REVIEW BOARD ON THE USE OF HUMAN VOLUNTEERS
CRL

62

Principal Investigator David A. Sack Trainee investigator(if any) _____

Application No 79-001 Supporting Agency(if Non-CRL) _____

Title of study Psychological Aspects of Premenstrual Syndrome

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 possibly 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 None
   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
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 Board for review.

I agree to obtain approval of the Review Board on Use of Human Volunteers for any changes involving the rights and welfare of subjects before making such change.

David A. Sack
Principal Investigator

_____
Trainee

Please return 2 copies of entire protocol to Chairman, Review Board on Use of Human Subjects.

19-001

Rec'd 3/1/79

SECTION I - RESEARCH PROTOCOL

1. Title: Pathophysiology of Rotavirus Diarrhea.

2. Principal Investigator: David A. Sack, M.D.

   Co-Investigators: Dr. Majid Molla, Dr. Abu Eusof, Dr. Ayesha, Molla, Mr. Wahed

3. Starting Date: 20 January 1979

4. Completion Date: June 1979

5. Total Direct Cost: $7,720

6. Abstract Summary:

Twenty children aged 18-30 months with diarrhea typical of rotavirus or enterotoxigenic E. coli will be studied to determine certain features of the pathophysiology of rotavirus diarrhea. Balance studies will be done to determine the manner in which these patients handle sodium, potassium, acid and carbohydrates. One intubation will be done to compare fluid composition in the small bowel with that in the stool. The results of the study should lead to an improved understanding in the mechanisms by which rotavirus causes diarrhea, should verify a malabsorptive defect, and should improve the recommendations for fluid and electrolyte therapy in patients with rotavirus diarrhea.

7. Reviews:

   (a) Research Involving Human Subjects: _____

   (b) Research Committee: _____

   (c) Director: _____

   (d) BMRC: _____

   (e) Controller/Administrator: _____

SECTION I - RESEARCH PLAN

INTRODUCTION

1. Objective: The overall objective of this study is the prevention of the complications (dehydration and malnutrition) of rotavirus diarrhea through a better understanding of the pathogenic mechanisms of this virus. When the mechanisms are known, a more rationale approach to treatment of these complications is likely.

2. Background: Rotavirus is a recently discovered but common pathogen causing diarrhea all over the world. It is most common in infants up to 2½ years of age and likely infects virtually everyone at some time. Adult infection occurs but is much less common, and when it occurs is often asymptomatic.

Studies done in Bangladesh have documented the common occurrence of the virus as a cause of infantile diarrhea here. The incidence of rotavirus in Matlab patients coming to the treatment center for diarrhea is estimated to be 7.1 per 1000; the actual incidence is however much higher since many of the patients do not come for treatment. During one study in February 1978 60-90% of the patients (aged 6 months to 2½ years) admitted to an oral fluid study had rotavirus in the stool.

The previous CRL studies have outlined the clinical features of the disease which are consistent with other published clinical studies of rotavirus diarrhea. The usual clinical episode begins with vomiting which lasts for about two days. Shortly after the vomiting; diarrhea begins and gradually increases in rate, reaching a peak during the third

These findings are in marked contrast to patients with enterotoxigenic diarrhea. A comparison of some of the features of cholera and rotavirus diarrhea is shown on Table II.

Table II

Comparison of cholera and rotavirus diarrhea.

		Cholera	Rotavirus
1.	Mechanism of diarrhea	cAMP stimulation	relative imbalance of secretory to absorptive cells
2.	Composition of small bowel fluid secreted	isotonic with electrolyte composition same as stool	Unknown
3.	Stool pH	alkaline (approx. 7.5)	acid (approx. 5.0-5.5)
	Stool osmolarity	isosmotic	isosmotic
	Stool total electrolytes	approx. 300 mmol	approx. 60 mmol
	Stool carbohydrate	less than 500 mg %	greater than 3 grams %
4.	Acidosis	Uncompensated	Compensated
	Mechanisms of acidosis	HCO_3 loss in stool	?
5.	Malabsorption	Mild deficiencies of disacchardases; low concentration of stool carbohydrate	Decrease disaccharidases (animals); high concentration of stool carbohydrates

Table II points out several gaps in our understanding of the pathophysiology of rotavirus diarrhea. The mechanism of rotavirus diarrhea infection is

or fourth day of illness, followed by a diminution in purging. The illness lasts about seven days. Patients who are hospitalized usually are admitted on the second or third day of illness at a time when vomiting is nearly over but at a time when purging rate is still increasing. Dehydration in admitted patients is usually mild (approximately 5% dehydration) and patients have a compensated metabolic acidosis (decreased serum CO_2 with a normal arterial pH). Severe cholera-like diarrhea of acute onset has not been documented at CRL nor reported in other published reports; however, the total purged volume over a prolonged week long illness may match total cholera purging, and deaths due to rotavirus have been documented in Canada.

Laboratory findings on admission in patients with rotavirus are found in Table 1.

Table I

Laboratory findings of patients with rotavirus diarrhea.

Laboratory values - blood	
Haematocrit (%)	33±1
White Blood-cells/µl	18,700±1300
Na^+ (mmol/l)	137±1
K^+ (mmol/l)	3.9±1
Cl^- (mmol/l)	107±1
CO_2 (mmol/l)	14.2±0.6
Creatinine (mg/dl)	0.7±0.1
Glucose (mg/dl)	84±5
Serum specific gravity	1.027±<0.001
Arterial pH	7.4
Laboratory values - stool	
Na^+ (mmol/l)	23±3
K^+ (mmol/l)	32±4
Cl^- (mmol/l)	11±2
CO_2 (mmol/l)	5.5±1.1
Osmolarity (mosm)	300

From: Sack, et al. Lancet ii:280-283, 1978.

postulated from animal experiments to result from an imbalance of crypt-like secretory cells with villus-like absorptive cells. Since the virus preferentially attacks the villus cells there exists a temporary excess of crypt-like cells which cover the tip. The different cell types (crypt or villus) can be recognized by their enzyme markers; thymidine kinase being a marker of the immature crypt cells and the disaccharidases being markers of the more mature villus cells. Besides being a cell marker; however, the deficiency of disaccharidases have important nutritional consequences as will be discussed later.

The make up of the small bowel fluid in cholera is essentially that of normal small intestinal fluid, except for an over production. This "normal" small bowel fluid overwhelms the absorptive abilities of the large bowel and so appears, almost unchanged as stool. In rotavirus the small intestinal fluid has not been sampled; however the rotavirus stool is low in electrolytes while still being isosmotic. The make up of the osmotically active particles is not yet known, though may be bacterial breakdown products of ingested food which is malabsorbed. The large amounts of carbohydrate in rotavirus stool detected after boiling acid hydrolysis is not found in cholera stool and is more than expected with only a disaccharidase deficiency. The duration of the high levels of stool carbohydrate is not known but one patient studied in 1978 had decreasing amounts as the diarrhea lessened during the one week in hospital.

The acidosis in cholera is due to bicarbonate loss in the stool. In rotavirus the bicarbonate concentration in stool is very low suggesting either that the secreted small intestinal fluid was low in bicarbonate or that the bicarbonate combined with acids in the bowel before appearing

in the stool. With a stool pH of 5.0-5.5 the latter is more likely and the bowel acid production apparently exceeds the buffering capacity of the bicarbonate in the secreted small bowel fluid. What then is the mechanism of the acidosis? Most likely both bicarbonate loss in the small bowel and acid production in the colon; but the relative importance of these two is not yet known. Another less likely possibility is an impaired acid clearing capabilities by the kidneys (e.g. a type of renal tubular acidosis). This seems very unlikely but should not be ruled out.

Diarrhea is one of the leading causes of death in children not only because of dehydration but also because of malabsorption and malnutrition. A defect of absorption has been detected in rotavirus patients (increase stool carbohydrate) though the specific deficit has not yet been determined nor is it known if this is an isolated carbohydrate malabsorption or is only one defect in a malabsorption involving fats, proteins, important vitamins and minerals.

The practical importance of studies of pathophysiology lies with the proper management of patients with rotavirus. While it is known that rehydration is crucial in the treatment and that oral sugar-electrolyte solution will maintain hydration, management regarding proper diet is not know. Based on folk medicine, various feeding regimens are taught, ranging from complete fasting during illness to force feeding throughout illness. Certainly if malabsorption plays a major role in the pathogenesis of the diarrhea and acidosis, increasing food intake only worsens the diarrhea and lessens the nutrient absorption. If the malabsorption is selective, then certain foods should be encouraged and others discouraged

during the illness in order to maximize nutrient and calorie absorption. Finally, while the WHO formula of oral rehydration solution "works" in the treatment of rotavirus diarrhea, the sodium concentration of the formula far exceeds the sodium being lost in the stool, and some feel this formulation is too high in sodium to be used in rotavirus diarrhea. Knowledge of the total handling of sodium in patients with rotavirus diarrhea would be helpful in deciding on the proper formula for oral solution.

3. Rationale: The pathophysiology of rotavirus is incompletely known but involves selective infection of villus cells, with resulting imbalance in secretory versus absorptive cells. It also results however in associated defects of absorption which contributes to the acidosis and diarrhea. Knowledge of the mechanisms in the disease should help guide specific therapy in patients with disease, especially in relation to salts, fluids, and nutrition.

B. SPECIFIC AIMS

1. Compare small bowel fluid with stool fluid with regard to pH, electrolytes, osmolarity, nutrients.
2. Determine the way in patients with rotavirus diarrhea handle sodium and potassium.
3. Document a carbohydrate malabsorptive defect.

C. METHODS OF PROCEDURE

1. Subjects: Approximately ten male patients with mild dehydration between 18 and 30 months of age with history typical of rotavirus diarrhea and ten male patients of the same age with a comparably severe illness but

more typical of enterotoxigenic diarrhea will be admitted to the study. The patients will be selected only if they have already been weaned.

2. Clinical Procedures: Patients will be admitted directly to the study ward where they will have a history, physical exam, and will be rehydrate with standard Dacca solution plus 2% glucose. Estimated fluid deficit will be replaced over 16 hours (half in 8 hours). Patients will have the following specimens taken on admission: Stool - microscopic exam, culture (including ETEC), electrolytes, pH, titratable acid and osmolarity, and stool for special carbohydrate studies; Urine - routine, pH, titratable acid, electrolytes and osmolarity; Blood - CBC, electrolytes, BUN, creatinine.

The patients will be maintained on intravenous fluids to maintain hydration using Dacca solution with 2% glucose. Patients will be kept NPO on day of admission and the next day until after the intubation; then they will have a diet consisting only of measured amounts of a standard weanling food, water and rice.

During the hospitalization the patients will have sodium, and potassium studies done and will have special studies done to detect carbohydrate malabsorption. Studies are described in more detail.

Sodium and Potassium Balance: Intake of sodium and potassium during the first 1½ hospital days will consist only of the I.V. solution with a know.. electrolyte content. From day 2 onward the patient will be receiving food also. Alequots of this will also be measured for sodium and potassium content.

Output of sodium and potassium will be in the stool, urine and sweat, and rarely in vomit. Sweating is minimal during the cool season so this immeasurable sodium loss should be minimal. All urine will be collected and volume measured. Eight hourly urines will be pooled and will be sent to Biochemistry for electrolytes, pH and titratable acid. All stool will be collected using colostomy bags, or cholera cots. Volumes of uncollected feces will be approximated. The stool will be kept cold and 8 hourly pooled stools will be sent for electrolyte determination. If vomiting occurs alequots of this will also be sent for electrolyte determination.

Records will be kept so that total sodium and potassium intake and output can be calculated every 8 hours for the duration of the diarrhea.

Carbohydrate Studies: Alequots of stool will be measured daily for reducing substances before and after boiling acid hydrolysis. Representative samples of stool with increased levels and with low levels of reducing substance after hydrolysis will also be assayed for specific sugars with thin layer chrometography to document the type of sugars being passed in the stool.

Two days after hospitalization a xylose tolerance test will be done. D-xylose will be given and a five hour urine collection will be saved and measured for xylose. The group with rotavirus will be compared to the ETEC group to document a difference in xylose absorption.

Intubation Studies: On the day after admission the patients will have a naso-duodenal tube passed. The position of the tube will be judged on the basis of tube contents (color and pH) but x-rays will not be used. An alequot of small bowel fluid and a concurrent alequot of catheterized stool will be obtained to be assayed for electrolytes, pH, titratable acidity and carbohydrate content.

The balance studies will continue for five days or the duration of the diarrhea whichever is longer. The intubation will be done only once.

3. Analysis of Data: Analysis will be carried out by comparing each rotavirus patient with his own values over time and by comparing the rotavirus group to the enterotoxigenic group. It is likely that at least 60% of the patients will actually have the expected pathogen, (either rotavirus or enterotoxigenic E. coli), and six patients should be adequate for this type of analysis since we would be looking for major differences.

Specifically the analysis of data can be illustrated by the following tables and figures.

Figure I

Mean stool volume in patients with rotavirus and enterotoxigenic E. coli diarrhea.

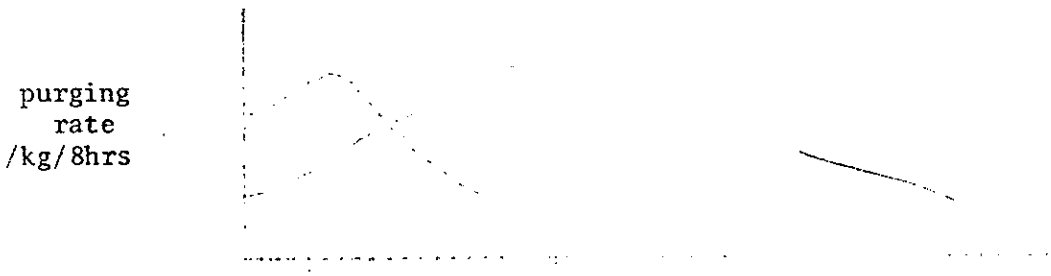

Figure II

Mean stool sodium concentration in patients with rotavirus and enterotoxigenic E. coli.

Figure III

Relation of stool sodium and potassium concentration to concurrent purging rate in patients with rotavirus and enterotoxigenic E. coli diarrhea.

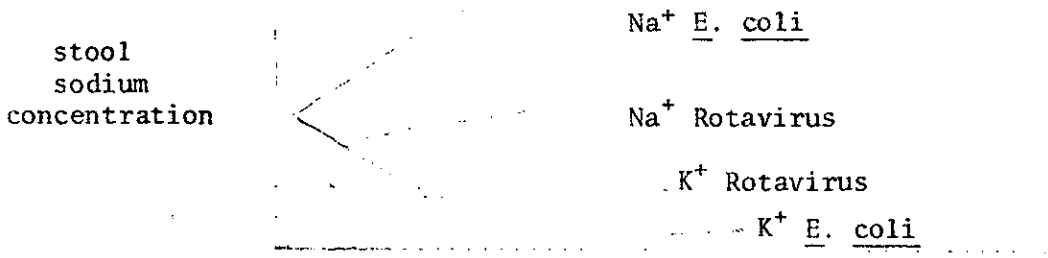

Table III

Sodium balance in patients with rotavirus or E. coli diarrhea treated with intravenous Dacca solution.

	Rotavirus					ETEC				
	Intake		Output		Net	Intake		Output		Net
	I.V.*	Diet	Urine	Stool		I.V.	Diet	Urine	Stool	
Day 1										
Day 2										
Day 3										
Day 4										
Day 5										
Day 6										

* meq sodium.

TABLE IV

Potassium balance in patients with rotavirus or E. coli diarrhea treated with intravenous Dacca solution.

(Table same as Table III)

Table V

Major carbohydrates in stools of patients with rotavirus and ETEC.

	Rotavirus	ETEC
Glucose	* ( )	
Sucrose		
Lactose		
Maltose		
Starch		

* mg% (approximate osmolarity).

Table VI

Comparison of small bowel fluid with stool in patients with rotavirus and ETEC.

	Small Bowel Aspirate		Stool	
	Rotavirus	ETEC	Rotavirus	ETEC
Na				
K				
Cl				
CO_2				
pH				
Osmolarity				
Carbohydrate				

SIGNIFICANCE

Rotavirus diarrhea is a major cause of infantile diarrhea world wide. An adequate understanding of the pathogenic mechanisms of this disease is necessary for optimal treatment of patients with this disease.

FACILITIES REQUIRED

1. Office space - already provided
2. Laboratory space - already provided
3. Hospital resources - 20 patients x 5 days per patient = 100 days
4. Animal resources - infant mice for ST testing (40 isolates or 100 mice).
5. Logistic support - none
6. Equipment - none
7. Other requirements - special handling of diets and I.V. fluids will be needed.

COLLABORATIVE ARRANGEMENTS

Mr. Mark Rhodes, a medical student from Johns Hopkins will participate in the clinical management of these patients.

REFERENCES

Davidson, G.P., Gall, D.G., Petric, M., et al. Human rotavirus enteritis induced in conventional piglets. J. Clin. Invest. 60:1402-1409, 1977.

Delage, G., McLaughlin, B., Berthiame, L. A clinical study of rotavirus gastroenteritis. J. Pediatrics 93:455-457, 1978.

Hieber, J.P., Shelton, S., Nelson, J.D., et al. Comparison of human rotavirus disease in tropical and temperate settings. Am. J. Dis. Child. 132:853-858, 1978.

Rodriguez, W.J., Kim, H.W., Arrobio, J.O., et al. Clinical features of acute gastroenteritis associated with human reovirus-like agent in infants and young children. J. Pediatrics. 92:188-193, 1977.

Ryder, R.W., Sack, D.A., Kapikian, A.Z., et al. Enterotoxigenic Escherichia coli and reovirus-like agent in rural Bangladesh. Lancet i:659-663, 1976.

Sack, D.A., Chowdhury, A.M.A.K., Eusof, A., et al. Oral hydration in rotavirus diarrhea: a double blind comparison of sucrose with glucose electrolyte solution. Lancet ii:280-283, 1978.

Tallett, S., MacKenzie, C., Middleton, D., et al. Clinical, laboratory, and epidemiologic features of a viral gastroenteritis in infants and children. Pediatrics 60:217-222, 1977.

Theil, K.W., Bohl, E.H., Cross, R.F., et al. Pathogenesis of porcine rotaviral infection in experimentally inoculated gnotobiotic pigs. Am. J. Vet. Res. 39:213-220, 1978.

Yolken, R.H., Wyatt, R.G., Zissis, G., et al. Epidemiology of human rotavirus types 1 and 2 as studied by enzyme-linked immunosorbent assay. N. Engl. J. Med. 299:1156-1161, 1978.

ABSTRACT SUMMARY

1. Children aged 18-30 months of age will be included in this study. This age group is the selected because this age group (and younger) are the people at risk of illness from rotavirus. Adults rarely have the disease and when they do it is mild and not typical of the children's illness.

2. The risks will be those associated with venapuncture and intubation. The venapuncture will be done three times and will remove 3ml each time. The intubation will be done once with a small lumen mercury-bag, tube. Intestinal intubation is temporarily uncomfortable for the child but has very low risk. Risks of intubation would include placement of the tube into the trachea rather than esophogus, perforation of lumen of esophagus or stomach. Small bowel biopsy would not be done. X-ray confirmation will not be done.

3. The venapuncture will both be done by one of the investigators. Intubation will be done by Dr. M. Molla, a pediatric gastroenterologist, who has much experience intubating children. Oxygen and other emergency equipment and supplies are immediately available in the highly unlikely event of a complication.

4. Research records are kept in a locked filing cabinet in the investigators office. Samples and records will be identified by code number and the link between patient and code number will be kept in a separate locked file.

5. A signed informed consent will be obtained from the parents.

6. No interview.

7. The individual will benefit from the treatment of his illness. Society will benefit if the proposed research leads to improved treatment of rotavirus diarrhea.

8. The research will use medical records, blood, stool, urine, and intestinal fluid.

SECTION III - BUDGET

A. DETAILED BUDGET

1. PERSONNEL SERVICES

Name	Position	% of effort or no. days	Annual Salary	Project Requirements TAKA	DOLLARS
Dr. David Sack	Investigator	10%	35,000		3,500
Dr. Majid Molla	Co-Investigator	10%	90,920	9,092	
Dr. Abu Eusof	Co-Investigator	10%	40,000	4,000	
Dr. A. Molla	Co-Investigator	10%	72,630	7,263	
Mr. Mark Rhodes	Student	20%	-		-
Mr. M.A. Wahed	Co-Investigator	10%	31,580	3,158	
To be named	Study Nurse	20%	20,000	4,000	
To be named	Microbiol. Tech.	10%	20,000	2,000	
To be named	Biochem. Tech.	25%	20,000	5,000	
			Sub Total:	34,513	3,500

2. SUPPLIES AND MATERIALS

Item		
Chemicals, reagents, media, glassware		500
Routine biochemistry tests	5,000	
Elisa assay	1,000	
Sub Total:	6,000	500

3. EQUIPMENT

4. PATIENT HOSPITALIZATION

100 patient days — Sub Total: 15,000

5. OUTPATIENT CARE

6. CRL TRANSPORT

7. TRAVEL AND TRANSPORTATION OF PERSONS

8. TRANSPORTATION OF THINGS

9. RENT, COMMUNICATIONS & UTILITIES

10. PRINTING AND REPRODUCTION

Mimeo Costs		150
Xerox Costs		150
	Sub Total:	300

11. OTHER CONTRACTUAL SERVICES

12. CONSTRUCTION RENOVATION, ALTERATIONS

B. BUDGET SUMMARY

Category	Project Requirements TAKA	DOLLARS
1. Personnel	34,513	3,500
2. Supplies	6,000	500
3. Equipment		
4. Hospitalization	15,000	
5. Outpatients		
6. CRL Transport		
7. Travel Persons		
8. Transportation Things		
9. Rent/Communication		
10. Printing/Reproduction	300	
11. Contractual Service		
12. Construction		
Total:	55,813	4,000
Total $:	7,720	

Conversion Rate $ 1 = Tk. 15

PERMISSION FORM

Pathophysiology of Rotavirus

The International Center for Diarrheal Disease Research, Bangladesh (formerly Cholera Research Laboratory) is carrying out research into the causes and treatment of diarrheal disease. We would like your child to participate in a study of the way in which rotavirus causes diarrhea in babies. We are doing this research in hopes that we can learn the most effective way to treat children with diarrhea. If you agree to have your child included in this study, you can expect the following:

1. We will treat your child's illness. For this (s)he will have to be in the hospital until the diarrhea stops. Usually this is about five days.

2. We will do special studies to determine if your child is absorbing his food. To do this he will receive a special food beginning on the third day of hospitalization and we will measure everything (s)he eats and drinks. We will also collect all his stool and urine for special tests.

3. As part of his medical treatment he will need three blood tests taken: today, tomorrow and on the last day of his hospitalization.

4. On the second day of hospitalization we will pass a small tube into his intestine to obtain a sample of fluid from the small intestine. This test is somewhat uncomfortable, but has a very small risk of complication.

5. Your child does not have to participate in this study. If (s)he does enter it, (s)he can leave it at any time. If you decide not to have your child entered into the study, or if (s)he leaves the study your child can still be treated here for his illness. Your decision regarding the study will not jeopardise his medical care.

6. The medical records will be kept confidential.

If you agree to enter your child into the study, please sign your name here.

_____
Name

_____
Date

সম্মতি পত্র

"রোটা ভাইরাস জীবাণুর সংক্রামকতা পরীক্ষা"

আন্তর্জাতিক ডায়রিয়া গবেষণা কেন্দ্র, বাংলাদেশ, বর্তমানে পেটের পীড়ার কারণ ও তার চিকিৎসার উপায় গবেষণা চালিয়ে যাচ্ছে। আমরা আশা করব আপনার অসুস্থ বা সহ আপনি আমাদের গবেষণায় অংশ গ্রহণ ও সহযোগিতা করবেন। এর ফলে রোটা ভাইরাস নামক ডা দ্বারা আক্রান্ত উদারাময় রোগের কারণ জানা যাবে। এই রো সম্বন্ধে পূর্ণ জ্ঞান লাভ করা ও তার একটি উপযুক্ত চিকিৎ উদ্ভাবন করাই হল এই গবেষণার মূল উদ্দেশ্য। যদি আ আপনার অসুস্থ বাচ্চাকে এই গবেষণায় অংশ গ্রহনে ইচ্ছা পোষণ করেন, তবে আপনি নীচে লেখা বিষয় গুলী আশা করতে পারেন ঃ—

① আপনার বাচ্চার অসুখের পূর্ণ চিকিৎসা করা হবে তার জন্য রোগীকে এই হাসপাতালে সর্বোচ্চ পাঁচ দিন ভর্তি হয়ে অবস্থান করতে হবে।

② আমরা বিশেষ ভাবে পরীক্ষা করে দেখবো আপনার বাচ্চার খাদ্যদ্রব্য চিকিৎসায় হজম হ কিনা। এর জন্য ভর্তির দ্বিতীয় দিনে রোগীকে বিশেষ ধরনের খাবার দেয়া হবে। এবং তার খাদ্যদ্রব্যের পরিমাপ করা হবে। পরীক্ষার জ রোগীর মল ও মূত্র গ্রহণ করা হবে।

③ রোগীর সুচিকিৎসার জন্য তার রক্ত পরীক্ষা দেখা হবে। প্রথম, দ্বিতীয় ও হাসপাতাল পরি দিন এই রক্ত পরীক্ষার জন্য নেয়া হবে।

④ ভর্তির দ্বিতীয় দিনে একটি রবারের নলের মা খাদ্য নালী থেকে সামান্য পাচক রস নেয়া হ এর জন্য সামান্য একটু অস্বস্তি বোধ লো পারে, তবে কোন অসুবিধার কারণ নেই।

৫) আপনি ইচ্ছা করলে এই গবেষনায় আপনার বাচ্চাকে নাও ভর্তি করাতে পারেন অথবা ভর্তি পরও যে কোন সময় ইচ্ছা করলে গবেষনা পরিত্যাগ করতে পারেন। তার জন্য আপনার বাচ্চার স্বাভাবিক চিকিৎসার কোন প্রকার ব্যত্যয় হবেনা।

৬) চিকিৎসার বিস্তারিত পত্র সম্পূর্ন গোপন রাখা হবে।

যদি আপনি মনে করেন আপনার বাচ্চা গবেষনায় অংশ গ্রহন করুক তবে দয়া করে নীচে নাম লিখুন ঃ

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