Officer and later as Sr. Medical Officer in Dhaka Hospital of ICDDR,B since February 1985.

Bibliography

Attached

Abstract Summary for Ethical Review Committee

Recently, there has been increasing concern among international agencies and national governments over the loss of human potential in children growing up with poverty and malnutrition and possible ways of improving the situation are being explored. Bangladesh Integrated Nutrition Program (BINP) is a major governmental effort to improve malnourished children's nutritional status. This program should reduce mortality and morbidity in children but it is unlikely to also improve their general cognitive, social and emotional development. This proposal concerns incorporating a low cost, feasible, and culturally appropriate program of child development activities into BINP feeding centers with the aim of improving the social and cognitive development of malnourished children and the child rearing skills of their mothers. It is a randomized controlled trial involving the BINP feeding centers, where a group of malnourished children and their mothers will participate in an intervention on child development activities and will be compared with a control group of malnourished children attending other feeding centers. They will also be compared with a group of wellnourished children living in the intervention areas and matched for age, sex, maternal education, and standard of housing. Intervention will include teaching mothers how to play with their children in a way to promote good development, and how to make toys from waste materials. Attention will also be paid to improving maternal child verbal interaction and to improving mothers' self esteem. The intervention program will last for one year. Stimulation at home and the socio-economic status of the family will be measured during a home visit. Before and after the study, the children's developmental levels, behavior, temperament and anthropometry and the mothers' knowledge of child development and child rearing practices will be assessed.

1. This study aims to improve the mental development of malnourished children and we therefore need to work with children.
2. No physical, psychological, social or legal risk is involved in this study. However, since the study subjects are malnourished and are always at risk of acquiring illnesses, they will be checked by the study physicians upon enrollment. During the study, minor illnesses will be treated and for any major illness, they will be referred to health centers. Liaison with the nearby health centers will be established and maintained to facilitate the referral.
3. There is no potential risk in this study.
4. Some of the information collected may be considered sensitive in nature. Therefore, following measures will be taken to ensure strict confidentiality of the information obtained.

   Mothers will be interviewed individually in their homes.
   Access to collected data will be restricted to the investigators only.

5. Signed informed consent of the parent will be obtained after thorough explanation of the purpose of the study, requirements of participation, and the benefits to the child. Another family member/neighbour will be acting as witness.
6. Mothers will be interviewed at their homes for about one hour at the beginning of the study.
7. As the study is an intervention program, it is likely to be useful for the mental development of malnourished children. The control group will also receive same type of intervention at the end of data collection. Once the objectives of the study are obtained, there will be improvement in development of these children, who are the future hope of the society.
8. Not applicable.

Principal Investigator: Last, first, middle Hamadani, Jena, Derakhshani

DETAILED BUDGET

	Pay level	# of staff	% pf effort	Monthly Rate	US$/Yr 1st yr 12 mths	2nd yr 12 mths	3rd yr mths	Total
Personnel								
Dr Jena D Hamadani, PI	NO-B/11	1	30%	1075	3,870	3,870	1,290	9,030
Co-PI,Dr. N.Huda	NO-B/11	1	35%	1075	4,515	4,515	1,505	10,535
Psychologist	GS-6/I	2	100%	455	10,920	10,920	-	21,840
Play leaders	Spl level	10	100%	60	7,200	7,200	-	14,400
Health Workers-Control villages	Spl level	4	100%	40	1,920	1,920	640	4,480
Driver	GS-2/1	1	100%	189	2,268	2,268	756	5,292
Research Assistant	GS-3/1	1	100%	224	2,688	2,688	896	6,272
	Sub-total				**33,381**	**33,381**	**5,087**	**71,849**
Travelling								
PI & Co-PI to Jamaica for training					6,000	-	-	6,000
Dr. McGregor to Bangladesh twice					2,000	-	2,000	4,000
PI to London for 4 weeks at the end for writing the manuscript					-	-	3,000	3,000
Travelling of play leaders and health					1,000	1,000	500	2,500
					9,000	**1,000**	**5,500**	**15,500**
Others								
Computer and its accessories					3,000	-	-	3,000
Play materials					500	500	200	1,200
Wage loss to mothers					1,000	1,000	500	2,500
Accommodation at the project site @ US$ 100/month					1,200	1,200	400	2,800
Vehicle					12,000	-	-	12,000
Gasoline					2,400	2,400	800	5,600
Maintenance of vehicle					1,200	1,200	400	2,800
Stationery					700	300	200	1,200
Contingencies					1,000	500	300	1,800
	Sub-total				**23,000**	**7,100**	**2,800**	**32,900**
Total					**65,381**	**41,481**	**13,387**	**120,249**
Overhead @ 15%								**18,037**
Grand total								**138,286**

4/8/99

Md. Bazlur Rahman
Senior Budget & Cost Officer
ICDDR, B, Mohakhali
Dhaka-1212, Bangladesh

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.

Personnel

PI and Co-PI will supervise the overall activities of the project. They will play the leading role in implementing the research in the field. they will pilot and train the appropriate personnel in all measurements. plan data entry. conduct analyses and write reports.

Co-PI is working at another institution and will give 35% of his time for this project.

The two psychologists will test 300 children and interview the mothers at the beginning and end of the study.

For the intervention group. we need one play leader at each intervention center making a total of 10.

For the control group health workers will arrange for the testing of the children and keep trace of their whereabouts. Therefore. one health worker can cover 2-3 feeding centers making a total of 4 health workers.

To make frequent visits to the project sites. which are situated outside the city in the rural area. we require a vehicle and a driver.

To supervise the work of the play leaders and help in record keeping, we need a research assistant.

Travelling

To learn the stimulation methods. the PI and Co-PI will visit Jamaica where the same program has been used with success. They will stay there for about 2 weeks.

To start the project. co-investigator. Prof. Sally McGregor will visit Bangladesh from UK for 2 weeks. She will also come after the intervention has begun to assess its progress.

The PI will go to UK to report the findings with Prof Sally McGregor at the end of the project.

Others

A computer and its accessories is required for data entry and manuscript writing.

Materials will be procured to make play materials for the play program.

For the developmental testing, we require a quiet room with no outside disturbance. Such a place is not available at the rural areas. We therefore. need to rent a house at the Narsingdi town to conduct the tests properly.

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.

Personnel

PI and Co-PI will supervise the overall activities of the project. They will play the leading role in implementing the research in the field. they will pilot and train the appropriate personnel in all measurements. plan data entry. conduct analyses and write reports.

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Principal Investigator: Last, first, middle Hamadani, Jena, Derakhshani

APPENDIX

International Centre for Diarrhoeal Disease Research, Bangladesh

Voluntary Consent Form

Title of the Research Project:

Principal Investigator:

Before recruiting into the study, the study subject must be informed about the objectives, procedures, and potential benefits and risks involved in the study. Details of all procedures must be provided including their risks, utility, duration, frequencies, and severity. All questions of the subject must be answered to his/ her satisfaction, indicating that the participation is purely voluntary. For children, consents must be obtained from their parents or legal guardians. The subject must indicate his/ her acceptance of participation by signing or thumb printing on this form.

Intervention Group

The Clinical Sciences Division of ICDDR,B is conducting a study to improve the mental development of the children and the child rearing practices of their mothers.

Malnutrition is a common problem in our country. It causes delay in physical growth as well as mental development. Your child is under the care of BINP nutrition center and will be benefitted for his/her physical growth. To obtain a maximum of mental development your child needs to receive more frequent attention & care. Apart from the diet your child is receiving, we will teach you how to care for your child, like making home-made toys, how to interact with your child, etc., every week for one year. In addition, we will test your child twice, once before and once after program , for his/her psychomotor function.

There is no risk to your child and your child will rather be benefitted by the above program. Any information thought to be secret for you will remain strictly confidential. You have the right to decline from participating into this program, but you will always receive the BINP nutrition facilities. After entering into the program, if you wish to stop the participation, you are at liberty.

Signature of Investigator/ or agents
Date:

Signature of Subject/ Guardian
Date:

Signature of the witness:
Date:

Principal Investigator: Last, first, middle Hamadani, Jena, Derakhshani

APPENDIX

International Centre for Diarrhoeal Disease Research, Bangladesh

Voluntary Consent Form

Title of the Research Project:

Principal Investigator:

Before recruiting into the study, the study subject must be informed about the objectives, procedures, and potential benefits and risks involved in the study. Details of all procedures must be provided including their risks, utility, duration, frequencies, and severity. All questions of the subject must be answered to his/ her satisfaction, indicating that the participation is purely voluntary. For children, consents must be obtained from their parents or legal guardians. The subject must indicate his/ her acceptance of participation by signing or thumb printing on this form.

Control Group:

The Clinical Sciences Division of ICDDR,B is conducting a study to improve the mental development of the children and the child rearing practices of their mothers.

Malnutrition is a common problem in our country. It causes delay in physical growth as well as mental development. Your child is under the care of BINP nutrition center and will be benefitted for his/her physical growth. We are testing a program aiming to obtain a maximum of mental development in children where apart from the diet we will teach the mothers how to care for their child, like making home-made toys, how to interact with their child, etc., every week for one year. We would like to compare those children who will receive this program with your child. We will test your child twice, once before and once after the program, for his/her psychomotor function. At the end of the program, we will also teach you the same program.

There is no risk to your child and your child will rather be benefitted by the above program. Any information thought to be secret for you will remain strictly confidential. You have the right to decline from participating into this program, but you will always receive the BINP nutrition facilities. After entering into the program, if you wish to stop the participation, you are at liberty.

Signature of Investigator/ or agents
Date:

Signature of Subject/ Guardian
Date:

Signature of the witness:
Date:

Principal Investigator: Last, first, middle Hamadani, Jena, Derakhshani

APPENDIX

International Centre for Diarrhoeal Disease Research, Bangladesh
Voluntary Consent Form

Title of the Research Project:

Principal Investigator:

Before recruiting into the study, the study subject must be informed about the objectives, procedures, and potential benefits and risks involved in the study. Details of all procedures must be provided including their risks, utility, duration, frequencies, and severity. All questions of the subject must be answered to his/ her satisfaction, indicating that the participation is purely voluntary. For children, consents must be obtained from their parents or legal guardians. The subject must indicate his/ her acceptance of participation by signing or thumb printing on this form.

Comparison Group:

The Clinical Sciences Division of ICDDR.B is conducting a study to improve the mental development of the children and the child rearing practices of their mothers.

Malnutrition is a common problem in our country. It causes delay in physical growth as well as mental development. We are testing a program aiming to obtain a maximum of mental development in children where apart from the diet we will teach the mothers how to care for their child, like making home-made toys, how to interact with their child, etc., every week for one year. We would like to compare those malnourished children with your child who is not malnourished. We will test your child twice, once before and once after the program, for his/her psychomotor function.

There is no risk to your child and you will be able to know the level of intelligence of your child. Any information thought to be secret for you will remain strictly confidential. You have the right to decline from participating into this program. After entering into the program, if you wish to stop the participation, you are at liberty.

Signature of Investigator/ or agents
Date:

Signature of Subject/ Guardian
Date:

Signature of the witness:
Date:

আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র
মহাখালী, ঢাকা-১২১২

বিনিপ সেন্টারে অপুষ্টিতে আক্রান্ত শিশুদের বুদ্ধিবিকাশে বিভিন্ন উৎসাহব্যাঞ্জক কার্যক্রমের মাধ্যমে মায়েদের পরিচর্যা ও যত্নের ভূমিকা

ইন্টারভেনশন গ্রুপ

সম্মতি পত্র

কলেরা হাসপাতালের ক্লিনিক্যাল সায়েন্স ডিভিশন শিশুদের বুদ্ধি বিকাশে মায়েদের যত্ন এবং লালন পালনের ভূমিকার উপর একটি গবেষণা কাজ হাতে নিয়েছে।

আপনি অবগত আছেন যে, বাংলাদেশে অপুষ্টি একটি মারাত্মক স্বাস্থ্য-সমস্যা। অপুষ্টির কারণে শিশুদের দৈহিক বৃদ্ধি যেমন বাধাপ্রাপ্ত হয়, তেমনি মানসিক বুদ্ধি বিকাশেও সমস্যা দেখা দিতে পারে। আপনার বাচ্চার পূর্ণ মানসিক বিকাশের জন্য আপনাকে আরো যত্নবান হতে হবে। বিনিপ ফিডিং সেন্টরে প্রতিদিন আপনার বাচ্চাকে পুষ্টিকর খাবার খাওয়ানো হয়। এ ছাড়াও আমরা প্রতি সপ্তাহে একদিন আপনাকে ট্রেনিং দেব - কিভাবে শিশুকে সুষ্ঠু ও পরিপূর্ণ যত্ন নিতে হয়, আপনার বাড়ীতেই পরে থাকা বিভিন্ন জিনিষ দিয়ে খেলনা তৈরী করে কিভাবে আপনি আপনার বাচ্চার সাথে খেলবেন - এ সমস্ত বিভিন্ন বিষয়ে আমরা আপনাকে প্রশিক্ষণ দেব।

আমরা এ কাজের শুরুতে এবং শেষে মোট ২ বার আপনার বাচ্চাকে পরীক্ষা করে দেখব - বাচ্চার মানসিক বুদ্ধিবৃত্তি কতটুকু বৃদ্ধি পেয়েছে। এ কাজে অংশগ্রহণ করলে আপনার বাচ্চার কোনভাবেই কোন সমস্যা দেখা দেবে না। এছাড়া আপনার বাড়ীতে গিয়ে আর্থ-সামাজিক অবস্থা এবং বাচ্চার বুদ্ধিবিকাশের উপযোগী পরিবেশের উপর বেশ কিছু প্রশ্ন করব। যে সমস্ত তথ্য আপনি দেবেন তার একান্ত গোপনীয়তা রক্ষা করা হবে।

আপনার যদি আমাদের সাথে সহযোগিতায় কোন প্রকার আপত্তি থাকে, আপনার সম্পূর্ণ স্বাধীনতা আছে এ কাজে যোগদান না করার। কিন্তু সে জন্য আপনাকে কোনভাবেই ক্ষতিগ্রস্থ করা হবে না। আপনি বরাবর যেমন খাবার পাচ্ছিলেন, তা চলতে থাকবে। এ কাজ চলাকালে কখনোও আপনি যদি মনে করেন যে আমাদের সাথে আর কাজ করবেন না আপনি আপনার অসম্মতি সরাসরি জানাতে কোন প্রকার সংকোচ করবেন না।

আপনি যদি আমাদের এ কাজে সহযোগিতা করতে রাজী থাকেন, তবে নিম্নে অনুগ্রহ করে আপনার স্বাক্ষর/ বাম হাতের বৃদ্ধাঙ্গুলির টিপ সহি দিবেন।

আমাদের এ কাজে সহযোগিতা করার জন্য আপনাকে অশেষ ধন্যবাদ।

প্রধান গবেষকের স্বাক্ষর	সাক্ষীর স্বাক্ষর	পিতামাতা বা অভিভাবকের স্বাক্ষর/বাম হাতের বৃদ্ধাঙ্গুলির ছাপ
তারিখ ঃ	তারিখ ঃ	তারিখ ঃ

আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র
মহাখালী, ঢাকা-১২১২

বিনিপ সেন্টারে অপুষ্টিতে আক্রান্ত শিশুদের বুদ্ধিবিকাশে বিভিন্ন উৎসাহব্যাঞ্জক কার্যক্রমের মাধ্যমে মায়েদের পরিচর্যা ও যত্নের ভূমিকা

কন্ট্রোল গ্রুপ

সম্মতি পত্র

কলেরা হাসপাতালের ক্লিনিক্যাল সায়েন্স ডিভিশন শিশুদের বুদ্ধি বিকাশে মায়েদের যত্ন এবং লালন পালনের ভূমিকার উপর একটি গবেষণা কাজ হাতে নিয়েছে।

আপনি অবগত আছেন যে, বাংলাদেশে অপুষ্টি একটি মারাত্মক স্বাস্থ্য-সমস্যা। অপুষ্টির কারণে শিশুদের দৈহিক বৃদ্ধি যেমন বাধাপ্রাপ্ত হয়, তেমনি মানসিক বুদ্ধি বিকাশেও সমস্যা দেখা দিতে পারে। বিনিপ ফিডিং সেন্টারে কিছুকিছু মায়েদের আমরা ট্রেনিং দেব কিভাবে বাচ্চাকে পরিপূর্ণ যত্ন নিতে হয় এবং ঘরে তৈরী বিভিন্ন খেলনা দিয়ে বাচ্চাদের সাথে কিভাবে খেলতে হয়, সে বিষয়ে আমরা আপনার বাচ্চার সাথে সে সব বাচ্চাদের তুলনা করে দেখব বুদ্ধিবৃত্তিতে কোন পার্থক্য আছে কিনা। এ কাজের শেষে আমরা আপনাকেও পূর্ণ প্রশিক্ষণ দেব এ সমস্ত বিষয়ে।

আমরা এ কাজের শুরুতে এবং শেষে মোট ২ বার আপনার বাচ্চাকে পরীক্ষা করে দেখব - বাচ্চার মানসিক বুদ্ধিবৃত্তি কতটুকু বৃদ্ধি পেয়েছে। এ কাজে অংশগ্রহণ করলে আপনার বাচ্চার কোনভাবেই কোন সমস্যা দেখা দেবে না। এছাড়া আপনার বাড়ীতে গিয়ে আর্থ-সামাজিক অবস্থা এবং বাচ্চার বুদ্ধিবিকাশের উপযোগী পরিবেশের উপর বেশ কিছু প্রশ্ন করব। যে সমস্ত তথ্য আপনি দেবেন তার একান্ত গোপনীয়তা রক্ষা করা হবে।

আপনার যদি আমাদের সাথে সহযোগিতায় কোন প্রকার আপত্তি থাকে, আপনার সম্পূর্ণ স্বাধীনতা আছে এ কাজে যোগদান না করার। কিন্তু সে জন্য আপনাকে কোনভাবেই ক্ষতিগ্রস্থ করা হবে না। আপনি বরাবর যেমন খাবার পাচ্ছিলেন, তা চলতে থাকবে। এ কাজ চলাকালে কখনোও আপনি যদি মনে করেন যে আমাদের সাথে আর কাজ করবেন না আপনি আপনার অসম্মতি সরাসরি জানাতে কোন প্রকার সংকোচ করবেন না।

আপনি যদি আমাদের এ কাজে সহযোগিতা করতে রাজী থাকেন, তবে নিম্নে অনুগ্রহ করে আপনার স্বাক্ষর/ বাম হাতের বৃদ্ধাঙ্গুলির টিপ সহি দিবেন।

আমাদের এ কাজে সহযোগিতা করার জন্য আপনাকে অশেষ ধন্যবাদ।

প্রধান গবেষকের স্বাক্ষর	সাক্ষীর স্বাক্ষর	পিতামাতা বা অভিভাবকের স্বাক্ষর/বাম হাতের বৃদ্ধাঙ্গুলির ছাপ
তারিখ ঃ	তারিখ ঃ	তারিখ ঃ

আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র
মহাখালী, ঢাকা-১২১২
বিনিপ সেন্টারে অপুষ্টিতে আক্রান্ত শিশুদের বুদ্ধিবিকাশে বিভিন্ন উৎসাহব্যাঞ্জক কার্যক্রমের মাধ্যমে মায়েদের পরিচর্যা ও যত্নের ভূমিকা

কম্পারিজন গ্রুপ

সম্মতি পত্র

কলেরা হাসপাতালের ক্লিনিক্যাল সায়েন্স ডিভিশন শিশুদের বুদ্ধি বিকাশে মায়েদের যত্ন এবং লালন পালনের ভূমিকার উপর একটি গবেষণা কাজ হাতে নিয়েছে।

আপনি অবগত আছেন যে, বাংলাদেশে অপুষ্টি একটি মারাত্মক স্বাস্থ্য-সমস্যা। অপুষ্টির কারণে শিশুদের দৈহিক বৃদ্ধি যেমন বাধাপ্রাপ্ত হয়, তেমনি মানসিক বুদ্ধি বিকাশেও সমস্যা দেখা দিতে পারে। আপনি নিশ্চয় জানেন, আপনার এলাকায় বিনিপ সেন্টোরে অপুষ্টিতে আক্রান্ত বাচ্চাদের পুষ্টিকর খাবার দেয়া হচ্ছে। এ সমস্ত ফিডিং সেন্টারে কিছুকিছু মায়েদের আমরা ট্রেনিং দেব কিভাবে বাচ্চাকে পরিপূর্ণ যত্ন নিতে হয় এবং ঘরে তৈরী বিভিন্ন খেলনা দিয়ে বাচ্চাদের সাথে কিভাবে খেলতে হয়, সে বিষয়ে আমরা এ কাজের শুরুতে আপনার বাচ্চাকে পরীক্ষা করে দেখব আপনার বাচ্চার মানসিক বুদ্ধিবৃত্তি অপুষ্টিতে আক্রান্ত বাচ্চার তুলনায় কতটুকু এগিয়ে আছে। এ কাজে অংশগ্রহণ করলে আপনার বাচ্চার কোনভাবেই কোন সমস্যা দেখা দেবে না। এছাড়া আপনার বাড়ীতে গিয়ে আর্থ-সামাজিক অবস্থা এবং বাচ্চার বুদ্ধিবিকাশের উপযোগী পরিবেশের উপর বেশ কিছু প্রশ্ন করব। যে সমস্ত তথ্য আপনি দেবেন তার একান্ত গোপনীয়তা রক্ষা করা হবে।

আপনার যদি আমাদের সাথে সহযোগিতায় কোন প্রকার আপত্তি থাকে, আপনার সম্পূর্ণ স্বাধীনতা আছে এ কাজে যোগদান না করার। কিন্তু সে জন্য আপনাকে কোনভাবেই ক্ষতিগ্রস্থ করা হবে না।

আপনি যদি আমাদের এ কাজে সহযোগিতা করতে রাজী থাকেন, তবে নিম্নে অনুগ্রহ করে আপনার স্বাক্ষর/ বাম হাতের বৃদ্ধাঙ্গুলির টিপ সহি দিবেন।
আমাদের এ কাজে সহযোগিতা করার জন্য আপনাকে অশেষ ধন্যবাদ।

প্রধান গবেষকের স্বাক্ষর	সাক্ষীর স্বাক্ষর	পিতামাতা বা অভিভাবকের স্বাক্ষর/বাম হাতের বৃদ্ধাঙ্গুলির ছাপ
তারিখ ঃ	তারিখ ঃ	তারিখ ঃ

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Principal Investigator: Last, first, middle Hamadani, Jena, Derakhshani

Reviewer's Comment: Reviewer # 1

To: Dr. Jena Hamadani

From: Professor Andrew Tomkins

31/7/99

cc: Prof Sally McGregor

Dear Dr. Jena,

Re: Effect of Psychosocial stimulation on the development of malnourished children in BINP centres in Bangladesh.

I was sent your proposal yesterday and asked to review it by Sally. I have a number of comments which will be brief because of my immediate travel plan.

1. The combination of stimulation and nutrition as a means of enhancing child development is established in middle income situations such as Jamaica but there is need to evaluate the intervention in the more harsh microenvironment of Bangladesh.
2. Most previous studies have focussed on cognitive function and the proposal to include assessment of social development is novel and of great importance.
3. Assessment of children's behaviour is constrained by the availability of robust instruments and the development and testing of new instruments as in this proposal is novel and important.
4. The inclusion of a randomised controlled trial is an appropriate way of studying these phenomena.
5. The choice of centres is important. Most studies of behavioural change insist on epidemiological grounds of inclusion of at least 6 pairs of communities and I see that you aim to reach as many as 10 pairs.
6. I note that these children will be assessed for nutritional status by weight and length. If possible I would recommend that they have Hb measured using a Hemocue to assess whether there are any differences in anemia in the groups.
7. I was particularly glad to note your inclusion of a series of indicators of temperament. These are novel and will be of great interest.
8. Overall I score this proposal very highly and recommend it strongly for funding.

Yours sincerely,

Andrew Tomkins

Response to reviewer's comment: Please see measurements Page # 10

Attention Dr M.A. Salam CSD
URGENT

Title The effect of psychosocial stimulation on the development of malnourished children in BNIP centres in Bangladesh

Summary of Referee's Opinions: Please see the following table to evaluate the various aspects of the proposal by checking the appropriate boxes. Your detailed comments are sought on a separate, attached page.

	Rank Score		
	High	Medium	Low
Quality of project	✓		
Adequacy of project design	✓		
Suitability of methodology	✓		
Feasibility within time period	✓		
Appropriateness of budget	✓		
Potential value of field of knowledge	✓		

CONCLUSIONS

I support the application:

a) without qualification ✓

b) with qualification

- on technical grounds / /
- on level of financial support / /

I do not support the application / /

Name of Referee: Ann Ashworth Hill

Signature: Ann Ashworth Date: 2.8.93

Position: Reader in Community Nutrition

Institution: London School of Hygiene & Tropical Medicine

Reviewer # 2

Forwarded Message Follows

From : Self <EPSI/EPHNAHIL>

To : masalam@icddrb.org (Dr. M.A. Salam - CSD)
Subject: URGENT External Review (Dr Jena Hamadani)
Date sent: Tue, 3 Aug 1999

Dear Dr. Salam

I strongly support this proposal. To establsih and evaluate in a service setting a programme of child development makes this a very important study and will be of great interest and value. It has enormous potential implications, not only to the children themselves, but to national development.

I rank it as follows:-

Quality	-	High
Design	-	High
Methods	-	High
Feasible	-	High
Budget	-	Appropriate
Value	-	High

My only comment for consideration is that all children in the intervention centres are included in the play activities, not just the ones that meet the enrolment criteria in the enrolment period (to avoid the other mothers and children feeling 'left out'.)

I will fax the summary sheet.

Yours sincerely

Ann Ashworth Hill

Response to reviewer # 2. According to our initial survey, there are only 8-10 malnourished children in each center, so actually no one will be left out. However, in case we find more malnourished children who do not fulfill the enrolment criteria.We will definitely include them in play activities.

Behaviour Ratings

A. Approach

Initial response to the examiner. The examiner addresses a few introductions, remarks to the child and then talks with the mother first giving the child a toy.
Response in the first 5 to 10 minutes is rated. It should be rated immediately, not at the end of the test.

1. Avoiding: shows stray signs of fear - clinging onto the mother / fussing / looking away, withdrawing.
2. Between 1 and 3
3. Hesitant: Some fear/ obviously worried/wary and watchful/ not happy/ not smiling/ not fussing/ not readily playing but may be slight touching of toy. May look fleetingly at examiner.
4. Between 3 and 5
5. Accepting : No sign of fear but aware of examiner / not offering / not vocalizing or smiling at examiner / but looking at her from time to time without fear. Plays with toy but not with vigour.
6. Between 5 and 7
7. Friendly : Not afraid. May smile or vocalize or offer toy to examiner after a few minutes, plays with toy readily.
8. Between 7 and 9
9. Inviting : Fully accepts examiner, happily. Interacts with her smiling, vocalizing and/or approaching. Obviously enjoys toy, may show enthusiasm in playing.

B. General Emotional Tone

This scale refers to how unhappy and fussy or cheerful and happy the infant appeared during the examination.

1. Child seems unhappy throughout assessment, gets very upset, cries and fusses for long periods or frequently may protest and wail.
2. Between 1 and 3
3. At times rather unhappy, begins to fuss often with cries, shout, verbal protests, but may respond happily to some procedures.
4. Between 3 and 5
5. Moderately happy or contented (smiles and positively vocalizes in response to some tasks), may become upset occasionally but recovers fairly easily.
6. Between 5 and 7
7. Generally appears to be in a happy state of well-being smiles often with some excitement, only becomes briefly unhappy once or twice during the whole assessment.
8. Between 7 and 9.
9. Radiates happiness, highly excited, nothing is upsetting (never becomes upset), animated, expressive, smiling, gleeful.

C. Activity

This scale refers to how physically active the infant was during the testing (gross motor activity).

1. Very still, little gross motor movement, stays quietly in one place, with practically no self-initiated movement, never wiggles around.

2. Between 1 and 3.
3. Usually quiet and inactive, rarely wiggles but responds appropriately in situations calling for some gross motor activities (motor tasks).
4. Between 3 and 5.
5. Moderate activity, wiggles occasionally and may get up or change position a number of times, can be quieted for sedentary tests without much difficulty.
6. Between 5 and 7.
7. In action during much of the assessment period, gets up frequently, moves around the room, wiggles, movements are consolable and can be quieted for sedentary tests, however with difficulties sometimes.
8. Between 7 and 9.
9. Overactive, on the move all the time, wiggles a lot, cannot be quieted for most of the sedentary tests.

D. Co-operativeness

This is a measure of how well the infant cooperates with the examiner and complies with his/her requests.

1. Resists all suggestions or requests which are assessment related, very resisting and uncooperative.
2. Between 1 and 3.
3. Refuses or resists several specific examinations initially or refuses to cooperate during part of the session (e.g. initially or towards the end).
4. Between 3 and 5.
5. Accepts the assessment or situation, neither cooperative nor resistant in relation to examiner, may occasionally say 'No' but will conform.
6. Between 5 and 7.
7. Seems to enjoy the interaction with the examiner, is happy to participate most of the time.
8. Between 7 and 9.
9. Enjoys the session and always complies, readily accepts the examiner's manipulations.

E. Vocalizing

Vocalizations refer to non-crying utterances or to recognizable utterances embedded in crying. These may be cooing, babbling, consonant sounds or words. Crying, per se, no matter how varied, does not qualify.

1. Definitely quiet, 1 or 2 vocalizations
2. Between 1 and 3.
3. Few vocalizations and of short duration.
4. Between 3 and 5.
5. Vocalizations occur as part of activities but too intermittent to constitute vocal excitement, chatter or the like.
6. Between 5 and 7.
7. Vocalizations constitute an obvious part of the infant's activity: infant vocalizes for the sake of vocalizing.
8. Between 7 and 9.
9. Excessive vocalizations, high vocal excitement.

Principal Investigator: Last, first, middle Hamadani, Jena, Derakhshani

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 ☑

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

INTERIM/FINAL

SUMMARY COMPLETION FORM FOR PROTOCOLS

Title : **The Effect of Psychosocial Stimulation on the Development of Malnourished Children in BINP Centres in Bangladesh**

Investigator(s): **Dr. Jena D. Hamadani, Dr. N. Huda, Prof. G. J. Fuchs, Prof. S.M. Grantham Mc-Gregor**

Protocol No. : **99-021** **Budget Code: 102261/102161/102541**

Findings (Abstract): Psychosocial stimulation was offered to a group of malnourished children and they were compared with a group of malnourished children who did not receive any stimulation and another group of well-nourished children. On enrollment the well-nourished children were significantly better than both groups of malnourished children in their mental and psychomotor development, temperament, and home stimulation. One year after the intervention, the intervened children did significantly better than the non-intervened group.

Policy Implications: Treatment of malnourished children should include psychosocial stimulation to ensure appropriate mental development.

Dissemination plans: I will present the results in ASCON X as well as any other conference. Final results will be published in international peer-reviewed journal.

Date: 14.3.02

Jena

Signature of the P.I.

RESEARCH PROTOCOL

FOR OFFICE USE ONLY

Protocol No: Date received:

RRCApproval: Yes/ No Date:

ERC Approval: Yes/No Date:

AEEC Approval: Yes/No Date:

Project Title:

Theme and key words:

Principal Investigator: **Division:** **Phone:**

Address: **Email:**

Co-Principal Investigator(s):

Co-Investigator(s):

Student Investigator/Intern:

Collaborating Institute(s):

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

Gender
- ☐ Male
- ☐ Females

Age
- ☐ 0 – 5 years
- ☐ 5 – 9 years
- ☐ 10 – 19 years
- ☐ 20 +
- ☐ > 65

- ☐ Pregnant Women
- ☐ Fetuses
- ☐ Prisoners
- ☐ Destitutes
- ☐ Service providers
- ☐ Cognitively Impaired
- ☐ CSW
- ☐ Others (specify _____)
- ☐ Animal

Project / study Site (*Check all the apply*):
- ☐ Dhaka Hospital
- ☐ Matlab Hospital
- ☐ Matlab DSS area
- ☐ Matlab non-DSS area
- ☐ Mirzapur
- ☐ Dhaka Community
- ☐ Chakaria
- ☐ Abhoynagar
- ☐ Mirsarai
- ☐ Patiya
- ☐ Other areas in Bangladesh _____
- ☐ Outside Bangladesh
  name of country: _____
- ☐ Multi centre trial
  (Name other countries involved)

Type of Study *(Check all that apply)*:
- ☐ Case Control study
- ☐ Community based trial / intervention
- ☐ Program Project (Umbrella)
- ☐ Secondary Data Analysis
- ☐ Clinical Trial (Hospital/Clinic)
- ☐ Family follow-up study
- ☐ Cross sectional survey
- ☐ Longitudinal Study (cohort or follow-up)
- ☐ Record Review
- ☐ Prophylactic trial
- ☐ Surveillance / monitoring
- ☐ Others

ICDDR,B
CENTRE
FOR HEALTH AND
POPULATION RESEARCH

INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH
Mail : ICDDR,B, GPO Box 128, Dhaka-1000, Bangladesh
Phone : 871751-60, Telex : 675612 ICDD BJ
Fax : 880-2-883116, 886050, 871568, 871686, Cable : Cholera Dhaka

Memorandum

31 October 1999

To : Dr. Shafiqul Alam Sarker
Clinical Sciences Division

From : Professor Mahmudur Rahman
Chairman, Ethical Research Committee

Subject: Approval of protocol # 99-020

This has reference to your memo of 18th October 1999 along with a modified copy of your protocol # 99-020 entitled "Helicobacter Pylori infection associated hypochlorhydria and iron deficiency anemia in child-bearing women in Bangladesh". I am pleased to inform you that the protocol is hereby approved upon your appropriate addressing of the issues raised by the Committee in its meeting held on 6th October 1999.

Thanking you and wishing you success in running the said study.

copy: -Division Director
Clinical Sciences Division

INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH
Mail : ICDDR,B, GPO Box 128, Dhaka-1000, Bangladesh
Phone : 871751-60, Telex : 675612 ICDD BJ
Fax : 880-2-883116, 886050, 871568, 871686, Cable : Cholera Dhaka

CENTRE FOR HEALTH AND POPULATION RESEARCH

Prof SAR Chowdhury
For comments please
Samad

October 18, 1999

To : Professor Mahmudur Rahaman
Chairman, Ethical Review Committee

From : Dr. Shafiqul Alam Sarker SA Sarker
Clinical Sciences Division

Thru: Division Director, CSD

Sub : Protocol # 99-020

Thank you very much for your letter with the comments on the above protocol. Please find below the answers to the comments:

a) We will initially study 160 women to determine the prevalence of *Helicobacter pylori* infection, low gastric acid secretion and iron deficiency anemia. For the Part 2 of the study, we will screen another 138 women. Therefore, the total number of women to be screened will be 160 + 138=298. The figure (500) as mentioned in page 9 has been corrected.

b) The subjects will be screened for worm infestation. And those with heavily infested with *Ankylostoma duodenale* will not be included. The comment has been incorporated in page 16, section 2.4.

c) Lactating women below 2 months of lactation will not be included. (page 16, section 2.4).

d) The adverse events those related to Injection pentagstrin are rare. However, possible side effects have been mentioned and the appropriate measure to manage such events has been included in page. 11, section 1.1.3, paragraph #3.

e) The placebo and the group (iii) with iron therapy alone will be provided anti-Hp therapy plus iron and Anti-hp therapy respectively after completion of the study. The comments have been included in page 14, section 2.1, last paragraph.

f) The comment on Bangla consent form has been incorporated to reflect the English consent form.

g) Provision of obtaining signature or thump impression of the subject (in stead of signature of thump impression of guardian) has been made in the Bangla consent form.

h) Ref # 64 as mentioned in page 14 is correct

i) We have included history of chronic blood loss as a excluding criteria in the protocol in page 16, section 2.4.

A Revised Version of the protocol incorporating the comments is submitted herewith for your kind approval please.

The PI has incorporated all the comments made in the last meeting and addressed these issues appropriately. The Protocol may now be approved for ethical clearance. Secretary (PI Research Branch)

INTERNATIONAL CENTRE FOR DIARRHOEAL DISEASE RESEARCH, BANGLADESH
Mail : ICDDR,B, GPO Box 128, Dhaka-1000, Bangladesh
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CENTRE FOR HEALTH AND POPULATION RESEARCH

Memorandum

27 September 1999

To : Dr. S. A. Sarker
Clinical Sciences Division

From : Professor V. I. Mathan
Chairman, Research Review Committee

Sub : Protocol # 99-020

This has reference to your memo of 27th September 1999 attaching a modified copy of your protocol # 99-020 entitled "Helicobacter Pylori infection associated hypochlorhydria and iron deficiency anemia in child-bearing women in Bangladesh". The protocol is hereby **approved** upon your appropriate addressing of the observations made by the Research Review Committee in its meeting held on 20th September 1999.

Thanking you and wishing your success in running the protocol.

copy:- Interim Head
Clinical Sciences Division

Attachment 1.

Date

(FACE SHEET) ETHICAL REVIEW COMMITTEE, ICDDR,B.

APPROVED COPY 10.10.99

Principal Investigator Dr. S.A. Sarker Trainee Investigator

Application No. 99-020 (Revised) Supporting Agency (if Non-ICDDR,B)

Title of Study Helicobacter pylori infection-associated hypochlorhydria and iron deficiency anemia in Bangladeshi women in childbearing age.

Project status:
(X) New Study
( ) Continuation with change
( ) No change (do not fill out rest of form)

Circle the appropriate answer to each of the following (If Not Applicable write NA).

1. Source of Population:
   (a) Ill subjects — Yes (No)
   (b) Non-ill subjects — (Yes) No
   (c) Minors or persons under guardianship — Yes (No)
2. Does the study involve:
   (a) Physical risks to the subjects — Yes (No)
   (b) Social Risks — Yes (No)
   (c) Psychological risks to subjects — Yes (No)
   (d) Discomfort to subjects — (Yes) No
   (e) Invasion of privacy — Yes (No)
   (f) Disclosure of information damaging to subject or others — (Yes) No
3. Does the study involve:
   (a) Use of records, (hospital, medical, death, birth or other) — (Yes) No
   (b) Use of fetal tissue or abortus — Yes (No)
   (c) Use of organs or body fluids — (Yes) No
4. Are subjects clearly informed about:
   (a) Nature and purposes of study — (Yes) No
   (b) Procedures to be followed including alternatives used — (Yes) No
   (c) Physical risks — (Yes) No
   (d) Sensitive questions — (Yes) No
   (e) Benefits to be derived — (Yes) No
   (f) Right to refuse to participate or to withdraw from study — (Yes) No
   (g) Confidential handling of data — (Yes) No
   (h) Compensation &/or treatment where there are risks or privacy is involved in any particular procedure — Yes N/A
5. Will signed consent form be required:
   (a) From subjects — (Yes) No
   (b) From parent or guardian (if subjects are minors) — Yes No
6. Will precautions be taken to protect anonymity of subjects — (Yes) No
7. Check documents being submitted herewith to Committee:
   ___ Umbrella proposal - Initially submit an overview (all other requirements will be submitted with individual studies).
   ✓ Protocol (Required)
   ✓ Abstract Summary (Required)
   ✓ Statement given or read to subjects on nature of study, risks, types of questions to be asked, and right to refuse to participate or withdraw (Required)
   ___ Informed consent form for subjects
   ___ Informed consent form for parent or guardian
   ___ Procedure for maintaining confidentiality
   ___ Questionnaire or interview schedule *

* If the final instrument is not completed prior to review, the following information should be included in the abstract summary:
1. A description of the areas to be covered in the questionnaire or interview which could be considered either sensitive or which would constitute an invasion of privacy.
2. Examples of the type of specific questions to be asked in the sensitive areas.
3. An indication as to when the questionnaire will be presented to the Cttee. for review.

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

S A Sarker

Principal Investigator

Trainee

International Centre for Diarrhoeal Disease Research, Bangladesh	FOR OFFICIAL USE ONLY	
RESEARCH PROTOCOL 99-020	Protocol No: 99-020	Date:
	RRC Approval: Yes/No	Date:
	ERC Approval: Yes/No	Date:

1. **Title of Project (Do not exceed 60 characters including spaces and punctuations):** *Helicobacter pylori* infection-associated hypochlorhydria and iron deficiency anemia in Bangladeshi women in childbearing age.

2a. Name of the Principal Investigator(s) (Last, Middle, First),	2b. Position/title	2c. Qualifications
Sarker Shafiqul Alam (ICDDR,B)	Associate Scientist	M.D.
Fuchs J George	Interim Director	M.D.

3. **Name of the Division/Branch/Programme of ICDDR,B under which the study will be carried out:**
Clinical Sciences Division

4. Contact Address of the Principal Investigator	
4a. Office Location: ICDDR,B Mohakhali, Dhaka 1212, Bangladesh	**4b. Fax No:** 880-2-883116 **4c. E-mail:** ssarker@cis.icddrb.org **4d. Phone/Ext**: 880-2-871751-60 Ext, 2313

5. Use of Human Subjects	5a. Use of Live Animals	5b. If Yes, Specify Animal Species
Yes ☐ No ☐	Yes ☐ No ☐	Not applicable

6. Dates of Proposed Period of Support (Day, Month, Year-DD/MM/YY)	7. Cost Required for the Budget Period
	7a. I[st] Year ($): 42,589 2[nd] Year ($): 21,489 3[rd] Year 7b. Direct Cost ($) 64,061 Total Cost ($)

8. **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.

Dr. M.A. Salam
Name of the Division Director

Signature

18.10.99
Date of Approval

9. Certification by the Principal Investigator	1. Signature of PI
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.	SA Sarker **Date :** 18/10/99

Table of Contents

☐ Check here if appendix is included

Principal Investigator (Last, first, middle): Sarker Shafiqul Alam

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: Dr. Shafiqul Alam Sarker

Project title: *Helicobacter pylori* infection-associated hypochlorhydria and iron deficiency anemia in Bangladeshi women in childbearing age.

Total Budget: US $ 64,061 **Beginning Date:** July 01, 1999 **Ending Date:** December, 2000

Helicobacter pylori (Hp) is a major gastrointestinal pathogen that causes gastritis and low gastric acid production. Gastric acid is one of the most important luminal factors necessary for optimal non-haeme iron (Fe) absorption. Thus, low gastric acid is a risk factor for iron deficiency anemia (IDA), which affects millions of people, primarily infants and women in the reproductive age. We hypothesize that poor bioavailability of iron in these countries might be related to low gastric acid output resulting from Hp infection. The frequency of low gastric acid secretor and IDA in such population is not known. We, therefore, propose to investigate the frequency of *H. pylori*-associated low gastric acid secretor (hypochlorhydria) and to evaluate its role in causing IDA in women. One hundred sixty women in the reproductive age, living in Nandipara, a peri-urban community of Dhaka city will be studied to ascertain the frequency of *H. pylori*-associated low acid output and IDA. To investigate the role of Hp in causing hypochlorhydria and IDA, an intervention study is also planned. Four groups (25 in each group) of Hp-infected women with IDA and hypochlorhydria, and another group (fifth group) of 25 women with normochlorhydria will be studied. Hp infected women with IDA and hypochlorhydria will be assigned to one of the four interventions: (i) anti-Hp therapy (triple-therapy with clarithromycin, amoxicillin and omeprazole), (ii) anti-Hp triple therapy plus iron (ferrous fumarate), (iii) iron therapy alone, or (iv) placebo. The fifth group of women with Hp infection and IDA but without hypochlorhydria will be treated with anti-Hp therapy.

Urea breath test will be used for identification of *H. pylori* infection. Iron status will be determined by analyzing hemoglobin, serum ferritin, and circulating transferrin receptor. Electrical Impedance Tomography (EIT) will be used to assess basal and pentagastrin-stimulated gastric acid outputs. Urea breath test, iron status, and EIT will be repeated at the end of intervention, and at 3 and 6 months from the time of initiation of intervention therapy.

This study is expected to provide useful, new information on the role of *H. pylori* infection and hypochlorhydria in the etiology of IDA. The findings of this study, therefore, are likely to influence the design of iron fortification strategies/programmes for reducing the burden and consequences of IDA in the developing countries.

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

Name	Professional Discipline/Specialty	Role in the Project
1. Shafiqul Alam Sarker (ICDDR,B, Bangladesh)	Physician/Gastroenterologist	PI
2. George Fuchs (ICDDR,B, Bangladesh)	Pediatrician/Gastroenterologist	Co-PI
3. Lena Davidsson (ETH, Zurich, Switzerland)	Nutritionist	Co-investigator
4. Nurul Haque Alam (ICDDR.B, Bangladesh)	Physician/Gastroenterologist	Co-Investigator
5. Hasan Ashraf (ICDDR, B)	Physician/Gastroenterologist	Co-investigator
6. MA Wahed (ICDDR, B)	Nutritional Biochemist	Co-Investigator
7. Prof. KS Rabbani (Dhaka University)	Biophysicist	Consultant
8. Pius Hildebrand (University Hospital, Basel, Switzerland)	Gastroenterologist	Co-investigator
9. Prof. Klaus Gyr (University Hospital, Basel, Switzerland)	Gastroenterologist	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 Aim of the proposed study. Provide the scientific basis of the hypothesis, critically examining the observations leading to the formulation of the hypothesis.

Iron deficiency anaemia (IDA) is the single largest nutritional deficiency globally, and is a major health problem in the developing countries. *Helicobacter pylori* (Hp) infections are also very common in the developing countries. This important gastrointestinal pathogen causes chronic gastritis, which ultimately progress to gastric atrophy and may thus impair absorption of iron. We, therefore, hypothesize that in Bangladeshi women in the reproductive age:

1. chronic *Helicobacter pylori* infection is a major cause of low gastric acid output (hypochlorhydria), which in turn

2. significantly contributes to the development of iron deficiency anaemia in this population.

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).**

The two specific aims of this study are:

1. to determine the prevalence of hypochlorhydria and iron deficiency anemia in *H. pylori*-infected women in the reproductive age, in a peri-urban slum of Dhaka city, and
2. to determine the if *H. pylori* infection is causally linked to iron deficiency anemia in this population.

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).**

1. *H. pylori* infections and gastric acid secretion

Hp is a major gastrointestinal pathogen, which occurs naturally and inhabits the protective, mucus layer of the gastric epithelial cells. It is the most frequent, known cause of chronic gastritis, and it also plays an important role in the etiology of peptic ulcer disease, gastric cancer, and non-ulcer dyspepsia. [1](reviewed by McGowan et al. 1996). The bacterium is highly adaptive to the unusual ecological niche in the human stomach, perhaps due to its production of large amounts of urease, and enzyme that hydrolyzes urea to ammonia and carbon dioxide leading to its better survival. An important adaptation of Hp to the gastric environment may be related to its ability to alter gastric physiology and function. Although the present discussion is related to Fe nutrition, reduced gastric acid output has other adverse consequences. For example, low gastric acid secretion is associated with increased susceptibility to enteric infections, a major public health problem, and has also been linked to diarrhea, malnutrition and growth failure in children in the developing countries ([2]Weaver 1995).

Acute Hp infection causes gastritis and transient hypochlorhydria, however its mechanism is unclear. One hypothesis is that the parietal cell functions are directly affected by this pathogen ([1]McGowan et al. 1996). Another possible explanation is the increased production of interleukin-1, a cytokine with powerful inhibitory action on acid secretion ([3]Wallace et al. 1991). The most severe outcome of chronic, Hp-induced gastritis is gastric atrophy, which leads to decrease gastric acid secretion and eventually results in achlorhydria. Individuals with reduced gastric acid output may absorb some Fe fortification compounds less well, while those with achlorhydria will have reduced absorption of all non-heme Fe ([4]Skikne et al. 1981).

In some other studies, HP-infection has actually been found to be associated with increased gastric acid output ([5]El-Omar et al. 1995a). Thus, the relationship between Hp infection and gastric acid secretion remains to be fully elucidated. This discrepancy may be related to the site of infection-antral colonization may increase gastric acid secretion as has been observed in Hp-infected individuals with duodenal ulcer ([6]El-Omar et al. 1995b). In a hospital-based study, gastrin-releasing peptide (GRP)-stimulated acid secretion was increased in significantly higher proportion of Hp-infected non-ulcer patients, compared to Hp-negative healthy subjects ([5]El-Omar et al. 1995).

It was reported later by the same group ([7]El-Omar et al. 1997) that Hp was predominantly responsible for gastric hypochlorhydria in a sub-group of Hp-infected Scottish subjects. Eradication of Hp resulted in variable degrees of restoration of gastric secretory function, ranging from minimal

increase to full restoration of gastric secretion. However, despite improvement in inflammation, eradication of *H. pylori* infection did not result in significant change in gastric atrophy and intestinal metaplasia, although partial recovery was observed in some of the subjects ([6]El-Omar et al. 1997). Restoration of gastric acid secretion was observed after successful treatment of dyspeptic patients with HP infection in a recent study ([8]Gutierrez et al. 1997). Finally, there is a serious lack in data from developing countries with regards to gastric functional abnormalities, specifically gastric acid secretion in Hp-infected population.

2. Iron deficiency anemia

Iron (Fe) deficiency anemia (IDA) is a major nutritional problem in the world that affect millions of people in the developing countries, particularly infants, children and women of child-bearing age ([9]Bothwell et al. 1979, [10]DeMaeyer & Adiels - Tegman 1985). The consequences of IDA include higher perinatal morbidity and mortality among mothers and children; impaired immune function and increased susceptibility to infections; decreased work performance; poor growth and potentially irreversible effects on cognition and motor function during early life ([11]Scrimshaw 1984, [12]Dallman 1987, [13]Lozoff et al. 1991, [14]Walter 1992). Thus, prevention and treatment of IDA are important in delivering health care to such population.

2.a Gastrointestinal function and iron deficiency anaemia

The relationship between IDA and gastrointestinal functions including gastric acid secretion has been studied in children and adults. Nieman and his colleagues studied 14 iron-deficient infants and children, and observed profound suppression of gastric acid secretion in majority of the subjects ([15] Niemann et al 1964). Studies in India have observed reduced gastric acid secretion in children ([16] Ghosh et al 1972) and in adults ([17] Sherman et al 1966) with iron deficiency anaemia. Reduction of acid secretion including histamine-fast achlorhydria also been reported in other Indian studies ([18]Desai et al 1967, [19]Desai et al 1968); compared to controls, acid outputs were significantly reduced in patients with iron deficiency. Histological abnormalities of the gastric mucosa suggestive of chronic gastritis were demonstrated in 61% of the patients in these studies. Other studies have observed very high incidence (75%) of chronic gastritis with iron deficiency anaemia ([20] Ikkala & Siuarala 1964). However, it is not known if these abnormalities precede iron deficiency anemia. An early acquisition of infection in children in developing countries suggests that Hp-related chronic gastritis might precede iron deficiency anaemia in these countries.

2.b Etiology of IDA

In the developing countries, IDA may result from several, overlapping etiologies, however, low Fe bioavailability plays a major role ([21]Taylor et al. 1995). Diets in many developing countries are cereal-based, and thus high in phytic acid, a potent inhibitor of Fe absorption ([22]Hallberg et al. 1987, [23]Hurrell et al. 1992, [24]Davidsson et al. 1994a). They are also low in major Fe absorption promoters such as ascorbic acid ([25]Layrisse et al. 1968, [26]1984, [27]Martinez-Torres et al. 1970, [28]Taylor et al. 1986, [29]Hallberg et al. 1986, [30]1989, [31]Siegenberg et al. 1991, [24]Davidsson et al. 1994a). The overall Fe bioavailability from such diets can be expected to be low or very low, resulting in reduced absorption of Fe while the requirements are relatively high in infants, children and women of childbearing age. High prevalence of infectious diseases, and other nutritional deficiencies in

developing countries can also contribute to the development of IDA; gastrointestinal parasites such as hookworm ([32]Stoltzfus 1997a), malaria ([33]Stoltzfus 1997b), and vitamin A deficiency ([34]West 1996) are factors important in the etiology of anemia.

Hp infection is considered a factor for anemia and IDA- Hp infection, common in such condition, has been discussed in the etiology of anemia and IDA ([35]Dufour et al. 1993, [36]Rosenstock et al. 1996, [37]Marignani et al. 1997, [38]Yip et al. 1997). This gastrointestinal pathogen has a worldwide distribution, however, it is more prevalent in the developing countries. The frequency of Hp infection is high in India, where >80% become infected by 20 years of age ([39]Graham et al. 1991); in Bangladesh, where its prevalence in adults and children has been reported to be as high as 85% ([40]Sarker et al. 1995). Once infected, Hp infection is believed to remain throughout the life causing chronic gastritis, which is a risk factor for development of gastric atrophy and gastric cancer ([41]Kuipers et al. 1995). Gastric acid is considered to be one of the most important luminal factors necessary for optimal absorption non-haeme Fe (reviewed by [4]Skikne et al. 1981). It is possible that Hp infections may reduce absorption of Fe by causing gastric atrophy and achlorhydria, or by causing transient hypochlorhydria during the active infections. Both of these mechanisms would result in an increased susceptibility to IDA. Furthermore, increased fecal blood loss in Hp-infected individuals may contribute to IDA ([38]Yip et al. 1997).

3. Importance of *H. pylori* infection in IDA and Food fortification program to combat Fe deficiency

Fe fortification of food is believed to be the most cost-effective approach to reduce Fe deficiency ([42]Hurrell 1997, [43]1998). While Fe fortification programs have been relatively successful in industrialized countries, they had limited success in the developing countries ([42]Hurrell 1997). This perhaps reflects differences in the aetiology of IDA in the developed versus the developing countries. If IDA is related to a lower bioavailability of Fe from diets such as cereals and legumes, fortification of such diets may not be the ideal method for Fe supplementation, unless it is protected from the inhibitors of absorption such as phytate. Ascorbic acid ([24]Davidsson et al. 1994a, [44]1997, [45]1998) or Na_2EDTA ([16]INACG 1993) could be suitable for this purpose. If IDA is partly due to increased blood loss from gastrointestinal parasites, then their treatment will be required for the food fortification program to be maximally effective. Similarly, treatment of malaria and Hp-infection could be important. Treatment of these infections in the developing countries would be very expensive and impractical due to higher incidences of treatment failure/reinfection. Thus, addressing these issues is critical for implementation of a successful Fe-fortification program in such countries.

3.1 Fe fortification

Fe is the most difficult mineral to add to the foods. When added as water-soluble, highly absorbable forms such as ferrous sulfate, the soluble Fe rapidly causes unacceptable color reactions in the presence of many fruits and vegetables, and in stored cereal flours it rapidly catalyzes fat oxidation reactions leading to rancid products ([42]Hurrell 1997). Food manufacturers are often obliged to use water-insoluble Fe compounds to fortify foods, especially in fortifying cereal flours and salt- food vehicles considered most useful for Fe fortification programs in the developing countries. These water-insoluble compounds cause no organoleptic problems, however, their absorption is largely dependent on the extent of their dissolution in the gastric juice.

Fortification compounds such as elemental Fe or ferric pyrophosphate, widely used to fortify cereal flours and weaning cereals, do not completely dissolve in the gastric juice of healthy subjects with normal gastric acid output, and also far less absorbed than ferrous sulfate ([42]Hurrell 1997). On the other hand, ferrous fumarate is almost insoluble in water, however, it is readily dissolved in the gastric juice of healthy subjects, and its absorption in adults has been observed to be equivalent to ferrous sulfate ([47]Hurrell et al. 1989). Ferrous fumarate is an interesting Fe fortificant, which has been used to fortify maize flour in Venezuela ([48]Layrisse et al. 1996), has been proposed as a fortificant of chocolate drink powder ([49]Hurrell et al. 1991), and has recently been selected for a pilot salt fortification programme organized by the Micronutrient Initiative in Bangladesh, Ghana and Guatemala (Micronutrient Initiative 1997, personal communication). However, there is a concern that a proportion of the population in the developing countries such as Bangladesh, are likely to have hypochlorhydria or achlorhydria due to Hp-infection and thus they may not be able to absorb Fe from ferrous fumarate fortified foods.

4. Study objectives

Once acquired, Hp infection remains throughout the life, causing chronic gastritis, a risk factor for development of gastric atrophy and gastric cancer ([41]Kuipers et al 1995). Gastric acid is the most important luminal factor necessary for optimal absorption of non-heme iron Fe ([4]Skikne et al 1981). It is possible that Hp infection may reduce absorption of Fe consequent to gastric atrophy and achlorhydria, or due to a transient hypochlorhydria during active infections. Either of these mechanisms would result in an increased susceptibility of IDA. Hp-infected individuals have been found to have reduced levels of serum ferritin ([50]Milman et al. 1998).

There is no published information on the relationship between Hp infection and gastric acid secretion. We plan to obtain information on the prevalence of reduced gastric acid secretion among Hp-infected subjects, and also hope to evaluate if Hp infection *per se* is a factor in causing IDA.

If, as hypothesized, Hp-linked hypochlorhydria is found to be a factor for IDA, it will help address an important issue with regards to effectiveness of Fe-fortification program since ferrous fumarate, that requires gastric acid for its bioavailability, is the used as Fe-fortificant in the developing countries.

5. Significance

Results from the study will provide new information on prevalence of *H. pylori* infection, and its association with low gastric acid secretion as well as IDA. Thus, results of this study are expected to have important implications for the treatment and prevention of IDA in population of developing countries.

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).**

This study has two parts to address its two objectives, which complement each other, and will be done, in sequence to test our hypothesis.

1. **First part:** To determine prevalence of *H. pylori* infection, low gastric acid secretion and IDA in Bangladeshi women in the reproductive age living in a peri-urban community of Dhaka City.

2. **Second part**: To conduct a randomized, double-blind, placebo-controlled field trial in the same population to determine if *H. pylori* infection is causally linked to iron deficiency anemia in this population.

1. Part 1: First Objective of the Study

To determine the prevalence of *H. pylori* infection, low gastric acid secretion, and iron deficiency anaemia in Bangladeshi women in the reproductive age living in a peri-urban slum of Dhaka city.

One hundred sixty (160) adult women aged, 20-40 years, living in Nandipara, a peri-urban community of Dhaka city will be screened for *H. pylori* infection using the ^{13}C-urea breath test. Their gastric acid secretion will be assessed by the non-invasive, Electrical Impedance Tomotography ([40]Sarker et al. 1997); and their body iron status will be determined. All subjects will be fully informed about the aims of the study and the procedures to be followed, and written informed consent will be obtained before their enrollment in the study.

1.1 Methods

1.1.1 Screening of Women for *H. pylori* Infection

^{13}C-urea breath test (UBT) will be used for screening women for presence of *H. pylori* infection.

^{13}C-urea Breath Test

H. pylori produces an enzyme, urease, which breaks urea to ammonia and carbon dioxide and the later is exhaled in the breath. This forms the basis of the "Urea Breath Test (UBT). The ^{13}C-urea breath test (UBT) is based on the enzymatic degradation of labeled (^{13}C) urea to ammonia,

and labeled CO_2 that is exhaled in breath and thus can be collected and analyzed. The UBT has a high specificity (97-100%) and sensitivity (95-97%), and is widely used as a non-invasive technique for diagnosing current *H. pylori* infection ([51]Lerlang et al .1998, [52]Logan et al. 1991, [53]Vandenplas et al. 1992, [54]Sarker et al. 1997). This simple, non-invasive test is currently regarded as the "Gold Standard" for detection of *H .pylori* infection ([51]Lerlang et al. 1998).

Breath samples will be collected for determining the baseline $^{13}CO_2$ enrichment by blowing through a pipe directly into Vacutainer tubes after 2 hours of fast. Participating women will be asked to drink a glass of whole milk (200 ml), and 10 minutes later 100-mg ^{13}C-urea (99%, Tracer Technologies, Boston, MA) in 25 ml of water. Thirty minutes later breath samples will again be collected in duplicates. Breath thus collected will be analyzed for ^{13}C enrichment at the Department of Medicine and Research, University of Basal, Switzerland by mass spectrometry. Samples with excess enrichment over baseline (^{13}C enrichment of >3.5%) will be regarded as indicative of *H. pylori* infection.

1.1.2 Screening for Low Gastric Acid Secretor

Electrical impedance Tomography (EIT) method that produces qualitative estimates of gastric acid secretion will be used for screening low gastric acid secretor.

Electrical Impedance Tomography (EIT)

The Electrical Impedance Tomography (EIT) method has been described in detail earlier ([55]Brown et al. 1985, [56]Avill et al. 1987, [57]Mangnall et al. 1987, [58]Baxter et al. 1988). The principal of the test is that secretions of H^+ ion (acid) into the stomach alters the ionic conductivity, which can generate tomographic image and can be measured, like computer scan. The system and software were developed at the Institute for Biomedical Equipment Evaluation and Service in Sheffield, UK. The system includes a data collection unit to measure and process the signals received from electrodes placed on the body surface, and a microcomputer to reconstruct the EIT image. It uses 16 measuring electrodes plus a common electrode for noise rejection, and it operates with a current of 1mA at 50kHz. By applying more than 2 electrodes, the resistivity can be measured between any pair of electrodes, and a tomographic picture of resistivity (resistance per length) in the body can be produced. With a 16-electrode array, 208 measurements are made during each cycle of 100 ms. Several cycles are added together to form a data set. Electrode contact is monitored by reference to an oscilloscope. The total test time is 2 hours.

Gastric resistivity is measured through 16 electrodes separately placed at equal distance in a horizontal place around the abdomen at the level of the eight costal cartilage (5 cm above the umbilicus), a place transecting the gastric fundus. The common electrode is place in the left lower back. Following an initial reference image, 3-minute frames are obtained for 120 min. Subsequent data sets are then back-projected against the initial set to produce a cross-sectional image of the change in distribution of resistivity in the area of the electrodes. After 30 min., 6μ/kg body weight pentagastrin (Cambridge Laboratories, Newcastle upon Tyne, UK) is injected subcutaneously. EIT images are then obtained for 90 min. After 120 min., the subject is given 250 ml normal saline as a drink in order to visualize the position of the stomach. A fixed size of the gastric region of interest (ROI) is outlined from the image obtained immediately after ingestion of the drink. The ROI thus allows comparison of actual resitivity changes during the

examination. The changes in logarithms of impedance over time within ROI are measured and plotted. Values for total gastric acid output are expressed as Area under Curve (AUC) calculated from the graph using a standard formula ([59]Thompson et al. 1972). The change of resistivity after pentagastrin stimulation is calculated by subtracting the actual baseline AUC value extrapolated for 90 min, basal AUC, from that of the stimulated AUC. The technique was recently validated ([40]Sarker et al. 1997a). The AUC value <300 will be considered indication of hypochlorhydria. The equipment is not available at ICDDR,B and thus needs to be purchased.

The manufacturer of the EIT system now markets the portable version of the system. Therefore, we also plan to validate the portable system of EIT against the standard gastric intubation test in additional 40 women prior to screening for *H. pylori* infection.

1.1.3 Validation of Portable EIT System

Before application in the field, the portable EIT system will be validated against the standard intubation (Pentagastrin) test. Gastric intubation and EIT measurement will be performed on 40 women at two separate, randomly chosen occasions.

Gastric Intubation

After an overnight fast, a soft nasogastric tube will be introduced, and the tip of the tube will be positioned at the most dependent part of the stomach under fluoroscopic control. After aspirating resting gastric juice, basal samples will be collected for 30 minutes. Pentagastrin (Cambridge Laboratories, Newcastle upon Tyne, UK) will be administered (6µg/kg of body weight) subcutaneously and 15-minute cycles of aspiration of gastric juice will continue for an additional 90 minutes. Acidity of each sample will be measured by titration of 1.0 ml gastric juice with 0.01N sodium hydroxide to pH 7.4 using an automatic titrator (Metrohm, Herisau, Switzerland). Total acid output will be calculated for each time point by multiplying volume of gastric juice and acid concentration. Acid outputs/hour will be calculated based on 4 baseline samples (basal acid output) and the 4 first samples collected after administration of pentagastrin (stimulated acid output).

Adverse events related to Injection of 6µg/kg pentagastrin are extremely rare. However, there may be transient hypotension, nausea, light headedness, malaise, tachycardia, flushing, and rash; all rapidly responding to intravenous antihistamine, and hydocortisone. We will use hydrocortisone 5 mg/kg dose, and/or chlopheniramine maleate 2 mg/dose to manage the events.

The validation of EIT system against standard intubation test will be performed in two ways, as done before by Sarker et al 1995 [40]. Firstly, in term of overall correlation between gastric acid output and AUC in EIT system. Second, in term of sensitivity and specificity of EIT system as compared to the standard intubation test. AUC below 300, and total stimulated gastric acid below 10 mmol/h will be considered indicative of hypochlorhydria. A dose-response curve analysing the basal phase and with pentagastrin at different dose (1 µg/kg, 3 µg/kg, and 6 µg/kg) will also be performed.

1.1.4 Screening for Iron Deficiency Anaemia (IDA)

Venous blood samples (2.5 ml) will be collected in EDTA-treated tubes, and analyzed for Fe status parameters- hemoglobin (Hb), serum ferritin (SF), serum transferrin receptor (sTfR), and serum iron and iron binding capacity (TIBC).

1.1.4.1 Laboratory Diagnosis of Iron Deficiency Anemia

Measurement of Hb concentration is the most useful for screening test for IDA since it directly reflects the quantity of the most abundant essential iron compound in the body. However, the diagnosis of IDA requires estimation of SF concentration ([60] Linpisarn et al 1996), and sTfR ([61]Cook et al 1993) due to the fact that Hb concentration may be transiently depressed in inflammation or infection, and thus does not indicate pathological anemia under such circumstances. Of all the biochemical tests for assessing Fe status, a low SF is the most specific test for iron deficiency. However, the major disadvantage of SF is its readily elevation in response to infection or inflammatory conditions. The impact of infection on SF is often described as a "reticuloendothelial block" , which reduces the release of Fe from phagocytic cells breaking down Hb, and thus reduce the serum Fe concentrations by intracellular accumulation of ferritin iron ([62]Means & Krantz 1992).

Determination of sTfR is a promising new test for evaluation of Fe status. A major advantage of sTfR is that unlike SF infection, or inflammatory process does not significantly influence it. However, sTfR levels are increased under conditions of increased breakdown of RBC e.g. in hemolytic anemia such as thalassaemia. A uniform cutoff value of >8.5 mg/L is regarded as elevation of sTfR, and thus of IDA or hemolytic anemia. When performed in conjunction with SF measurements, the sTfR serves to distinguish true IDA from anaemia of chronic disease or inflammatory diseases, and thus offers a major advantage in determining true prevalence of IDA in population studies ([61]Cook et al 1993).

Transferrin saturation (serum iron/iron binding capacity) is the most widely available confirmatory tests for iron deficiency. Typically serum iron is depressed and the iron binding capacity is elevated in iron deficiency, but the later is not consistent finding and its absence by no means excludes the diagnosis. Low transferrin saturation and serum irons are characteristics of both iron deficiency, or recent or concurrent infection.

The following table indicates the indicators of iron deficiency and iron deficiency anemia.

Table: Laboratory indicators of iron deficiency and iron deficiency anaemia

Indicators	Iron deficiency	Iron deficiency anemia
Hb	⇔	↓
SF	↓	↓
sTfR	↑	↑

1.1.4.2. Definition of iron deficiency anaemia

Iron deficiency anaemia will be defined as: haemoglobin value below the WHO cut-off for women (12 g/dL) ([63]Dallman et al 1995) plus two out of three abnormal Fe status measurements; plasma ferritin values <12 g/L, plasma circulating transferrin receptor values >8.5 mg/L ([61]Cook et al 1993) and transferrin satuaration values <15%.

1.1.5 Sample Size

Prevalence of HP-linked IDA and Hypochlorhydria

The reported prevalence rate of *Helicobacter pylori* infection in the community is 80%. We assume 60% of the Hp-infected women will have hypochlorhydria and 70% of the Hp-infected hypochlorhydric women will have iron deficiency anaemia. However, we like to have an estimate of the prevalence of Hp infection plus hypochlorhytdria plus iron deficiency anaemia to be corrected within ± 5.0 % with 95% confidence

The required sample size will be:

$$\frac{\varepsilon}{\sqrt{PQ/n}} = Z_\alpha$$

Where
- ε = allowable error
- P= estimated prevalence
- Q= 1-P
- n= the required sample size
- Z_α= value of the normal variation for $(1-\alpha)$% confidence

Assuming:
$\varepsilon = 7.5\%$,
$P = 0.8 * 0.6 * 0.7$
$\cong 34\%$
$Q = 1-P = 66\%$
and $Z_\alpha = 1.96$ (95%confidence)

The required sample size of Hp infected women with hypochlorhydria and IDA:

$$\frac{\varepsilon}{\sqrt{PQ/n}} = Z_\alpha$$

$$\frac{0.075}{\sqrt{0.34*0.66/n}} = 1.96$$

Therefore $n = 1.96^2 * 0.34 * 0.66 / 0.075^2$
= 154 women. However, we will take 160 sample.

2. Part 2: Testing of the second objective

Randomized, double-blind, placebo-controlled, community trial

2.1 Methods

To determine if there is a causal relationship of IDA with Hp infection, or if Hp infection has any relationship with IDA, an intervention study will be conducted on 100 Hp-infected women with hypochlorhydria and IDA. They will be randomized in equal numbers to receive either of the following four interventions:

(i) Anti Hp therapy: A combination of 500mg clarithromycin twice daily + 500mg amoxicillin twice daily + 40 mg omiprazole once daily for 14 days

(ii) Anti Hp therapy plus iron: The above + ferrous fumarate containing 60-mg elemental iron each day for 60 days

(iii) Iron alone: Ferrous fumarate containing 60-mg elemental iron each day for 60 days

(iv) Placebo: Starch powder

Fifth group: There will be a fifth group of 25 women with Hp infection but without hypochlorhydria. This group is required to observe the influence of hypochlorhydria *per se* on IDA. This group will also be treated with Anti-Hp therapy plus iron.

The therapies will be provided in gelatin capsules and will be fed daily in morning and at the evening. The women in the placebo group will receive same amount of starch powder in identical capsules for 60 days. To keep the study blind, all therapies will be kept in identical container and will be fed by a health worker who will remain unaware of the nature of the study and the contents inside the bottles.

The women will be followed for six months after the end of intervention. Hb, SF, and sTfR will be determined at the end of intervention and also, 3 and 6 months after the intervention. Urea breath test will also be performed at the same time. EIT will be repeated 6 months after intervention. The women in the placebo groups will be given anti-Hp therapy plus iron as indicated above at the end of study period of 6 months. Similarly the group (iii) women will also provided anti-Hp therapy at the end of the study. The dose of iron conforms to that used in Bangladesh ([64] Kolsteren et al 1999).

2.2 Randomization

An experienced person not related in any way with the study will prepare a master randomization chart. A permuted block randomization with variable block length will be used. Box containing anti-Hp therapy, iron therapy, or placebo will be identical in appearance and will be arranged in sequence that corresponds to the randomization chart which will be sequentially numbered. The serial number of the box will correspond to the random number of women enrolled in the study. As one group of women would receive anti-Hp therapy and Fe therapy

simultaneously, there will be two boxes (boxes A and B) for each group of women to make the study double-blind. For women belonging to anti-Hp plus iron therapy, one box will contain anti-Hp therapy and the other box will contain Fe therapy. For women in the iron therapy or anti-Hp therapy groups alone, one of the boxes will contain active drug and the other will contain placebo for the other therapy. As the duration of therapy of anti-Hp therapy is 14 days, the women belonging to this group will be provided placebo capsules for the rest 44 days to maintain the double-blind nature of the study.

2.3 Sample size

The sample size is determined with the assumptions that anaemia will be corrected in 95% women with Anti-Hp therapy plus iron-therapy, while iron therapy alone will correct anaemia in 60% of the women. Thus, the worthwhile difference (D) in correction of anemia will be:

$D = 95 - 60 = 35\%$

At 5% level of significance (type I error of 5%) with 80% power (type II error of 20%), and to detect a 35% difference in the outcome (correction of anaemia), the sample size has been estimated as follows:

$$n = 2\,P(1-P) * (Z\alpha/2 + Z\beta)/D^2$$

Where: $P = (P_1 + P_2)/2 = (95 + 60)/2 = 77.5\%$

(P_1 is 95% and P_2 is 60%)

$$n = 2 * 0.775\,(1-0.775) * (1.96 + 0.86)^2 / (0.35)^2$$
$$= 1.55 * 0.225 * (2.82)^2 / 0.1225$$
$$= 0.34875 * 7.95 / 0.1225$$
$$= 22.6$$
$$\cong 23 \text{ subjects in each of the five groups}$$

Based on previous study in the same community, we anticipate a drop out rate of approximately 10%. Therefore, the number of women to be enrolled is 25 in each group i.e. 25 *5=125 women in total in 5 groups.

The reported prevalence of Hp infection is 80%. We estimate 60 % of infected population will be hypochlorhydric. of whom 70% will have IDA. We need to screen 298 (100/0.8*0.6*0.7) women to identify 100 infected women (for four groups) with hypochlorhydria and iron deficiency anemia. As 160 women will be enrolled under the first part of the study we will require138 (298-160=138) additional women to be screened under the second part of the study.

We need a fifth group of 25 women with Hp infection but without hypochlorhydria. They will be selected from among these 260 women.

2.4 Exclusion Criteria

Women with the following conditions will not be eligible for this study:

- Acute infection, or apparent inflammatory process

- Severe anemia (Hb of < 8g/dL)
- Severe malnutrition (body mass index <14)
- Presence of occult blood in stool as detected by HemoQuant test ([65]Schwartz et al 1983).
- History of chronic blood loss e.g. polymenorrhoea
- Presence of *Ancylostoma duodenale* (hook worm) in stool
- Pregnant and lactating women (initial 2 months of lactation)

2.5 Laboratory Methods

Hb will be analyzed using the cyanomethemoglobin method (Sigma kit, Sigma, St. Louis, MO). Transferrin saturation will be assessed by analysis of Fe and total Fe-binding capacity (TIBC) (Sigma kit), and plasma ferritin and circulating transferrin receptor will be measured by ELISA (Ramco, Houston, TX). Commercial quality control materials (DiaMed, Cressier sur morat, Switzerland, Sigma and Ramco) will be analyzed together with all series of samples analyzed for Hb, Fe, TIBC and plasma ferritin.

2.6.1 Outcome Measures

- Prevalence of Hp infection and hypochlorhydria before and after intervention
- Prevalence of IDA in each group before and after the intervention
- Rise of serum Hb and SF, transferrin saturation, and reduction in sTfR before and after intervention
- Change of gastric acid output before and after intervention.

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 equipment 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).**

The study will be carried out under the Clinical Science Division of ICDDR,B. The study population will be recruited from Nandipara, a peri-urban community, situated 7 miles northeast of Dhaka city Centre. The community has a population of 4,500 with about 750 reproductive age women, in an area of approximately 3 square miles. The prevalence of Hp infection in women of this community is about 80%. Since 1985, ICDDR,B operates a weekly clinic for provision of care to the population for their minor illnesses.

Blood analysis including Hb, SF and sTfR, and measurement of gastric acid concentration will be performed in the laboratories of the Laboratory Sciences Division of ICDDR, B. Breath samples for UBT will be sent to the University of Basel, Switzerland where ^{13}C will be measured by mass spectrometry (IRMS).

Data Analysis

Describe plans for data analysis. Indicate whether data will be analyzed by the investigators themselves or by other professionals. Specify what statistical software 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).**

Principal Investigator (Last, first, middle): Sarker Shafiqul Alam

Data will be entered onto personal computer (PC) and analyzed by the investigators themselves using the Windows version of the Statistical Package for Social Science (SPSS).

Chi square test will be used for comparison of the proportions of IDA in Hp-infected women with normal acid secretion (>300 AUC) versus women with low acid secretion (AUC <300).

Clinical characteristic such as age and weight, and laboratory characteristics such as Hb, SF, and sTfR concentration will be compared among the groups by one way analysis of variance (ANOVA). When significant F ratio ($p<0.05$) is obtained, means will be compared by student's t-test using multiple comparison procedure. Outcome variables e.g. change in the Hb, SF and sTfR, and gastric acid output before and after intervention in each group will be compared using paired t-test. Data with skewed distribution will be normalized using log transformation, and the t-test will be applied on transformed data. Chi-square (X^2) test will be applied for comparison of binary variables e.g. the incidence of Hp infection with hypoclorhydria and IDA before and after therapy, and also for comparison between groups. The Odd's Ratio (OR) and Confidence Interval (CI) will be calculated. Multivariate analysis (logistic regression and multiple regression) will be done for adjustment of confounding variables such as age, socioeconomic status, and nutritional status .

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.

IDA is a major public health problem in the developing countries that afflicts millions of people, primarily infants, children and women of reproductive age. This study has been designed to address this important public health issue, and the results of this study may help formulate strategies for fortification programme to improve body iron status of women in the reproductive age.

Only after full explanation of the aims and procedures of this study, and securing the written informed consent subjects will be enrolled in the study. The subjects will reserve the right to not participate in the study, and also to withdraw their consent at any time during the course of the study. The population will be directly benefited from the study as they will be diagnosed and will be treated with appropriate medication. Information derived from this study will also have practical implications for the design of successful food fortification strategies in developing countries, and thus benefit the society.

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.

Not applicable

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 judgement in assessing the "standard" length.

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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 program.

It is expected that the information generated from this study will lead us to a better understanding of IDA among women in the reproductive age. Thus, results are expected to have major public health implications in terms of prevention and treatment of IDA in population of developing countries with high prevalence of Hp infection.

Results of this study will be disseminated within the country through scientific conference(s), and internationally through scientific congress/conference/symposium as well as through publication in international biomedical journal.

Collaborative Arrangements

This study is collaborative one between ICDDR, B, the University of Basel, Switzerland, and Institute of Food Science, Laboratory for Human Nutrition, ETH, Zurich, Switzerland. We will also collaborate with Prof. S. R. Rabbani of the University of Dhaka, who will be involved in setting and validating Electrical Impedance Tomography at ICDDR,B. The investigators from Switzerland will be actively involved in analyzing UBT by mass spectrometry for the diagnosis of Hp infection (University of Basel), and for measurement of iron status parameters (ETH).

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.

Name	Position	Date of Birth
Name: Shafiqul A. Sarker, MBBS, MD	Associate Scientist	January 21, 1953

Academic Qualifications (Begin with baccalaureate or other initial professional education)

Institution and Location	Degree	Year	Field of Study
Rajshahi University, Bangladesh	**MBBS**	**1976**	Medicine & Surgery
University of Basle, Switzerland	**MD**	1991	Internal Medicine

Research and Professional Experience

Concluding with the present position, list, in chronological order, previous positions held, experience, and honours. Indicate current membership on any professional societies or public committees. List, in, chronological order, the titles, all authors, and complete references to all publications during the past three years and to representative earlier publications pertinent to this application. **(DO NOT EXCEED**

A. Professional Experience

Service: Position	**Institution**	**Year**
Medical Officer	International Centre for Diarrhoeal Diseases Research, Bangladesh (ICDDR,B)	1982-87
Assistant Scientist/ Sr. Medical Officer	ICDDR, B	1987-92
Associate Scientist	ICDDR, B	1992 till date

Clinical Research Fellowships/Training:

Field of Training	Place	Date
Clinical Nutrition	ICDDR, B, Dhaka Hospital	1979-81
Internal Medicine/ Gastroenterology	University Hospital, Basel, Switzerland	1989-91
G.I. Endoscopy	Division of Gastroenterology, University Hospital, Basel, Switzerland	September-December 1996

B. RESEARCH PRODUCTIVITY

Sl #	Title/Journal name/year
1	Molla AM, Rahaman M, **Sarker SA**, Sack DA, A Molla. Stool electrolytes content and purging rates in diarrhoea caused by rotavirus, enterotoxigenic *E. coli* and *V. cholerae* in children. *J Pediatr*1981;98:835-8.
2	Molla AM, Hossain M, Islam R, Bardhan PK, **Sarker SA**,. Hypoglycemia: A complication of diarrhoea in children. *Indian Pediatr* 1981; 18: 181-5.
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12	Molla AM, **Sarker SA**, Molla A, Khatun M, Greenough III. Rice based oral rehydration therapy in acute diarrhoea: a superior therapy and a medium for calorie supplementation. In Eeckels RE, Ransome-Kuti O, Kroonberg OC, eds. *Child health in the tropics; Sixth Nutrition-Cow & Gate Symposium*, Leuven, 1983. Dordrecht, The Netherland: Nijhoff, 1985;65-70.
13	Molla AM, Molla A, **Sarker SA.** Malabsorption in Acute Diarrhoea. In: Chagas C. Keutch GT eds. Interaction of parasitic infection and Nutrition. Pontificia Academia Scientivarm, Citta Del Vaticano, Roma, 1985;35-41.
14	**Sarker SA,** Wahed MA, Rahaman MM, Islam A, Jahan F. Persistent Protein losing Enteropathy in post-measles diarrhoea. *Arch Dis Childhood,* 1986,61:739-43.
15	Alam AN, **Sarker SA,** Molla AM, Rahman MM, Greenough WB-III. Hydrolyzed wheat based oral rehydration solution for acute diarrhoea. *Arch Dis Child* 1987;62:440-44.
16	Molla AM, Molla A, **Sarker SA**. Management of acute infectious diarrhoea. *Bailler's Clinical Gastroenterology* 1987; 1:377-95.
17	**Thesis:** Infectious Diarrhoea and Gastrointestinal Defense with special reference to non-invasive assessment of gastrointestinal function. University of Basel, Switzerland, 1991.

18 **Sarker SA,** Gyr K. Non-Immunological Gastrointestinal Defense. *Gut* 1992;33:987-93.

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24 Nahar Q, **Sarker SA**, Karim SR, Malek MA. Factors Related to Birth Weight in an Urban Maternity Centre of Bangladesh. *Bangladesh J Nutrition* 1995;8:13-19.

25 Miraj AM, Albert MJ, **Sarker SA**, Bhattacharya MK, Azad AK. Septicemia due to *Vibrio cholerae* O139 Bengal. *Diagn Microbiol Infect Dis* 1995;22:337-338.

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33 **Sarker SA,** Casswall TH, Mahalanabis D, Alam NH, Albert MJ, Fuchs G, Hammarström L. Successful treatment of rotavirus diarrhoea in children with immunoglobulin from immunized bovine colostrum. Pediatr Infect Dis J (in press).

34 Casswall T, Nilsson HO, Bergström M, Aleljung P, Wadström T, Dahlström AK, Albert MJ, **Sarker SA.** Evaluation of serology, ^{13}C-urea breath test and PCR of stool to detect *Helicobater pylori* in Bangladeshi children. Eur J Ped Gastro Nutr (in press).

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APPENDIX

International Centre for Diarrhoeal Disease Research, Bangladesh
Voluntary Consent Form

Title of the Research Project: *Helicobacter pylori* infection-associated hypochlorhydria and iron deficiency anemia in Bangladeshi women in childbearing age.

Principal Investigator: Dr. Shafiqul Alam Sarker

Before recruiting into the study, the study subject must be informed about the objectives, procedures, and potential benefits and risks involved in the study. Details of all procedures must be provided including their risks, utility, duration, frequencies, and severity. All questions of the subject must be answered to his/her satisfaction, indicating that the participation is purely voluntary. For children, consents must be obtained from their parents or legal guardians. The subject must indicate his/her acceptance of participation by signing or thumb printing on this form.

[This form will be read and clearly explained in local language before obtaining the consent]

You are suffering from anemia as well as infection due to a germ called *Helicobacter pylori*, both of which are major health problems in Bangladesh. This germ causes changes in the stomach that leads to decreased production of acid, which is required for absorption of iron from the intestine. In this way, the germ may finally cause anaemia.

We are conducting a research in this Nandipara area to examine how many women in the reproductive age have infection due to this germ, reduced production of gastric acid and anaemia. We invite you to participate in this study, and if you agree to our proposal:

1. One of the investigators of this study will examine you to determine your nutritional status and other health problems if any.

2. We will collect 2.5 millilitre (1/2 teaspoonful) of blood from a vein on your forearm for diagnosis of anemia and determination of its type.
3. To determine if you are infected with *Helicobacter pylori*, we will collect your breath sample twice- before and after feeding you a powder of ^{13}C-urea in 25.0 millilitre (five teaspoonful) of water. For this purpose you will be required to blow your breath into a tube through a pipe.
4. To measure the amount of acid secretion into your stomach, we will take tomographic images of your stomach after an overnight fast. Sixteen electrodes (small piece of metals connected by wires) will be placed around your abdomen in a circle, and image of your stomach content will be obtained for 30 minutes by a computer. After this, pentagastrin, a medicine that increases the secretion of gastric acid will be injected beneath your skin, and further images of your stomach will be taken for another 2 hours.
5. You may be provided one of the following four treatments:
   - Antibiotics for 14 days to kill the germs
   - Iron for 60 days
   - Antibiotics for 14 days plus Iron for 60 days, or
   - Placebo

   We will repeat breath test and impedance test at 1, 3 and 6 months after therapy. 2.5 millilitre venous blood will also be taken at the same time for evaluating correction of anaemia.

6. **For intubation test**
We may request you to be admitted in the metabolic study ward of the Dhaka Hospital (Cholera Hospital) of ICDDR,B for 3 days in order to see how good the tomographic image test is for assessment of gastric acid secretion.

The followings will be done:

After an overnight fast, a soft, flexible rubber tube (10 French) is to be swallowed slowly to place its tip in the stomach. Fluids from the stomach will be collected through tube for ½ hour. Then, 500 µg of Pentagastrin, a medicine that stimulates stomach acid production, will be injected under your forearm skin. Your stomach fluid will then be collected for another hour. Collected fluid will be tested for acid concentration.

7. There are no major risks involved in this study. At the time of collection of blood, you may experience momentary pain, and there is a small risk of bluish discoloration of the skin around the needle stick due to minor leakage of blood from the vein, which fades away in a few days without causing any further problem. Chances of infection at the site of needle sticks will also be very little since blood will be collected using sterile, disposable plastic syringe and needles, after thorough cleansing of the skin with iodine and alcohol.

8. The drugs that will be used for treatment of iron deficiency anemia are quite safe and well tolerated. You may, however, experience minor side effects of the drugs such as vomiting tendency or vomiting, loose motion, and allergic reactions. They will not cause any permanent effect, and they are reversible upon withdrawal of the drug.

9. You will be benefited from participating in this study because of identification of your anemia, determination of its type and getting its proper treatment. Additionally, the results of this study will enrich our knowledge and help us in determining better treatment options for such conditions, and thus benefit the society.

10. You are the one to decide for and against participation in this study. You may also withdraw your consent at any time after inclusion in the study. Whether or not you participate in this study, and also in the event you withdraw your consent, you will continue to receive the usual, good care of this clinic as offered to other patients.

11. If you have any further questions about this study, or if you want to know further, you may contact Dr. Mohammed Abdus Salam, Chief Physician of Dhaka Hospital of ICDDR,B. personally or by telephone (Telephone No. 871751, Ext. 2302 or 9886734).

12. If you agree to our proposal to participate in this study, please indicate that by providing your signature or left thumb impression at the space specified below.

Thank you for your cooperation and assistance.

Declaration by the investigator:
I have obtained assent of the subject after explaining the purpose and procedures of the study to her in a simple, understandable, local language.

Signature of Investigator	**Signature/left thumb impression of subject**	**Signature of witness**
Date: _____	**Date:** _____	**Date:** _____
_____	_____	_____

স্মরণী

আন্তর্জাতিক উদরাময় গবেষণা কেন্দ্র
মহাখালী, ঢাকা-১২১২

স্বেচ্ছা স্বম্মতি পত্র

গবেষণা প্রকল্প শিরোনামঃ হেলিকোব্যাক্টর পাইলোরী জীবাণু জনিত স্বল্প অম্লরস নিঃসরণ বাংলাদেশের সন্তান ধারণ ক্ষমতা সম্পন্ন মহিলাদের রক্তশূন্যতা

হেলিকোব্যাক্টর পাইলোরী নামক এক প্রকার জীবাণুর সংক্রমনে সৃষ্ট রোগের কারণে আপনি রক্তশূন্যতা রোগে ভুগছেন। এই সমস্যা আমাদের দেশের অন্যতম স্বাস্থ্যজনিত সমস্যা হিসেবে চিহ্নিত। এই সংক্রমন পাকস্থলীর অম্লরসের নিঃসরণ কমিয়ে দিতে পারে, যা পরবর্তীতে লৌহের শোষণ ক্ষমতা কমিয়ে দিয়ে লৌহের অভাবজনিত রক্তশূন্যতা রোগ দেখা দেয়।

আমরা কেন্দ্রের নন্দীপাড়া চিকিৎসাকেন্দ্রে একটি গবেষণা কার্য চালাতে যাচ্ছি, যেখানে আমরা পরীক্ষা করে দেখতে চাই যে, কতজন মহিলা হেলিকোব্যাক্টর পাইলোরী নামক জীবাণুর সংক্রমনে পাকস্থলীর নিঃসরণ ক্ষমতা কমার কারণে রক্তশূন্যতা রোগে ভুগছেন। আমরা আপনাকে এই গবেষণা কার্যে অংশ গ্রহণের জন্য অনুরোধ করছি। আপনি যদি আমাদের এই গবেষণা কার্যে অংশগ্রহণ করতে রাজী থাকেন তাহলে -

১। একজন গবেষক আপনাকে পরীক্ষা করে আপনার পুষ্টিজনিত অবস্থা, রক্তশূন্যতা আছে কিনা বা অন্য কোন স্বাস্থ্যজনিত সমস্যা আছে কিনা তা পরীক্ষা করবেন।

২। আপনার হাতের শিরা থেকে ২.৫ মিঃ লিঃ (আধা চা-চামচেরও কিছু কম) পরিমাণ রক্ত নেয়া হবে, যা দিয়ে আপনার রক্তশূন্যতার লক্ষণসমূহ এবং প্রকারভেদ নির্ণয় করা হবে।

৩। হেলিকোব্যাক্টর পাইলোরীর সংক্রমণ নির্ণয়ের জন্য আপনার কাছ থেকে নিঃশ্বাসের নমুনা সংগ্রহ করা হবে। এই নিঃশ্বাসের নমুনা প্রথমে ১৩C ইউরিয়া ২৫.০ মিঃলিঃ (পাঁচ চা-চামচ) পরিমাণ পানির সাথে মিশিয়ে খাওয়ার আগে ও পরে দুইবার করে নেয়া হবে। একটি সরু নলের মাধ্যমে ফু দিয়ে এ নমুনা সংগ্রহ করা হবে।

৪। আপনার পাকস্থলীর অম্লরস নিঃসরণের অবস্থা বোঝার জন্য এক রাত উপবাস থাকতে হবে। কম্পিউটারের সাহায্যে আপনার পেটের উপরের অংশে বৃত্তাকারে ১৬টি ইলেকট্রোড লাগিয়ে ৩০ মিনিট ধরে পাকস্থলীর বিভিন্ন ছবি সংগ্রহ করা হবে। এর ৩০ মিনিট পর আপনাকে একটি ইনজেকশন দেয়া হবে, যার নাম পেন্টাগাসট্রিন। এটা পাকস্থলীর অম্লরস নিঃসরণ বাড়িয়ে দেয়। আবার ১ ঘন্টা (দুই ঘন্টা) ধরে একই পদ্ধতিতে আপনার পাকস্থলীর ছবি সংগ্রহ করা হবে।

৫। আপনাকে নীচের চারটির যে কোন একটি দ্বারা চিকিৎসা করা হতে পারেঃ-

ক) ১৪ দিন ব্যাপী জীবাণু নাশক ঔষধ (এন্টিবায়োটিক)
খ) ৬০ দিন ব্যাপী লৌহ চিকিৎসা
গ) জীবাণু নাশক ঔষধ ও লৌহ চিকিৎসা (এন্টিবায়োটিক ১৪ দিন, লৌহ চিকিৎসা ৬০ দিন)
ঘ) প্লাসিবো বা শর্করা জাতীয় পাউডার

উপরোক্ত চিকিৎসা শেষে ১ম, ৩য় ও ৬ষ্ঠ মাসে পুনরায় ১৩ কার্বন খাইয়ে নিঃশ্বাসের পরীক্ষা করা হবে এবং কম্পিউটারের সাহায্যে পাকস্থলীর অম্লরসের পরিমাণও নিরূপন করা হবে। এ সময় হাতের শিরা থেকে ২.৫ মিঃ লিঃ রক্ত সংগ্রহ করে রক্তশুন্যতা ভাল হয়েছে কিনা তা দেখা হবে।

৬। " ইনটিউবেশন পরীক্ষা "

" আপনাকে কলেরা হাসপাতালের মেটাবলিক ইউনিট ওয়ার্ডে ৩ দিনের জন্য ভর্তি করা হতে পারে। তখন আমরা আপনাকে নিম্নের পরীক্ষাগুলো করবো।

সারারাত উপবাস করার পর সকালে একটি নরম রবারের নল পাকস্থলীতে ধীরে ধীরে প্রবেশ করানো হবে। এই রবারের নল দিয়ে আধা ঘন্টা ব্যাপী আপনার পাকস্থলীর তরল পদার্থ সংগ্রহ করা হবে। তারপর, আপনাকে ৫০০ মাইক্রোগ্রাম ক্যালসিয়াম

পেন্টাগাস্ট্রিন নামক একটি ইনজেকশন দেয়া হবে, যা পাকস্থলীর অম্লরস নিঃসরণ বাড়িয়ে দেয়। এখন আমার ১ ঘন্টা ধরে পাকস্থলীর তরল পদার্থ সংগ্রহ করা হবে। এই সংগৃহীত তরল পদার্থে অম্লরস কতটুকু আছে তা পরিমাপ করা হবে।

৭। এই গবেষণা কার্যে কোন ঝুঁকি নেই। রক্ত নেওয়ার সময় আপনি অল্প ব্যথা পেতে পারেন এবং সুঁই ফুটানোর জায়গায় একটু নীল হয়ে যেতে পারে, যদিও এই নীল হওয়া অংশ অল্প কয়েকদিনের মধ্যে কোন অসুবিধা ছাড়াই এমনি ঠিক হয়ে যাবে, অল্প অল্প রক্ত নেয়া হওয়ার জন্য এমন নীল হতে পারে , যা কোন বড় ধরণের ঝুঁকি নেই। সুঁই ফুটানোর জায়গায় সংক্রমণ হওয়ার সম্ভাবনাও খুব কম, যেহেতু রক্ত নেয়ার সময় আপনার চামড়ায় আয়োডিন ও এ্যালকোহল দিয়ে পরিস্কার করা হবে এবং পরিস্কার ও পরিশোধিত প্লাষ্টিকের সিরিঞ্জ ও সুঁচ দ্বারা রক্ত নেয়া হবে। পেন্টাগাস্ট্রিন পরীক্ষায় পাকস্থলীতে সরু নল প্রবেশ করানোর সময় আপনি একটু অস্বস্তি বোধ করতে পারেন।

৮। যে ওষুধগুলি দ্বারা আপনার পাকস্থলীর জীবাণু নষ্ট করা হবে এবং যৌহের ঘাটতিজনিত রক্তশূন্যতা দূর করা হবে, সেগুলিতে সবগুলি নিরাপদ ও সুসহনীয়। যদিও এই ওষুধগুলি খেলে আপনার বমি বমি ভাব, বমি, পাতলা পায়খানা ও এ্যালার্জি দেখা দিতে পারে, এগুলি ক্ষণস্থায়ী। আপনি ওষুধ খাওয়া বন্ধ করার পর পরই এগুলি দূর হয়ে যাবে।

৯। এই গবেষণা কার্যে অংশগ্রহণ করে আপনি উপকৃত হবেন, কারণ আপনি আপনার রক্তশূন্যতার মাত্রা ও প্রকারভেদ সম্পর্কে জানতে পারছেন এবং রক্তশূন্যতার চিকিৎসা পাচ্ছেন। এই সাথে এই গবেষণা কার্যের লাভ ফলাফল আমাদের জ্ঞানবৃদ্ধি করবে যা ভবিষ্যতে এ রোগের আরও ভাল চিকিৎসা দিতে সাহায্য করবে।

১০। এই গবেষণা কার্যে অংশগ্রহণ করা না করা সম্পূর্ণ আপনার ইচ্ছা। আপনি এই গবেষণা কার্যে অংশগ্রহণ করার পরও যে কোন সময় আপনি আপনার সম্মতি প্রত্যাহার করতে পারবেন। আপনি এই গবেষণা কার্যে অংশগ্রহণ করেন আর না করেন অথবা অংশগ্রহণ করার পর আপনার সম্মতি প্রত্যাহার করেন, তবুও আপনি আর সকল রুগীদের ন্যায় এই চিকিৎসা কেন্দ্রের স্বাভাবিক ও সুচিকিৎসা পেতে থাকবেন।

১১। আপনার যদি এই গবেষণা কার্য সম্বন্ধে আরও কোন প্রশ্ন থাকে, অথবা আপনি যদি আরো জানতে চান, সেক্ষেত্রে আপনি নিম্নলিখিত ঠিকানায় যোগাযোগ করতে পারেন-

ডাঃ মোহাম্মদ আব্দুস সালাম
প্রধান চিকিৎসক, ঢাকা হাসপাতাল
আইসিডিডিআর,বি, মহাখালী, ঢাকা।
ফোন নং ঃ ৮৭১৭৫১-৬০ Ext।। ২৩০২
অথবা ৯৮৮৬৭৩৪

১২। আপনি যদি এই গবেষণা কার্যে অংশগ্রহণে রাজী থাকেন, তবে নীচে নির্দিষ্ট স্থানে আপনার নাম সই করুন অথবা টিপ সই দিন।

আপনার সহযোগিতার জন্য ধন্যবাদ।

গবেষকের বক্তব্যঃ

আমি এই মহিলাকে গবেষণা কার্যের সকল উদ্দেশ্য ও পদ্ধতি সমূহ সহজ, বোধগম্য ও আঞ্চলিক ভাষায় ব্যাখ্যা করার পর তার অংশগ্রহণের সম্মতি গ্রহণ করেছি।

গবেষকের স্বাক্ষর	সাক্ষীর স্বাক্ষর	অংশগ্রহণ কারীর স্বাক্ষর/অথবা বাম বৃদ্ধাঙ্গুলির টিপ সহি

Project Title: *Helicobacter pylori* infection - associated hypochlorhydria and iron deficience anaemia in child bearing women in Bangladesh

PI: Dr. Shafiqul A. Sarker

Project Duration: 18 months from starting

Line item		% effort	1st year	2nd year	Total US$
PERSONNEL (Local salaries)					
Dr.S. A. Sarker (#1747-5)		25	4,196	2,182	6,378
Dr. G.J. Fuchs		5	-	-	-
Dr. N.H. Alam (1698-0)		10	1,538	808	2,346
Dr. H. Ashraf (2927-2)		10	1,220	640	1,860
Study Physician-1		100	5,025	2,512	7,537
Health Assistant 2		100	4,000	2,000	6,000
Health Worker 4		100	2,000	1,000	3,000
Biostatistician-1			-	1,000	1,000
	Sub-Total		17,979	10,142	28,121
INTERNATIONAL TRAVEL					
Ticket Cost, per diem etc. for attending			-	3,000	3,000
Conference and Seminar					
	Sub-Total		-	3,000	3,000
LOCAL TRAVEL					
General Transportation for follow-up visits			400	400	800
	Sub-Total		400	400	800
SUPPLIES AND MATERIALS					
Ferritin Kit (US$ 100 per kit x 20)			1,000	1,000	2,000
Transferin Receptor Kit (US$ 300 per kit x 20)			3,000	3,000	6,000
Medicine (antibiotics, iron, vitamin etc.)			350	350	700
	Sub-Total		4,350	4,350	8,700
OTHER CONTRACTUAL SERVICES					
Printing and Publication of Forms			250	250	500
Patient food & Diet, ICDDR,B			400	400	800
Service Charge, Daily wager & Short-term staff			300	300	600
Compensation for wage loss			500	500	1,000
	Sub-Total		1,450	1,450	2,900
INTERDEPARTMENTAL SERVICES					
Transport			500	500	1,000
Medical Illustration			50	50	100
Xerox,Memo & Library Services			100	100	200
Laboratory Tests			1,500	1,500	3,000
Patient Hospitalization			2,500	-	2,500
	Sub-Total		4,650	2,150	6,800
CAPITAL EXPENDITURE					
Electrical Impedance Tomography & Others			13,740	-	13,740
	Sub-Total		13,740		13,740
Total Direct Cost			42,569	21,492	64,061

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M. R. Kabir Chowdhury
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ICDDR, B, Mohakhali
Dhaka 1212, Bangladesh.