ANTIMICROBIAL SENSITIVITY IN CHOLERA IN KENYA

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BY

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ABBREVIATIONS:

D.C.D.C. = Division of Communicable disease control

M.O.H. = Ministry of Health

CAMP = Cyclic Adenosine Monophosphate

UG = Microgram

MIC = Mean inhibitory concentration

S.D. = Standard deviation

W.H.O. = World Health Organisation.

CONTENTS:

LIST OF TABLES

LIST OF FIGURES

ANTIMICROBIAL SENSITIVITY IN CHOLERA IN KENYA.

SUMMARY

Investigations were carried out with a view to establishing vibrio cholerae susceptibility to various antimicrobial agents. Tetracycline, chlorampenicol, co-trimoxazole, Erythromycin, Ampicillin, Minocycline, Amoxycillin and Nalidixic acid were included.

Vibrio cholerae strains tested from 178 isolates were found to be completely resistant to Co-trimoxazole and amoxycillin. Complete resistance was encountered to Tetracycline, in Kirinyaga district (N=124) and highly resistant in Nyanza Province 67%(N=33). Variable high resistance was also encountered to Erythromycin 65.2% (N=178) and ampicillin 99.3%(N=178).

The V. cholerae strains were 100% sensitive to Minocycline and Nalidixic acid, and 84.3% sensitive to chloramphenicol.

The multiple drug resistance encountered is usually confered by plasmids.

INTRODUCTION

Acute diarrhoea and vomiting due to vibrio cholerae Eltor biotype, serotype Ogawa has been a persistently recurrent public health problem in Kenya since 1971. (Siongok T.K. personal communication & M.O.H. Records) (56). Tetracycline 2gm stat and then 500mg 6 hourly for one week and intravenous fluids have been used successfuly until 1984 when clinicians noticed no response in the course of diarrhoea. (Siongok T.K. D.C.D.C., Ministry of Health Division of communicable Disease control).

Therefore it became necessary to perform In-vitro antibiotic testing inorder to advise and guide clinicians on the pattern of antibiotic sensitivity to V.cholerae as part of management of these patients. Minimum inhibitory concentration (MIC) method Ericsson (50) has been used routinely to determine antimicrobial susceptibility. The MIC's should therefore guide the clinician in selecting the most appropriate antimicrobial.MIC's do correlate to effective serum drug levels. MIC's of antibiotics indicate levels at which inhibition of growth of the organism occurs rather than bacteriolysis. In vitro MIC's values do quite often correlate to effective serum levels, in vibrio cholerae infections MIC's should be the same as the effective therapeutic levels because there is no invasion by the organism. Moreover, Mic's for any antibiotic is not the same

effective serum value. Clinical trials are necessary to determine the minimum effective dose in vivo- for new antimicrobials and indications. The clinician, in prescribing any drug including antimicrobials takes into account indications and contraindications both for the drug and clinical state of the patient. Micro-organisms develop resistance under appropriate conditions. These include R-factor transfer from one gram negative organism to another and inadequate antibiotic dosage; (51). and invitro Resistance correlates with observed clinical response.(22) Antimicrobial resistance to microorganism is a universal problem, and may be either intrinsic or acquired. Multiple drug resistance is usually due to plasmids (22) and this form of resistance is acquired as above. The plasmids are transferrable from one gram negative organism to another (52). Cholera is an acute communicable epidemic disease characterised by profuse purging of colourless watery material, vomiting, muscular Cramps, oligoanuria, algidity and collapse, presence of vibrio cholerae in the gut, and high mortality over 60% without treatment. (1).

The disease was known to man for centuries until the 1883 pandemic when the causative agent was demonstrated by Robert Koch in Egypt from cholera patients (2).

Vibrio cholerae is a gram negative, aerobic bacillus measuring 1.5-2 um long and 0.5 - 0.6 um wide. It thrives optimally at alkaline P.H.'S 8-9.5, temperatures 15-42^{o}c (maximum 37.5^{o}c), and salinity of 15 parts per thousand (4). The organism survives for long periods under hot, humid climate with decaying vegetation.

It is known to survive for 285 days in sea water (1) vibrio cholerae exists in three serotypes, Ogawa, Inaba, and Hikojima. However, non-agglutinable forms have been shown to exist in nature between Outbreaks (5).

The organism is pathogenic only to man, in two biotypes: Classical and EL tor. Transmission is through the faeco-oral route. (6,7&8). Patients in hospitals must therefore be isolated (9).

When cholera first affects a community, adults are mainly affected (W.B. Baine et al (58). However in endemic areas all ages are affected and carrier rates are high. Carriers are high among house-hold contacts and may exist in an endemic area without overt manifestations of the disease. They are therefore important in maintaining endemicity (44 & 45).

Vibrio cholerae in the gut secretes an exotoxin, which activates the enzyme adenylcyclase in the gut Mucosa. Consequently gut mucosal cellular levels of cyclic adenosine monophosphate (camp) increase and this results in secretory diarrhoea and effortless vomiting (57). This results in dehydration, prerenal Oligonuria secondary to hypotension and metabolic acidosis.

Cholera in Kenya (10,11,12,13).

Cholera was first reported in Kenya in 1971 in North Eastern province. This was part of the spread of the 7th cholera pandemic which had originated and spread from South East Asia in 1960's. The disease affected predominantly nomadic people. Kenya has since then been removed from the list of affected areas.

The 1971 epidemic is thought to have been introduced into North Eastern Kenya from countries to the North (where the disease had been reported in August, 1970) by either healthy or convalescent carriers. Transmission was amplified by large numbers of Somali nomads from Somalia Crossing International boundaries due to a severe drought at the time, in search for food and water. Cattle traders travelling from place to place to sell their livestock probably, carried the disease further Inland.

In 1971, 301 cases were officially reported among a population of some 750,000. Control measures

led to a sharp decline in the number of cases during 1972 and 1973.

The clinical presentation was consistent with cholera. A few patients had mild disease with moderate diarrhoea and showed few signs of dehydration. The majority of patients, however, had severe disease. "Three patients were struck suddenly with vomiting and diarrhoea and on trying to reach the nearest treatment centre, soon collapsed and died in the bush track and were later discovered by the surveillance team half eaten by hyenas" (Mngola, E.N. (10).

In Hola in Tana river district among 142 bacteriologically proven cases, overall fatality was 17%. No fatality was recorded in the age group 7 - 16 years. Abortion rate was 50% in affected pregnant women. Apart from age, poor nutritional status, concurrent infections and other illnesses negatively influenced the prognosis.

In December 1974, cholera was reported in Western Kenya. It was probably introduced via Lake Victoria from neighbouring Tanzania where the disease was rampant. Affected districts were Kisumu, Siaya, South Nyanza, Busia and Kakamega. The number of reported active cases escalated six-fold from 402 in 1974 to 2455 in 1975. Effective control measures led to decline and only 71 active cases were reported throughout the country in 1977.

TABLE I

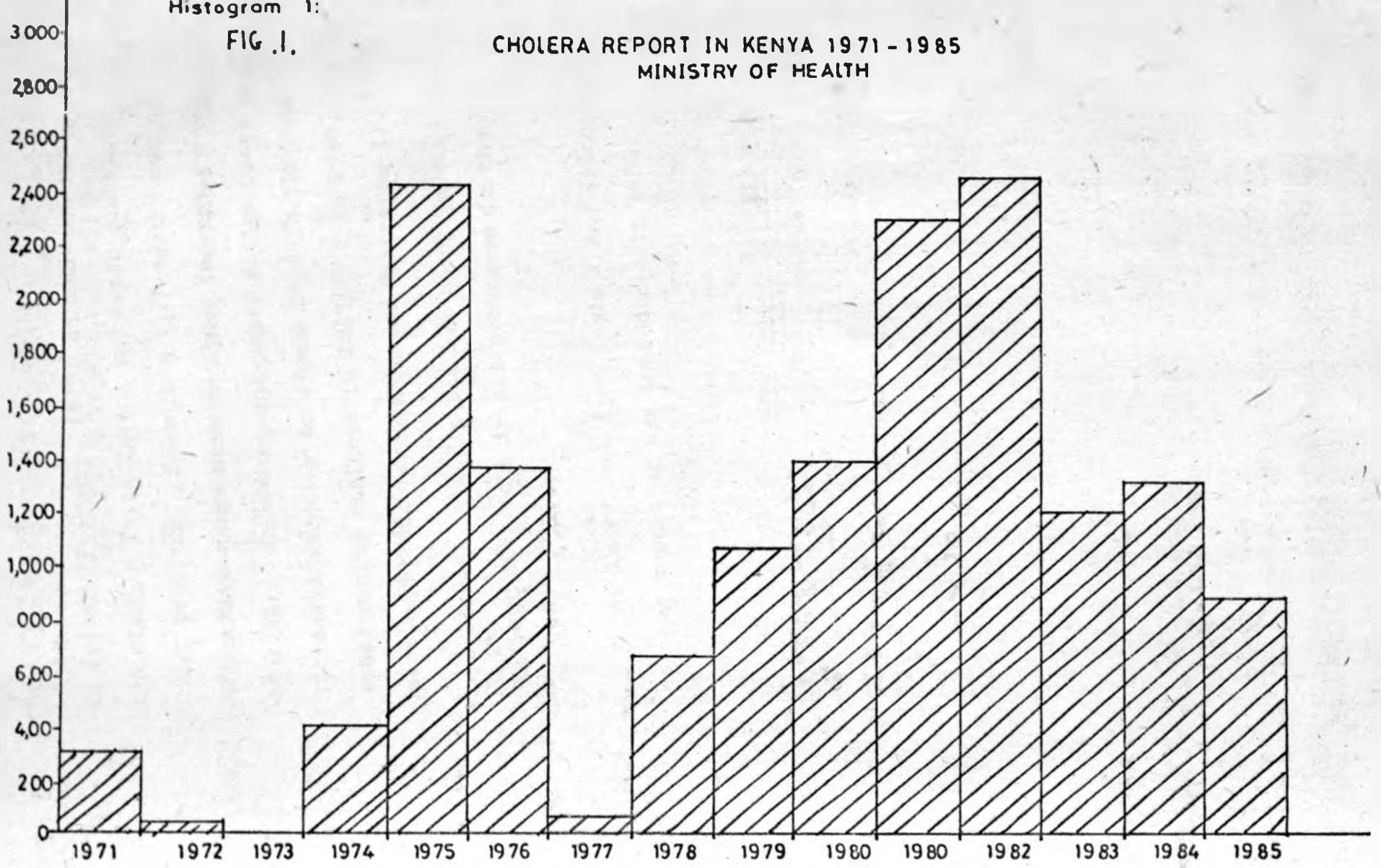
KENYA: CHOLERA REPORT 1971-1985

YEAR	1971	1972	1973	1974	1975	1976	1977	1978	1979	1980	1981	1982	1983	1984	1985	TOTALS
ADMISSIONS	-	-	-	-	-	-	-	-	-	-	-	-	2865	2537	2237	7639
CULTURES	-	-	-	-	-	-	-	-	-	123473	242755	283976	59260	39544	35634	784642
POSITIVE CULTURES	-	-	-	-	-	-	-	-	-	4331	9431	6327	2453	1989	2724	27255
ACTIVE CASES	301	51	0	402	2425	1359	71	672	1070	1398	2289	2458	1199	1313	894	15902
CARRIERS	-	-	-	-	-	-	-	-	-	2933	4537	2864	1246	661	1446	13687
DEATHS	-	-	-	-	-	-	-	17	2	61	-	-	78	96	75	329

Histogram 1:

FIG .1.

CHOLERA REPORT IN KENYA 1971 - 1985
MINISTRY OF HEALTH



KENYA: CHOLERA REPORT 1971 - 1985: ACTIVE CASES (PATIENTS:

In January/February, 1978, an outbreak was reported in Taita Taveta and Kwale districts in Coast province. Seventeen (17) deaths out of 672 active cases were recorded (mortality rate of 2.5%). In subsequent years active cases increased steadily to a peak 2458 in 1982 and subsequently declined in 1983/84. In 1985, 894 were reported, (see Table and Histogram I).

Todate, the disease has been reported from various districts in all provinces in the country.

As is evident from Table I and Histogram I, proper reporting was introduced in 1980.

OBJECTIVES:

1. To determine the pattern of antibiotic in-vitro sensitivity of vibrio cholerae to commonly used antibiotic drugs.

2. To determine the duration of healthy carrier state in vibrio cholerae. Healthy carriers for purposes of this study are defined as symptom-free individuals positive for vibrio cholerae and the duration is determined from the date of identification which is not necessarily the date of infection.

JUSTIFICATION OF THE STUDY:

In early 1984, clinicians in the districts started sending reports to the Ministry of Health about in-vivo unresponsiveness of cholera to the then routinely used Tetracycline 2gm stat then 0.5g q6h. as an adjunct to fluid and electrolyte replacement, (Siongok, T.K.D.C.D.C. & personal communication). There are no previous published data on this subject in the literature, on this country. Antibiotics do shorten duration and volume of diarrhoea by enhancing bacteriological cure (15,23).

It was therefore necessary for basic data on in-vitro sensitivity of vibrio cholera to commonly used antibiotics to be determined.

Carriers are important in disseminating infection to their associates particularly household contacts, (44,45,46). Duration of healthy carrier state is therefore important apart from other

preventive measures in controlling transmission particularly if quarantine restriction on proven carriers are to be imposed.

SUBJECTS MATERIALS & METHODS:

The study was conducted as part of an on-going surveillance and investigations of vibrio cholerae in the country by the Division of Communicable Disease Control (DCDC) of the Ministry of Health. The director, DCDC authorized the study and provided funds, technical staff and equipment. Consent from subjects was not necessary and therefore not sought as this was part of formal routine investigations and service by the Ministry of Health.

Patients of all ages admitted with acute diarrhoea with or without vomiting in suspected cholera areas were screened for vibrio cholerae and included in the study if positive stool specimens were obtained by using rectal swabs from the subjects; patients and their household contacts.

They were then transported to the hospital laboratory in cary and blair[53] transport medium and then cultured in Thiocitrate-Bile-Sucrose (TCBS) medium at 37°C for 18-24 hours. Characteristic colonies were serotyped with polyvalent serum to confirm their identity as Vibrio cholerae and then further serotyped with specific Ogawa and Inaba antisera to determine the serotype[54].. Pure cultures were then separately transported in Tryptose Soy Agar

to the central laboratory: National Public Health Laboratories (N.P.H.L.S.) Nairobi for antibiotic sensitivity testing.

Antimicrobial sensitivity to various antibiotics was tested by using Minimum Inhibitory concentration plate method Ericsson (50).

The antimocrobial drugs were prepared in distilled water to a final concentration of 100 ug/ml and stored at between 4°C and 8°C for a maximum of a week. Ten, two-fold serial dilutions of the test drug were prepared in test-tubes containing 2 mls of sterile Tryptic Soy broth kept at room temperature.

The test media plates were prepared by dispensing 18mls of tryptic soy agar (TSA) into universal bottles, sterilising and then holding them at 45°C in a thermostatically controlled water bath. The 18ml. of TSA media were then mixed thoroughly with the 2 ml serially diluted antimicrobial drug preparations avoiding bubble formation. The 20ml mixtures were then poured into petri dishes and then left to set. Cultures for testing were prepared by innoculating isolates into sterile tryptic soy broth and incubating at 37°C for 4 hours to obtain a young culture (Washington jA (54) page 410-427). The cultures were then transferred onto the test media using a standard loop and incubated at 37°C for 18-20 hrs.

W.H.O. standard E. coli. were set up with the inocular in each petridish as controls.

The petridishes were then read after 18-20 hrs. at 37°C for inhibition of growth and using the following M.I.C.'s in ug/ml as the limits at which antibiotics inhibit growth of gram negative organism (table II).

Since this study is prepared for a clinically orientated postgraduate course, some clinical features were studied in 50 patients.

TABLE II

MEAN INHIBITORY CONCENTRATIONS AT WHICH ANTIBIOTICS INHIBIT GROWTH OF GRAM NEGATIVE ORGANISMS

Chloramphenicol	0.2 - 5 ug/ml.
Tetracycline	0.1 - 10ug/ml.
Minocycline	0.1 - 4 ug/ml.
Ampicilin	0.2 - 5 ug/ml.
Nalidixic acid:	Not more than 10ug/ml.
Neomycin	0.5 - 8 ug/ml.
Co-trimoxazole	Not more than 1.4 ug/ml.
Erythromycin	Not more than 8 ug/ml.
Amoxycillin	0.2 - 5 ug/ml.

CONTROL W.H.O. E. COLI

Those clinical features which are excluded from the study; for instance volume of diarrhoea, could not be quantified due to administrative difficulties. Data on patients and carriers was obtained as per questionnaire I and II respectively.

The author was unable to visit Wajir and included fourteen isolates from there with permission of Director, D.C.D.C. Clinical data was omitted but cultures were tested for anti-microbial sensitivity.

RESULTS

TABLE V

SUMMARY OF FIELD WORK

District	Total Rectal swabs	Number Positive	% Positive
Kirinyaga	1419	124	8.7
Kisumu	1665	36	2.2
South Nyanza	4	4	100
Wajir	14	14	100
Totals	3102	178	5.74

Results: (178) One hundred and seventy eight out of 3,102 subjects tested were positive for vibrio cholerae el tor biotype serotype Ogawa including sixty eight (68) patients. Some characteristics of cholera were studied in fifty (50) patients. Their mean age was 29.7 years, median = mode = 25 yrs. One standard deviation S.D. from the mean was 21 yrs. (1xSD = 29.7± 25 years)(Histogram II).

Fourty two (42) 84% denied history of known family contact and the rest, 8 (16%) had contact with a person suffering from diarrhoea and vomiting.

Table III

V. cholerae sensitivity pattern to various antibiotics

District	TOTAL NO. OF RECTAL SWABS	NO. +Ve	SENSITIVITY TO NO. OF SUBJECTS							
			Tetracycline	Chloramphenicol	Nalidixic acid	[illegible]acin	[illegible]trin ([illegible]trimoxazole)	[illegible]thromycin	[illegible]icillin	[illegible]oxil
KIRINYAGA	1419	124	0	104	124	124	0	34	1	0
KISUMU	1665	36	12	31	36	36	0	10	4	0
WAJIR	14	14	14	14	14	14	0	14	14	-
SOUTH NYANZA (HOMA-BAY)	4	4	1	1	4	4	0	4	0	0
TOTALS	3102	178	27	150	178	178	0	62	19	0
%		100%	15.2%	84.3%	100%	100%	0%	34.8%	10.7%	0%

100% Sensitivity: Minocycline, Nalidixic acid.

Three patients household contacts had infact died of diarrhoea and vomiting four to seven days before onset of symptoms in patients as observed by visits by the surveillance team.

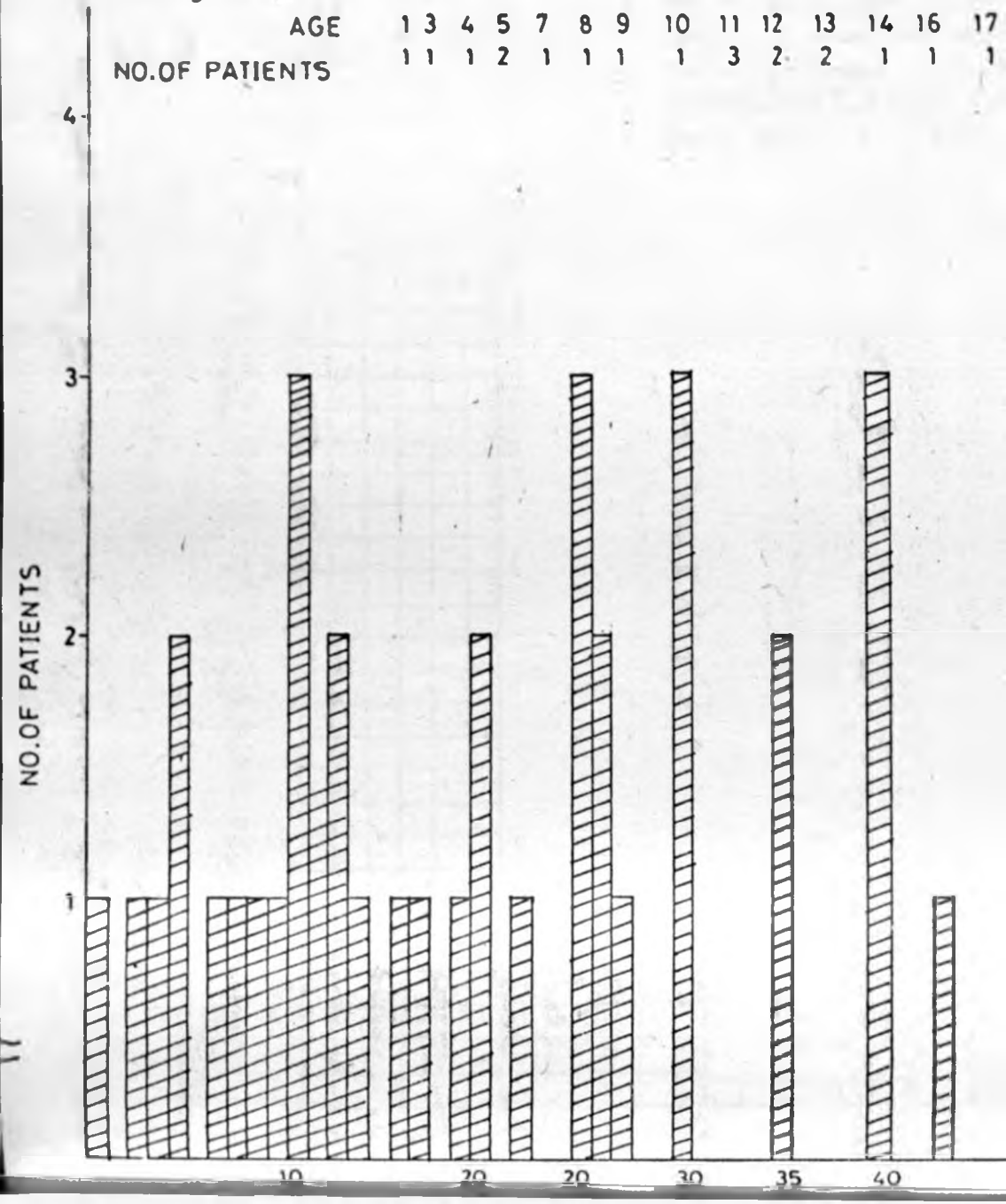
Thirty two (32) (64%) of patients had no treatment before admission; (histogram III) and the rest 18 (36%) had some form of treatment which included some antibiotic either tetracycline orally 2 gm stat in seven (7) (14%) patients or oral chloramphenicol 15 mg/Kg in one paediatric patient. Seven of the treated group (14%) did not know what treatment was administered.

Thirty two (32) (64%) of patients had moderately severe dehydration at admission. Sixteen (16) 32% had severe dehydration and two (2) 4% of patients died within four hours of admission, (Histogram VI).

All fifty patients had watery stool and thirty one 62% had characteristic rice water appearance of stools, (histogram VII). While in hospital fourty one (41) 82% were treated with tetracycline 2 gm stat then 0.5g 6 hourly for a minimum of five days or two days on after cessation of symptoms. Eight (8) 16% patients were treated with chloramphenicol 500mg 6 hourly for one week. One patient received co-trimoxazole 2 b.d. for five days (adult).

Histogram 2. FIG. 2.

AGE	1	3	4	5	7	8	9	10	11	12	13	14	16	17
NO. OF PATIENTS	1	1	1	2	1	1	1	1	3	2	2	1	1	1



19	20	22	25	26	27	30	35	46	43	50	55	60	65	70	80
1	2	1	3	2	1	3	2	3	1	2	1	3	4	1	1

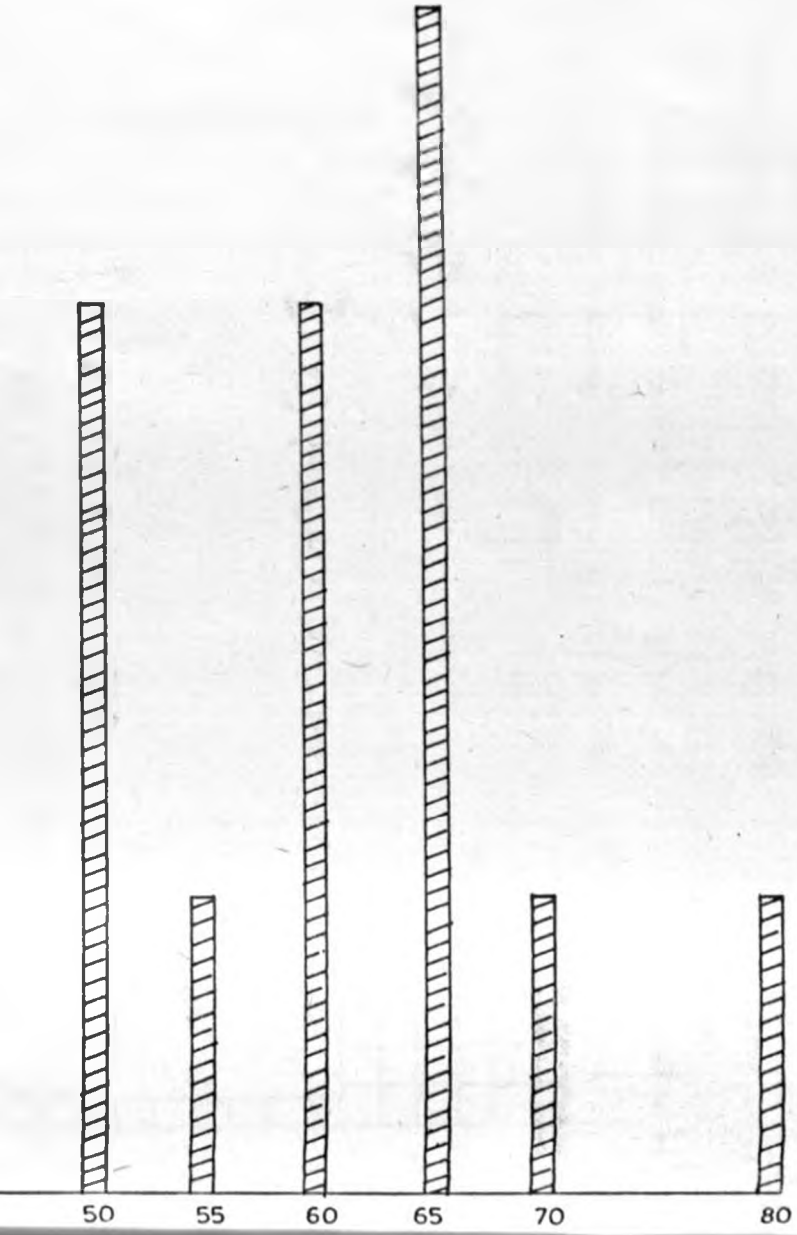


Fig.3. TREATMENT BEFORE ADMISSION

Histogram 3.

1 NONE # 32 64% N = 50
2 Tetracycline therapeutic dose # 7 14%
3 Oralite, Sulphadimidine, Chloroquine & Flagyl 1 2%
4 Chloraniphenicol 1 2%
5 Chloroquine & Flagyl 1 2%
6 Don't know 7 14%

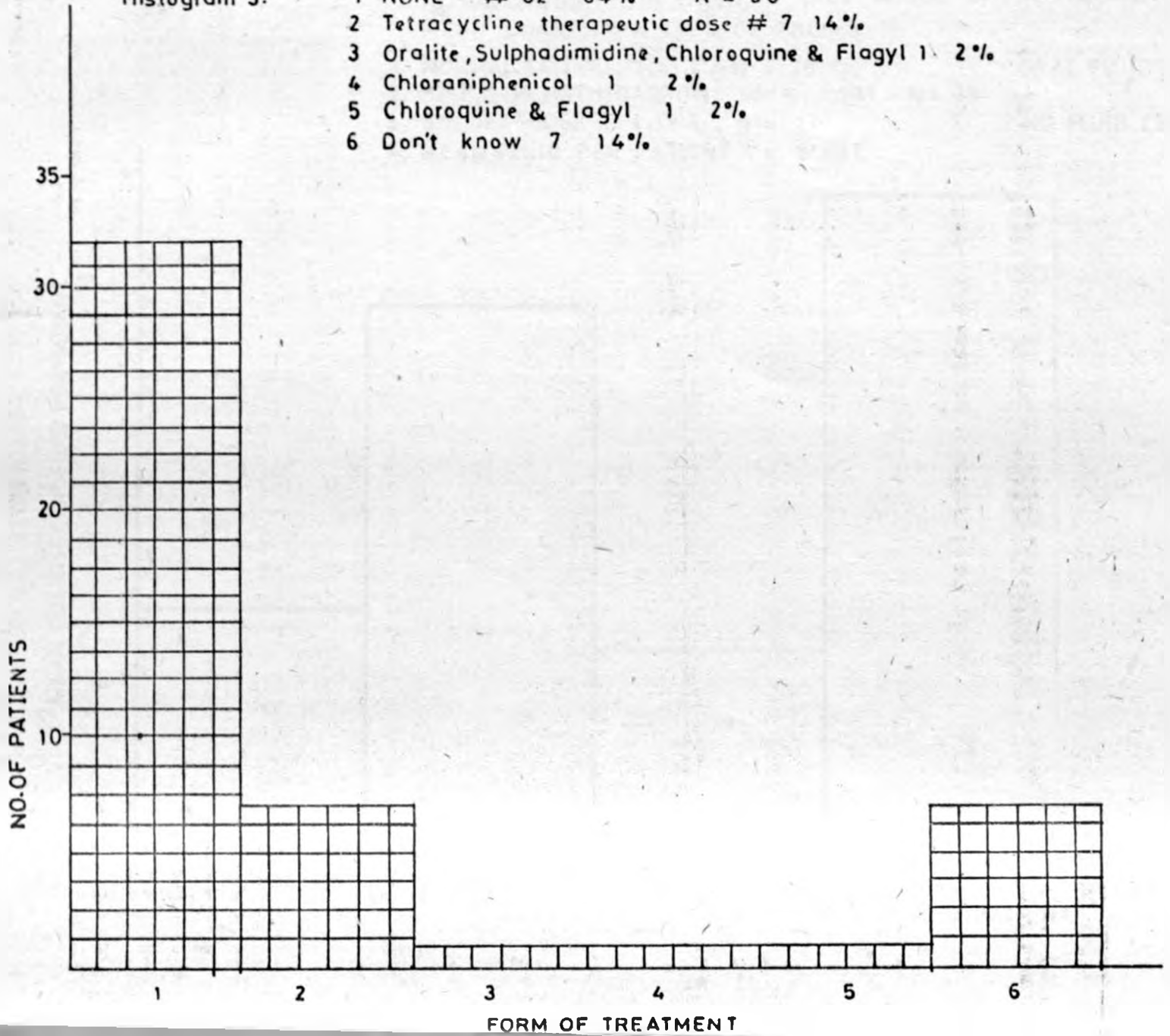


FIG.4.

Histogram 4

PATIENTS

INTRAVENOUS FLUID THERAPY (FOR WHOLE OF IN-PATIENT PERIOD).
MEAN QUANTITY & TYPE OF FLUID

1. NORMAL SALINE 1.41 l N = 16
2. HALF STRENGTH DARROWS 50/N 3.22 l N = 35.
3. 5% DEXTROSE 1.18 l N = 17
4. MEAN FLUID PER PATIENT = 3 88 l

ORAL FLUIDS N = 8

NO FLUID CHARTS

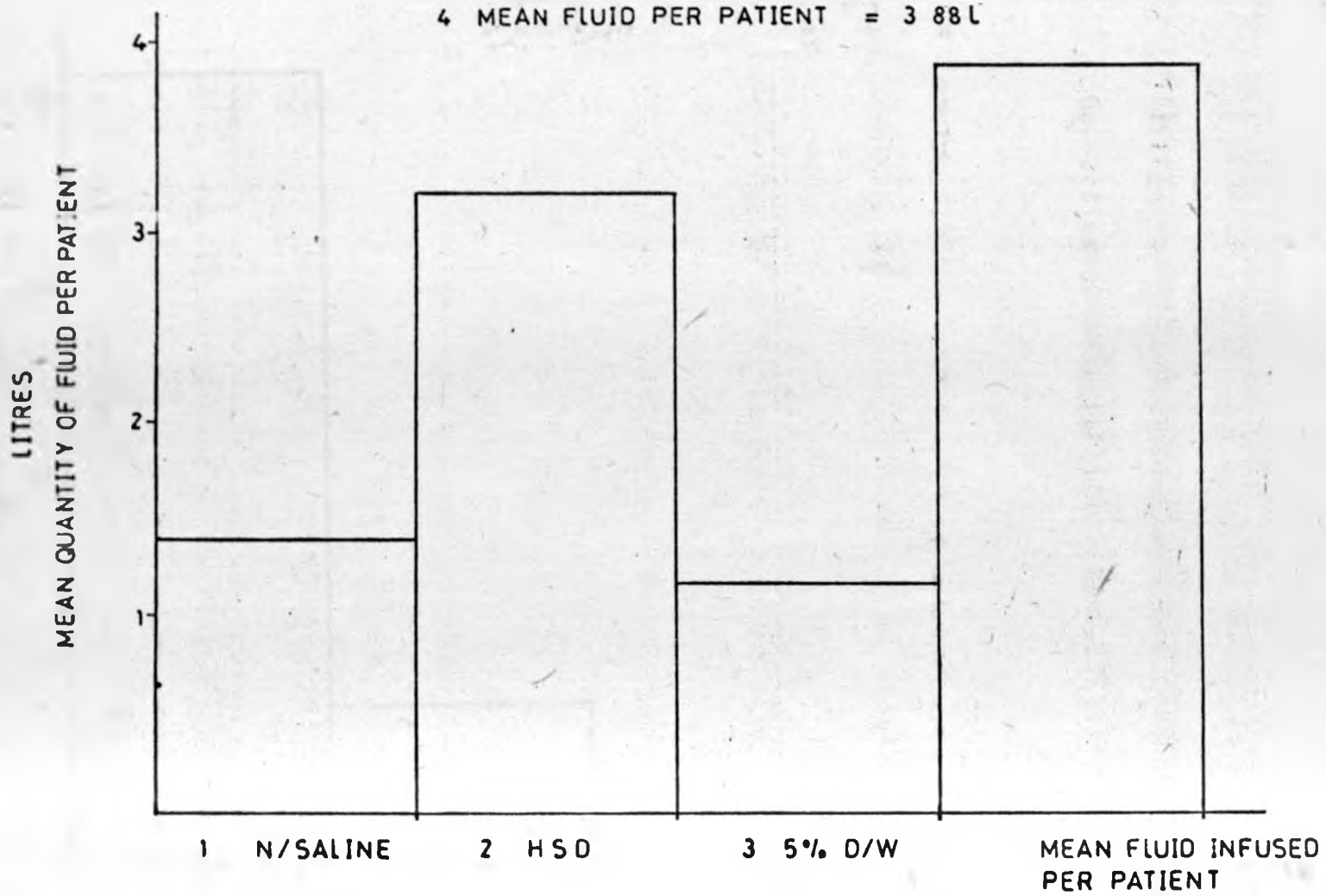


FIG. 5

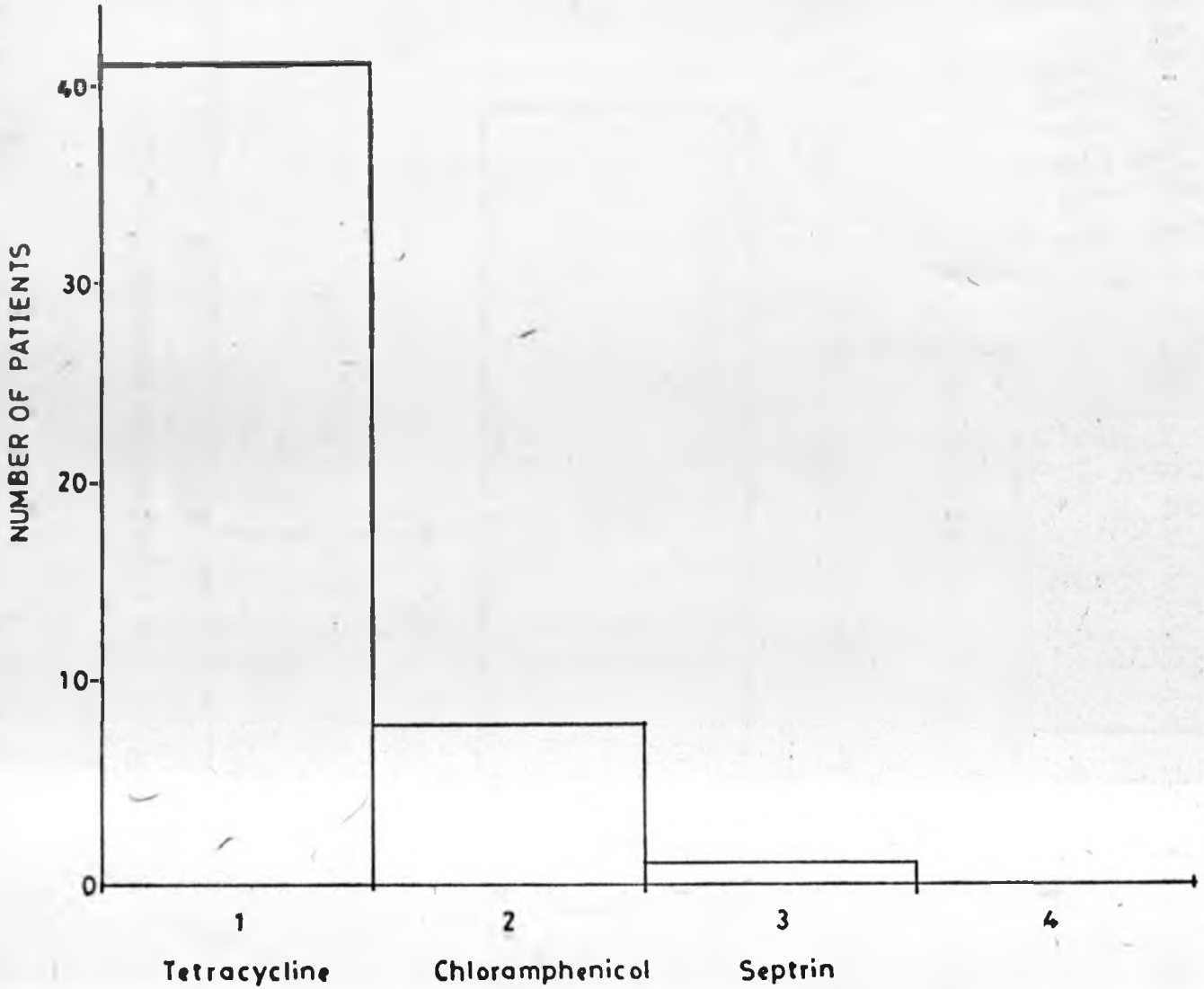
Histogram 5

PATIENTS

TREATMENT IN HOSPITAL N = 50

THERAPEUTIC DOSES

1.	Tetracycline 2 gm start then 0.5 gm Q6 hourly.	# 41	82 %
2.	Chloramphenicol	8	16
3.	Septrin	1	2



Histogram 6

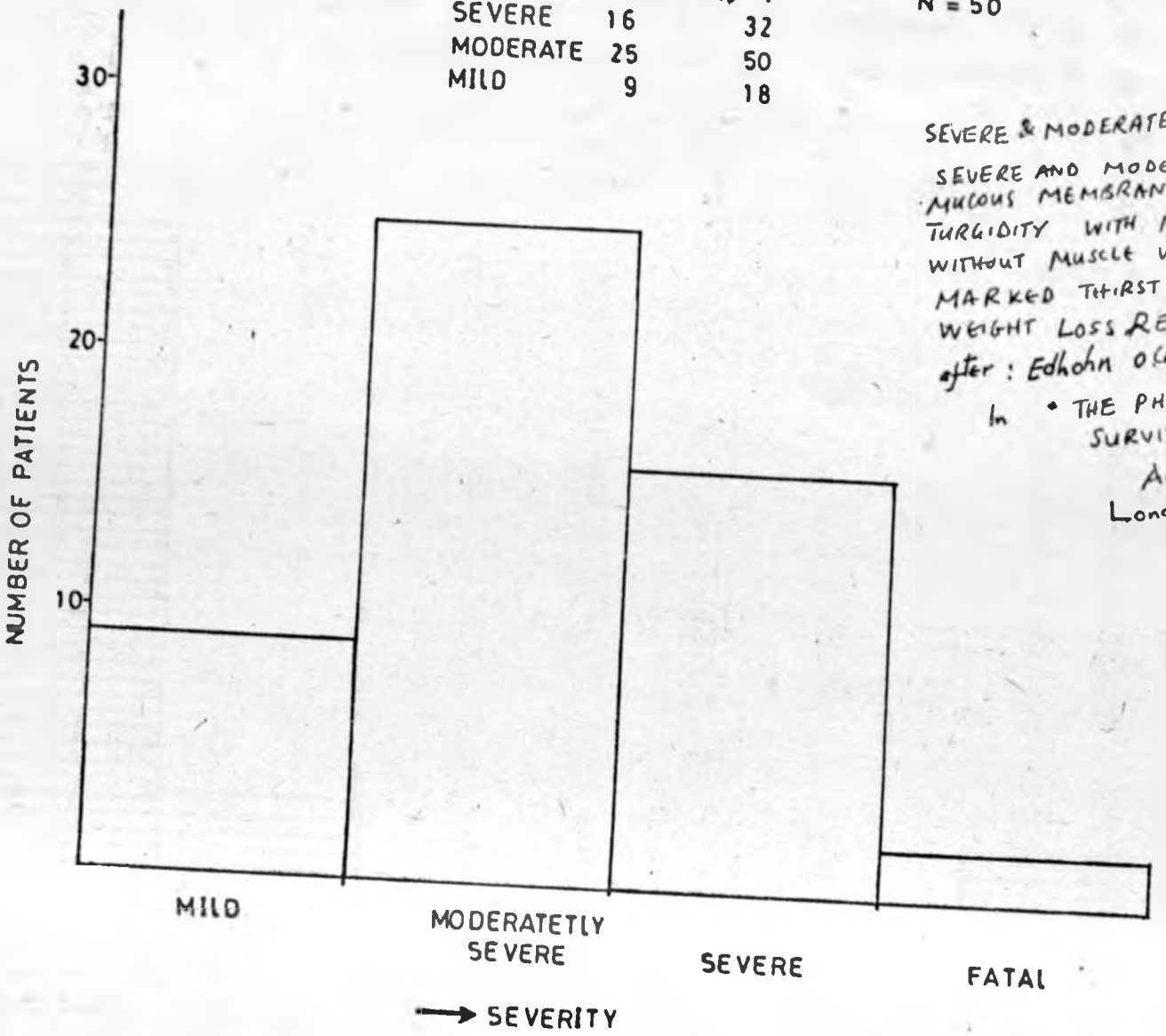
Fig. 6

PATIENTS

DEHYDRATION (DISEASE) SEVERITY AT ADMISSION

	#	%
FATAL	2	4
SEVERE	16	32
MODERATE	25	50
MILD	9	18

N = 50



SEVERE & MODERATE DEHYDRATION:

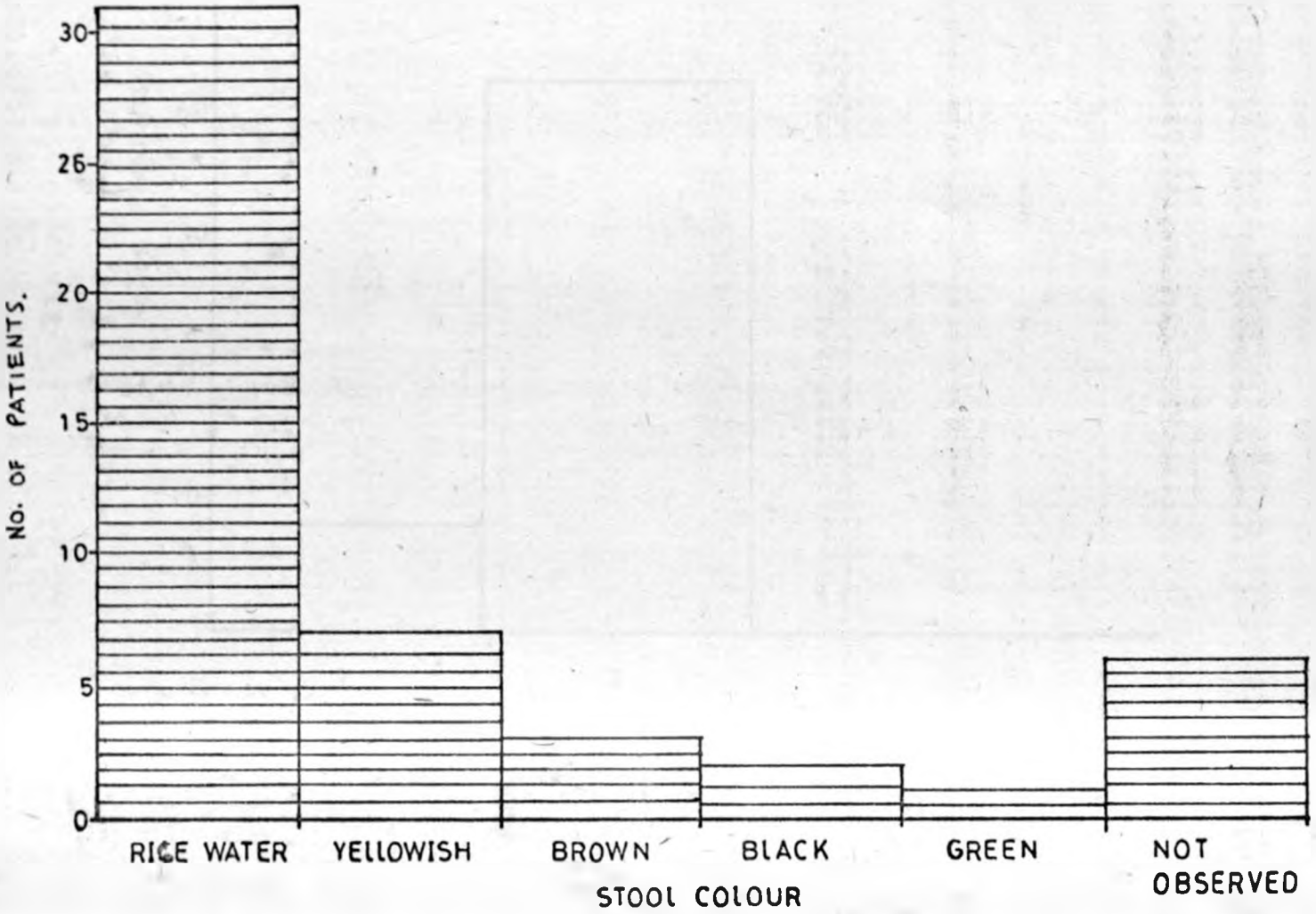
SEVERE AND MODERATE DRYNESS OF MUCOUS MEMBRANES, LOSS OF SKIN TURGIDITY WITH MARKED BONY PROMINENCES WITHOUT MUSCLE WASTING, RESTLESSNESS, MARKED THIRST WITH OLIGURIA AND WEIGHT LOSS RESPECTIVELY.

after: Edholm O.G. & Bacharach A.L. (1965) In "THE PHYSIOLOGY OF HUMAN SURVIVAL" Academic Press. London, New York.

Histogram 7.

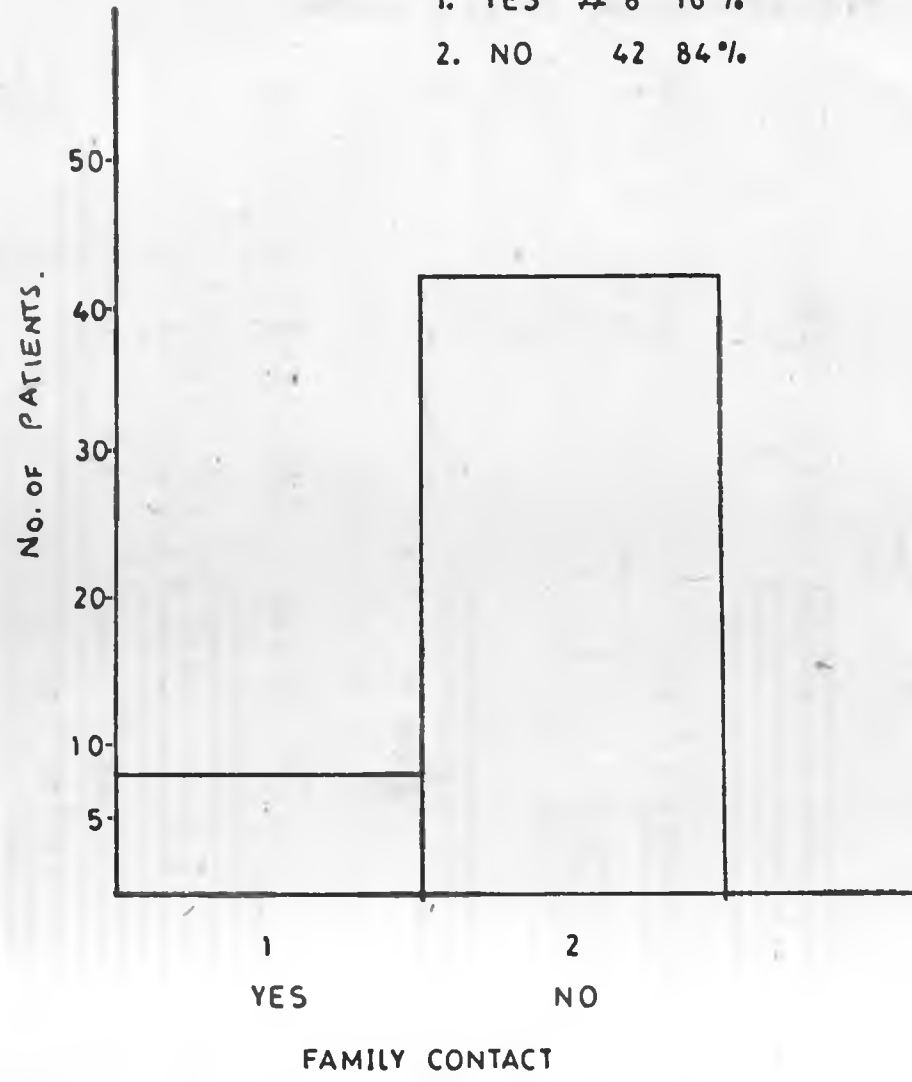
FIG.7.

STOOL CONSISTENCY WATER	100 %	N = 50				
COLOUR RICEWATER (whitish)	# 31	62 %	YELLOWISH	# 7	14 %
BLACK	2	4	BROWN	3	6
GREENISH	1	2	NOT OBSERVED	6	12



PATIENTS: KNOWN FAMILY CONTACT

1. YES # 8 16 %
2. NO 42 84 %



CARRIERS

Age	2/3	2½	4	5	6	7	9	8	13	21	22	25	27	31	1	34	35	37	43	45	47	50	63	65
No. of Subjects	1	1	4	1	2	2	2	2	1	1	2	1	1	1	1	2	2	1	1	2	1	2	1	1

MEAN = 23.46 YRS MEDIAN = MODE = 12 YRS SD = 23.46 ± 18.12 YRS

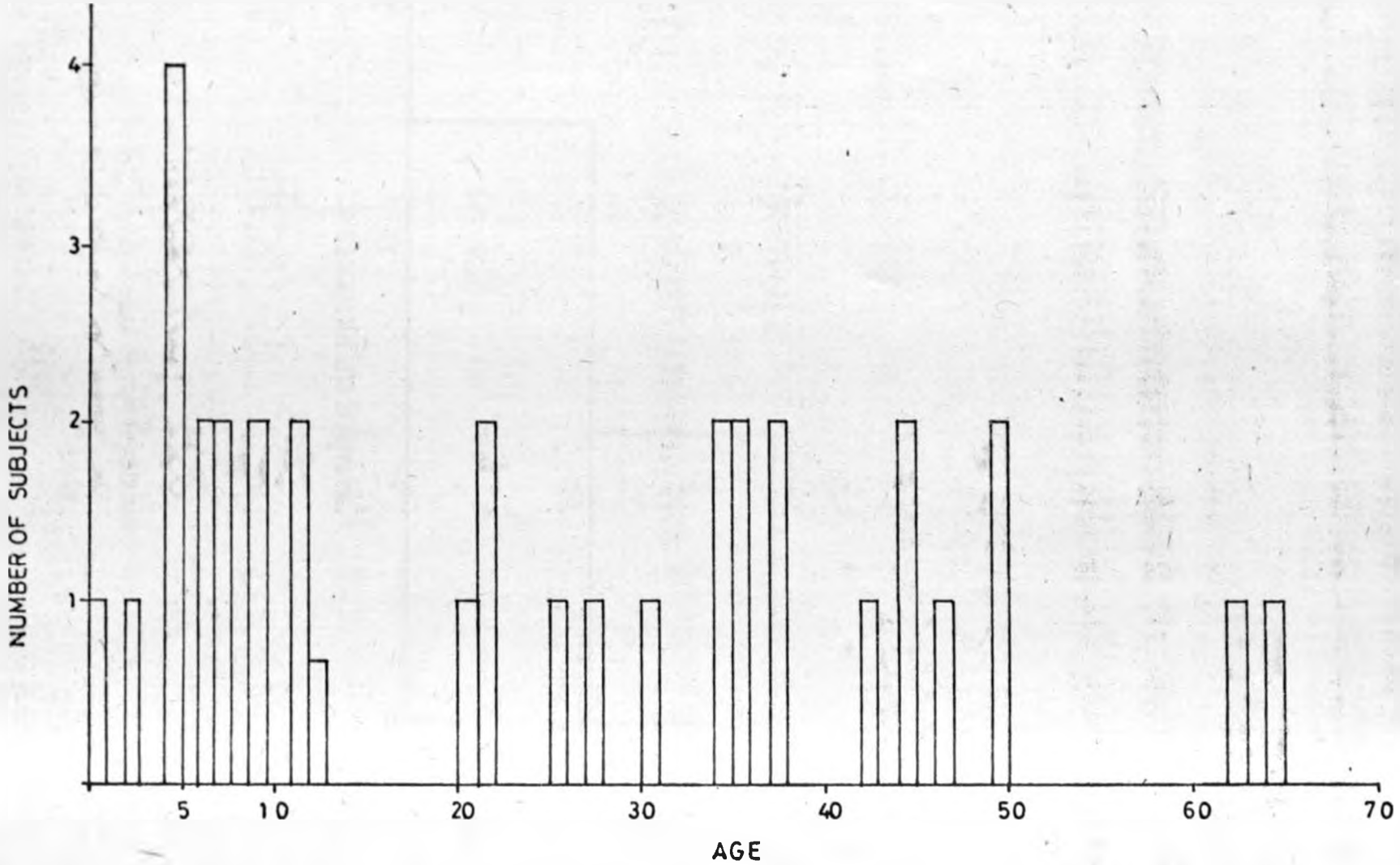


Fig. 9.

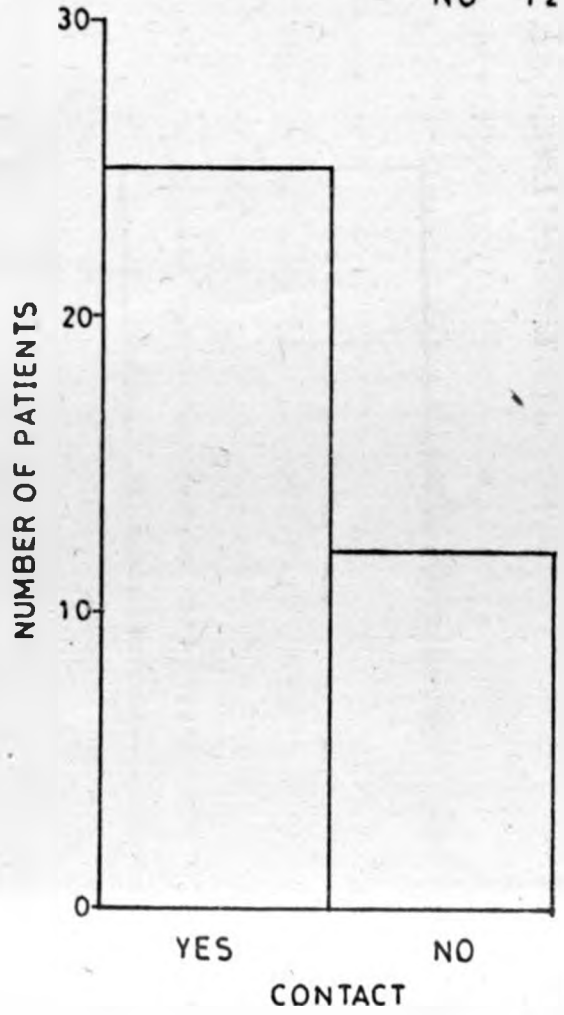
Histogram 8

FIG. 10

KNOWN HOUSEHOLD CONTACT N = 37

YES 25 67.6%

NO 12 32.4%

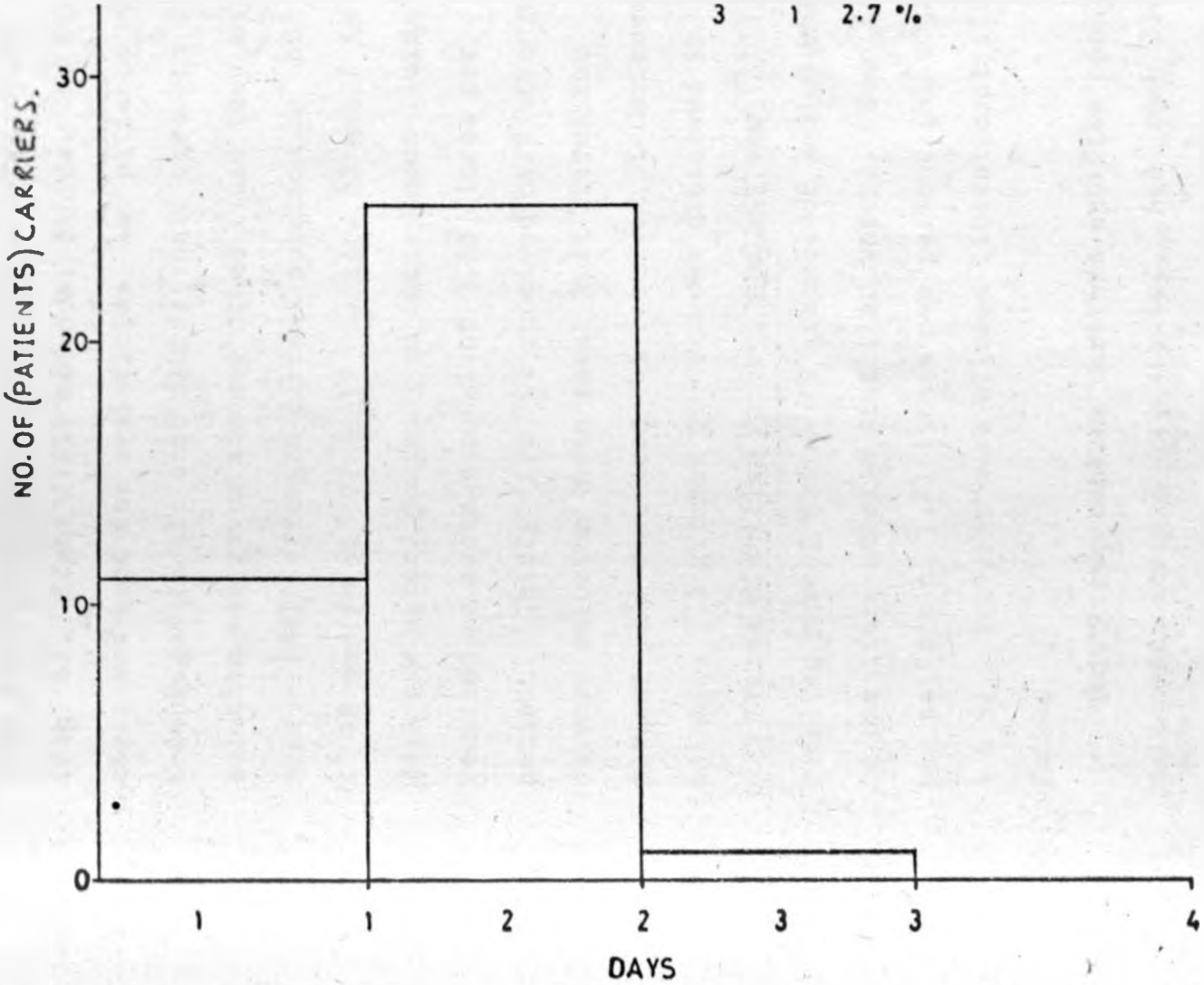


Histogram 9

Fig.11.

DURATION OF CARRIER STATE:

N = 37	DAYS		
	1	11	29.7 %
	2	25	67.6 %
	3	1	2.7 %



Parenteral fluid was administered to fourty two (42) 84% of patients mainly those presenting with moderately severe and severe dehydration (Fig. 6). Eight (16%) had oral fluids. No fluid chart was kept for oral fluids, and patients were encouraged to sip oral fluids; half strength darrows solution was given and any other fluid they may need. (Half strength darrows solution Na^+ 62 K^+ 18 mmol/M cL^- 27 mmol/ lactate 53 mmol/ in 5% dextrose water) patients on intravenous fluids received an average total of 3.88 litres per patient. Thirty five 70% received half strength darrows solution (mean total 3.22 litres for patient (17) seventeen 34% received 5% dextrose solution (25 grammes of dextrose dissolved in o.5 litres distilled water), and sixteen (32%) received normal saline (9 grammes of sodium chloride in one litre sterile distilled water). Mean total per patient of 1.41 litres per patient (histogram 4 & 5). Patients were allowed liberal oral fluid intake.

Thirty two healthy carriers and five convalescent carriers were studied. Ages mean 23.5 years mode= median = 12 years. One times standard deviation from mean 1xSD=23.5 $\pm$ 18.1 years. There was no significant difference between healthy and convalenscent carriers. Twenty five 67.6% had a known household contact. All 37 carriers were treated as soon as bacteriologically proven

positive for vibrio cholerae. They were given either tetracycline 2gm stat then 0.5 gm 6 hourly for five days or chloramphenicol 25 mg/Kg for paediatric patients or 500mg 6 hourly for one week. In Kirinyaga district, all carriers were admitted until bacteriologically negative. Elsewhere, carriers were dispensed with medicine by the mobile surveillance team in their homes.

Only one carrier was a breast feeding infant but his mother was negative for vibrio cholerae.

DISCUSSION

Antimicrobial agents inhibit growth of microbes by different mechanisms. Antibiotics act at different sites in bacterial metabolism to inhibit (bacteriostatic) growth or to lyse (bacteriocidal) the bacterium. The objectives of a clinician is to administer an appropriate effective antibiotic. In order to determine effectiveness or resistance of an antibiotic, minimum inhibitory concentration (MIC) has been used. It is applicable to vibrio cholerae (54). Tetracycline inhibits bacterial protein synthesis by binding to the 30s submit of the (bacterial) ribosome and thus impairs binding of Transfer Ribosenuclei acid to messenger Ribose nucleic acid. Their selective toxicity to bacterial cells attributed to their high intracellular concentrations*. Resistance to tetracycline develops slowly.

Chloramphenicol affects the function of the small bacterial ribosomes by preventing peptide bond formation.

Ampicillin is bacteriocidal and acts by breaking down the cell wall. Nalidixic acid inhibits bacterial deoxyribosenucleic acid gyrase and thus from forming a double helix.

Antibiotic resistance is said to occur when the level of susceptibility is beyond that normally achieved in human tissues in recommended therapeutic doses. Resistance may be intrinsic or acquired as described above (under introduction). From Table III is evident that the organism vibrio cholerae el tor biotype serotype ogawa currently isolated in patients and asymptomatic subjects in Kenya was 100% (N=178) sensitive to minolycline and nalidixic acid 0.1 - 4 mg/ml and not more than 10 mg/ml, respectively. 84.3% were sensitive to chloramphenico All 124 isolates from Kirinyaga district were resistant to tetracycline at 0.1 - 10mg/ml, compared to 67% resistance encountered in Kisumu district. All fourteen isolates from Wajir district were sensitive. The organism was 100% resistant to co-trimoxazole and amoxycillin at not more than 1.4 mg/ml and 0.2-5 mg/ml. Variable high resistance to erythromycin 65.2% and ampicillin 89.3% was elicited of vibrio cholerae.

Antibiotic sensitivity pattern Table III shows levels of sensitivity by percentage using standard minimum inhibitory concentrations M.I.C.'s as indicated in Table II.

All 178 isolates were sensitive to minocycline and nalidixic acid compared to 84.3% for chloramphenicol. The organism was resistant to co-trimoxazole and amoxycillin. The study was conducted between August 1985 and February, 1986 in two sessions six weeks each. During this period, the disease was reported by the D.C.D.C. & R. surveillance team in Kirinyaga district in central province, and Kisumu and Siaya districts in Nyanza province. Fourteen patients were also reported in Wajir district.

Carrier state:

All patients admitted for cholera were treated until negative bacteriologically for V. cholerae. All healthy carriers were started on antibiotics. Tetracycline in adults and chloramphenicol when available for children 15 years. In Kerugoya district hospital, carriers were admitted and treatment continued till bacteriologically negative. In Nyanza provincial general hospital, Kisumu, patients were also discharged as soon as they were negative and clinically improved, but healthy carriers were sent home on treatment or antibiotics dispensed to them in their homes. Tetracycline and chloramphenicol were used also in therapeutic doses.

My intention in the first place was to determine clearance rate without treatment. However, this was not possible since this would

contravene Ministry of health's policy on this issue.

Note: During my study, 402 subjects were reported positive for V. cholerae. This was a representative sample being 178. 44.3% of all reported positives.

Cross resistance to ampicillin and co-trimoxazole does occur (Dapoint M) et al 1985 (16).

Multiple antibiotic resistant vibrio cholerae in endemic areas has been shown from other studies to be due to plasmids (21, 22,23,24 & 16). A single plasmid coding for resistance against several antibiotics.

Tetracycline 2gm stat then 500mg 6 hourly for at least five days, co-trimoxazole 2 BD and erythromycin 1000mg four times a day and chloramphenicol 500mg four times a day have been considered and shown to be effective against vibrio cholerae during the last two decades (18, 19 and 20). Minocycline 200 mg stat then 100 mg BD has always been effective in the treatment of cholera compared to tetracycline, (Mazumdar D.N. et al 25). However, Nalidixic acid 1 gram four times a day, which in-vitro is as effective as minocycline and cheaper has not been cited in the literature.

In the management of cholera, antibiotics are an important adjunct to therapy. Fluid and electrolyte replacement are the mainstay of therapy in the treatment and prevention of complications of cholera, (14, 26, 35, 36, 37, 38, 39, 40). However, appropriate antibiotics do significantly shorten the duration and volume of diarrhoea

Poor nutritional status (34) intercurrent infections, immuno compromised status, and failure to breastfeed aggravate the prognosis in cholera. Fatal septicaemia (30) and endotoxaemia (31) due to vibrio cholerae have been reported in severely immunocompromised patients,Seigel M.I. et al (1982) and Onyemelukwe, G.C. et al (1982), R.1: Glass et al (1983) (32) and RA.Gunn et al 1979 (33) report on the benefit of breastfeeding. Although breastfeeding does not prevent infection, it does protect breastfed infants from pathogenesis of cholera. This is corroborated by experimental models: Guentzel M.N. et al (55). Non specific immunity and specific immunity against vibrio cholerae in breastfed infants apparently play a complimentary role. Patients in this series were well nourished and did not have any overt evidence of intercurrent infections or diseases. These factors may account for the favourable outcome for the majority 48 (96%) of documented patients. The mortality rate was 2 (4%)(N=50). Mortality in these patients may be explained by late arrival in hospital when they were already in hypovolaemic shock with oliguria and severe metabolic acidosis. Patients in this series presented with a syndrome consistant with cholera. They however presented late after onset mean 38.2 hours mode= median= 24 hours. One times standard deviation 38.2±35.5 hrs. Range 4 hrs - 6 days. and thus it is expected that these patients present with severe or moderately severe dehydration in 41 patients and this delay probably accounted for the two deaths. I did not account for domiciliary deaths due to diarrhoea and vomiting since although highly probable to have been cholera there is no bacteriological proof.

Treatment with antibiotics at health centres while in transit to hospital was administered to 24 (48%) of pattern. As is evident from the pattern of antibiotic sensitivity. The bulk of these drugs may have been wasted especially in an area with 100% resistance to the drug being administered. Although the duration and volume of diarrhoea were not quantified it is my observation that hospitalisation period was longer in the district with 100% resistance to tetracycline (about 5 - 6 days) compared with the district with =67% resistance (3 - 4 days).

Cholera carriers have been studied (42,43,44,45,46,47,48). In these studies a healthy carrier is an asymptomatic individual who is positive for vibrio cholerae on rectal swabing. Ideally the best method of determining the duration of carrier state would be to follow up non-infected individuals until they were infected and then follow them up until bacteriologically negative severally. However, in the studies under reference above and this one took day one as the day a subject was identified as positive.

Healthy carriers have a higher rate of household contact than the general population, Pal S.C. et al. (1973). (45) demonstrated a four fold rate in family contacts than in the general population 4.5% vs. 1.5%. They may excrete organisms intermittently and serotype interconversion may occur. They may exist in an endemic area without overt disease in the community and thus enhance endemicity, Sinha R. et al. (1967) (43). Duration of healthy carrier state is variable and short. About 75% of individuals take between 1 - 5 days for most studies with a range of 2 - 24 days

Sinha, R. (43) working in Calcutta obtained the following durations:

TABLE IV DURATION OF HEALTHY CARRIER IN CALCUTTA

Period in days	Number of positive intermmittent excretors
1	95
2–5	3
6–15	13
16–25	2
26–30	3
51–100	0
101–150	2
151–200	2
200	7

Pal S.C. et al 1973 working in New Delhi obtained a range of 2 - 24 days and a median period of 5 days. The longest carrier duration is 4 years; viz cholera Dolores in the Philipines.Azurin J.C. et al. (1967)(48).

In this study all cholera carriers were treated with tetracycline 2 gm stat then 500 mg 6 hourly for at least 5 days; or chloramphenicol 500 mg 6 hourly for one week and 25 mg/Kg body weight for children below 15 years of age.

The carrier duration was short. All 37 carriers studied were negative after 3 days. The variance between this finding and those of other workers is probably due to antibiotic therapy. Although the organism may be resistant in vitro, in-vivo response is unquantifiable in carriers and is modified by factors such as dosage of the antibiotic

nutritional and immunological factors.

There is strong corroboration between this study and others cited above since carriers had a history of house-hold contact two-fold compared to the general population or patients of whom 84% (N=50) denied known history of household contact. The household is therefore an important target in control measures apart from other public health control measures.

There was no evidence of sero-conversion as reported in other studies as all isolates were vibrio cholerae eltor serotype ogawa.

CONCLUSIONS:

1. Minocycline, Nalidixic acid chloramphenicol were found to be highly effective In-citro to Vibrio cholerae eltor serotype Ogawa found in Kenya today.

   The organism showed high resistance to Tetracycline, Co-trimoxazole, erythromycin, ampicillin and amoxycillin.

2. Antibiotic sensitivity in Vibrio cholerae eltor Ogawa varied from district to district.

3. Healthy carrier rate was high among family contacts more than two-fold compared to patients of the general population.

4. Natural healthy carrier duration was not established in this study due to treatment with antibiotics.

Recommendations:

1. Nalidixic acid 1gm 6 hourly for one week should be tried in vivo for clinical efficacy in cholera patients.

2. Cholera surveillance should continue and to incl
   i. Regular antibiotic sensitivity in all locali where cholera occurs.
   ii. Apart from other control measures concentrat more on patients and carriers household cont

3. Tetracycline should be withheld and sensitivity testing continued until sensitivity rates are on an upward trend.

4. Chloramphenicol 500 mg q iD for one week should continue to be used for cholera treatment.

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APPENDIX A

Serial No	Initial	Age	Sex	TETRACYCLINE	CHLORAMPHENICOL	ERYTHROMYCIN	AMPICILLIN	AMOXIL	NALIDIXIC ACID	SEPTRIN	MINOCYCLINE
6024	M.G.	45	M	50	3.1	12.5	50	100	1.5	100	0.7
026	G.W.	12	M	50	3.1	12.5	50	100	3.1	50	0.7
027	S.M.	11	M	50	1.5	25	25	50	3.1	100	1.5
028	N.M.	64	M	100	1.5	12.5	50	100	6.2	100	0.7
029	S.M.	8	M	25	3.1	12.5	50	50	1.5	50	0.7
030	W.M.	6	F	50	6.2	25	25	50	3.1	50	0.7
034	J.N.	15	F	12.5	1.5	12.5	12.5	50	1.5	100	0.7
035	W.A.	2	F	50	1.5	25	25	100	1.5	50	1.5
044	W.N.	9	F	100	3.1	12.5	50	100	3.1	100	0.7
052	J.N.	40	M	50	6.2	12.5	12.5	50	1.5	100	0.7
054	J.M.	30	F	25	3.1	12.5	50	100	3.1	100	1.5
058	F.M.	31	M	50	3.1	25	50	100	1.5	100	0.7
059	M.N.	7	M	25	3.1	12.5	25	50	3.1	100	0.7
060	M.N.	6	M	100	1.5	12.5	25	100	1.5	100	0.7
061	R.N.	4½	M	50	3.1	25	100	100	3.1	100	1.5
073	J.N.	7	M	50	3.1	12.5	50	100	1.5	50	0.7
075	J.W.	2½	F	50	1.5	25	50	50	3.1	100	0.7
076	F.W.	9	F	25	3.1	25	25	25	3.1	50	0.7
080	E.N.	18	F	12.5	3.1	25	25	25	1.5	100	0.7
102	R.W.	25	M	50	6.2	12.5	50	50	1.5	100	1.5
104	B.G.	22	M	50	3.1	12.	100	100	3.1	100	1.5
105	S.M.	32	M	25	0.7	1.5	50	100	3.1	100	0.7
123	N.K.	40	M	100	3.1	3.1	100	100	3.1	100	3.1
125	G.W.	55	F	50	1.5	6.2	50	50	1.5	50	0.7
135	W.G.	50	F	25	3.1	12.5	25	25	3.1	100	3.1
144	W.M.	45	F	12.5	3.1	12.5	50	100	3.1	50	0.7
163	J.N.	24	M	50	3.1	12.5	50	100	1.5	100	0.7
164	S.M.	42	M	50	3.1	12.5	50	100	1.5	100	0.7
186	S.W.	28	F	50	1.5	12.5	50	100	1.5	100	1.5
187	D.M.	1	M	50	6.2	12.5	50	100	3.1	100	1.5
188	J.N.		M	100	12.5	25	50	50	1.5	100	0.7

Serial No.	Initials	Age	Sex	TETRACYCLINE	CHLORAMPHENICOL	ERYTHROMYCIN	AMPICILLIN	AMOXIL	NALIDIXIC ACID	SEPTRIN	MINOCYCLINE
8	J.M.	15	M	25	1.5	12.5	50	50	1.5	50	0.7
17	V.N.		F	50	3.1	12.5	50	100	1.5	100	1.5
201	S.R.	25	M	50	1.5	12.5	25	100	3.1	100	1.5
254	S.I.	20	M	100	3.1	25	25	50	1.5	100	3.1
405	G.W.	50	F	100	3.1	25	100	100	3.1	100	3.1
408	F.W.	50	F	25	1.5	12.5	50	50	6.2	50	0.7
425	G.N.	65	F	50	3.1	12.5	100	100	3.1	100	1.5
386	W.M.	50	F	50	3.1	6.2	25	100	1.5	100	1.5
397	A.K.	65	M	100	3.1	12.5	50	50	3.1	50	0.7
605	B.W.	28	F	50	0.7	6.2	100	50	3.1	100	3.1
608	R.N.	60	M	25	0.7	6.2	50	100	1.5	50	0.7
609	S.M.	35	M	50	25	12.5	100	100	3.1	100	1.5
627	J.G.		M	12.5	1.5	25	50	100	1.5	100	0.7
641	A.M.		M	50	3.1	12.5	100	100	3.1	100	1.5
651	M.M.		CM	25	0.7	6.2	50	50	3.1	50	1.5
653	W.W.	3	F	100	1.5	12.5	25	100	3.1	100	3.1
674	A.W.	35	F	100	3.1	12.5	50	50	1.5	100	1.5
677	P.M.	17	M	50	0.7	25.	100	50	1.5	100	0.7
678	A.M.	45	M	25	1.5	12.5	100	100	3.1	50	0.7
807	M.K.	8	M	25	1.5	6.2	50	505	1.5	100	1.5
808	L.W.	25	F	50	0.7	3.1	100	50	3.1	100	0.7
809	P.N.	22	F	100	3.1	6.2	25	100	1.5	100	0.7
816	E.W.	39	F	50	0.7	12.5	50	100	3.1	50	0.7
993	I.N.	4	M	50	1.5	6.1	50	50	1.5	50	1.5
8023	N.G.	80	M	50	1.5	3.1	50	100	1.5	100	3.1
8031	A.K.	63	M	25	0.7	12.5	100	50	3.1	100	3.1
041	I.W.	7	M	100	0.7	25	25	50	1.5	50	1.5
081	J.W.	22	F	50	1.5	6.1	25	100	1.5	100	1.5
084	P.W.	3	M	25	1.5	3.1	100	50	1.5	50	1.5
085	M.M.	2	M	50	0.7	6.1	50	100	1.5	100	0.7
8102	L.M.			50	0.7	3.1	25	100	1.5	100	0.7
				50	25	1.5	12.5	100	100	100	1.5

No.		Age	sex	TETRACYCLINE	CHLORAMPHENICOL	ERYTHROMYCIN	AMPICILLIN	AMOXIL	NALIDIX ACID	SEPTRIN	MINOCYCLINE
595	M.N	55	M	25	1.5	12.5	50	50	1.5	50	0.7
603	B.W	16	F	50	1.5	12.5	25	50	3.1	100	0.7
606	N.K		M	25	3.1	6.2	100	100	1.5	100	0.7
609	G.M	65	M	50	3.1	12.5	50	100	3.1	100	3.1
614	R.W	70	F	100	1.5	12.5	50	50	3.1	50	0.7
620	N.W		F	50	0.7	6.2	25	50	1.5	50	1.5
637	F.N		M	50	0.7	6.2	12.5	100	1.5	100	0.7
640	G.M	39	M	25	1.5	12.5	25	50	3.1	50	0.7
655	S.N	70	F	50	0.7	6.2	50	50	3.1	100	0.7
656	J.M	15	M	50	0.7	6.2	50	50	1.5	50	1.5
657	P.K	14	M	25	1.5	6.2	100	100	1.5	100	0.7
660	T.S	50	F	25	3.1	6.2	100	50	3.1	50	1.5
662	L.N	18	F	50	1.5	12.5	50	50	3.1	50	1.5
663	H.N	15	M	25	1.5	12.5	25	100	0.7	100	0.7
667	J.K		M	100	3.1	12.5	25	50	3.1	50	1.5
702	D.M	37	M	50	3.1	12.5	100	100	1.5	50	1.5
704	J.W	30	F	50	0.7	6.2	50	100	3.1	100	0.7
744	F.M		M	50	3.1	12.5	100	100	3.1	100	1.5
745	S.N		F	100	6.2	12.5	100	100	6.2	50	1.5
736	J.W		F	50	25	12.5	100	100	3.1	100	1.5
853	T.M	65	F	50	3.1	6.2	100	100	0.7	100	3.1
854	J.W	30	F	50	3.1	12.5	100	50	3.1	100	0.7
863	F.M	42	M	50	3.1	12.5	50	100	0.7	100	1.5
864	J.K	20	F	50	12.5	12.5	100	100	0.7	100	0.7
870	T.M	4	F	100	0.7	6.2	100	50	1.5	50	0.7
874	G.W	12	M	50	6.2	12.5	25	100	3.1	100	0.7
879	S.M	8	M	50	3.1	12.5	100	100	1.5	100	0.7
883	I.W	13	F	50	3.1	6.2	100	100	1.5	50	0.7
896	M.W	65	F	100	1.5	12.5	100	100	1.5	100	0.7
897	M.G		AM	50	1.5	12.5	50	100	1.5	100	0.7

Serial No.	Initials	Age	Sex	TETRACYCLINE	CHLORAMPHENICOL	ERYTHROMYCIN	AMPICILLIN	AMOXIL	NALIDIX ACID	SEPTRIN	MINOCYCLINE
899	R.W	35	F	50	1.5	25	50	50	1.5	50	
901	W.J	30	F	25	1.5	12.5	25	100	1.5	100	
910	W.M	6	F	100	3.1	25	100	100	3.1	100	1.5
913	E.W	20	F	50	0.7	12.5	50	50	1.5	50	
914	J.K	28	M	100	3.1	12.5	100	100	3.1	100	0.7
922	J.K	19	M	50	3.1	25	100	100	3.1	100	1.5
925	E.W	7	F	100	3.1	25	100	100	3.1	100	1.5
932	J.M	35	M	50	3.1	25	100	100	3.1	100	0.7
933	B.N	35	M	25	0.7	12.5	25	50	1.5	25	
948	T.M.G	58	F	50	1.5	12.5	50	100	1.5	100	
951	P.K	7	M	50	1.5	12.5	25	50	1.5	50	
952	S.M	12	M	50	25	12.5	100	100	3.1	100	1.5
954	J.W	6	F	100	3.1	25	100	100	3.1	100	0.7
987	M.I		AM	25	0.7	12.5	50	50	1.5	100	
991	W.G	51	F	25	1.5	12.5	100	50	1.5	50	
992	G.W		AF	50	1.5	25	25	50	1.5	50	
993	G.N		MA	50	0.7	12.5	50	50	1.5	100	
991	C.M		F	25	0.7	25	100	50	1.5	50	
995	E.W		M	100	1.5	12.5	50	100	3.1	100	
997	E.W		F	50	3.1	12.5	25	50	1.5	100	
607	W.G		F	25	1.5	12.5	25	100	3.1	100	
007	K.K		M	25	0.7	25	50	50	1.5	50	
009	K.M		F	50	3.1	25	100	100	3.1	100	
010	F.M		AF	50	3.1	12.5	25	50	1.5	100	
011	W.M		F	25	1.5	12.5	50	50	1.5	50	
014	J.I		M	50	0.7	12.5	25	100	3.1	50	
021	E.W		F	25	3.1	12.5	50	50	1.5	50	
022	E.W		F	50	0.7	12.5	50	50	3.1	100	
			F	25	3.1	12.5	25	100	1.5	100	

NO.		Age	Sex	SEPTRIN	TETRACYCLINE	CHLORAMPHENICOL	ERYTHROMYCIN	AMPICILLIN	AMOXIL	NALIDIXIC ACID	LIDAPRIM	MINOCYCLINE
13	G.O	2½	M		3.1	0.7	25	6.2	25	0.7	3.1	0.7
279	G.O		MC	25	12.5	1.5	12.5	25	25	0.7	12.5	0.7
281	D.A	54	M	50	1.5	0.7	6.2	25	25	0.7	6.2	0.7
282	T.O	16	M	50	3.1	0.7	6.2	3.1	12.5	1.5	6.2	0.7
283	G.O	12	M	25	1.5	6.2	1.5	6.2	100	25		0.7
285	P.A		AM	100	25	6.2	3.2	3.2	50	1.5	0.7	1.5
369	E.O	4	M	12.5	1.5	1.5	6.2	3.1	12.5	0.7		0.7
378	N.A	2/12	F	12.5	25	0.7	50	25	50	1.5	12.5	0.7
406	L.A	12	EM	25	12.5	1.5	25	6.2	25	0.7	25	0.7
406	A.P	50	M	25	6.2	3.1	12.5	25	25	1.5	50	0.7
16	R.N	12	F	50	1.5	1.5	12.5	25	50	1.5	50	1.5
407	A.O	22	M	25	12.5	0.7	25	25	25	0.7	100	0.7
440	P.A	12	F	25	25	1.5	12.5	25	12.5	0.7	50	0.7
450	J.A	7	F	25	12.5	1.5	25	25	12.5	0.7	25	0.7
450	D.O	7	M	50	12.5	0.7	50	25	12.5	1.5	12.5	0.7
471	P.A	28	F	25	12.5	1.5	25	25	25	0.7	25	0.7
472	B.O	11	M	50	12.5	0.7	25	25	25	0.7	50	0.7
474	R.A	13	F	25	6.2	1.5	25	1.5	25	1.5	25	0.7
490	O.O		F	25	12.5	0.7	12.5	6.2	12.5	0.7	25	1.5
493	M.A		F	25	6.2	1.5	25	12.5	25	1.5	25	0.7
495	L.A		F	12.5	3.1	0.7	12.5	6.2	25	0.7	3.1	0.7
496	MN	5	F	25	6.2	0.7	25	12.5	25	0.7	6.2	0.7
569	CO		M	50	12.5	1.5	25	6.2	25	1.5	12.5	0.7
628	M.O	50	F	25	1.5	0.7	3.1	1.5	12.5	1.5	6.2	0.7
641	D.A	70	F	50	25	1.5	12.5	50	25	0.7	12.5	0.7
655	M.N	13	M	25	1.5	1.5	12.5	100	25	1.5	25	0.7
712	M.O	17	N	50	6.2	0.7	25	50	25	0.7	50	0.7
716	J.A	10	F	25	1.5	0.7	3.1	50	12.5	1.5	25	0.7
740	B.O			50	1.5	3.1	6.2	50	25	0.7	12.5	0.7
741	C.O			25	3.1	6.2	25	25	12.5	0.7	25	0.7
736	M.A			50	100	3.1	25	100	25	0.7	12.5	1.5
	W.			25	12.5	0.7	12.5	12.5	25	0.7	25	0.7

Serial No.	Initials	Age	Sex	TETRACYCLINE	CHLORAMPENICOL	ERYTHROMYCIN	AMPICILLIN	AMOXICILLIN	NALIDIXIC ACID	LIDAPRIM	MINOCYCLINE
739	P.O.			25	50	1.5	25	25	3.2		0.7
749	O.O			1.5	12.5	1.5	25	50	0.7	6.2	0.7
829	M.O			6.2	1.5	1.5	25	50	0.7	6.2	0.7
FROM HOMABAY											
750	J.A.	5	F	12.5	12.5	1.5	50	50	1.5	3.1	1.5
751	E.A		AF	25	6.2	1.5	25	25	6.7	3.1	0.7
752	S.O	25	M	6.2	6.2	1.5	25	25	0.7	3.1	0.7
753	D.A	3	M	25	3.1	0.7	12.5	25	1.5	6.2	0.7
FROM WAJIR				1.5	0.7	6.2	1.5		0.7	6.2	0.7
1	6686/WAJ /85			1.5	0.7	3.1	1.5		0.7	3.1	0.7
2	6725/WAJ /85			1.5	0.7	3.1	0.7		0.7	3.1	0.7
3	6761/WAJ /85			0.7	0.7	1.5	0.7		0.7	3.1	0.7
5	6769/WAJ /85			0.7	0.7	1.5	1.5		1.5	6.2	0.7
6	6758/WAJ /85			0.7	0.7	6.2	1.5		0.7	6.2	0.7
10	6742/WAJ /85			0.7	0.7	3.1	3.1		0.7	6.2	0.7
11	6695/WAJ /85			1.5	0.7	3.1	3.1		0.7	3.1	0.7
12	6790/WAJ /85			0.7	0.7	1.5	1.5		0.7	6.2	0.7
13	6791/WAJ /85			0.7	0.7	6.2	0.7		0.7	6.2	0.7
14	6792/WAJ /85			0.7	0.7	6.2	0.7		0.7	3.1	0.7
15	6793/WAI /85			0.7	0.7	3.1	1.5		0.7	6.2	0.7
16	6794/WAJ /85			1.5	0.7	3.1	0.7		0.7	6.2	0.7
17	6795/WAJ			0.7	0.7	3.1	0.7		0.7	6.2	0.7

Appendix B

I. QUESTIONAIRE FOR PATIENTS:

A. DATA AT ADMISSION

1. Name ---------- Age ----------

   Sex ---------- Serial No.----------

   IP.NO.----------

2. Duration of diarrhoea ----------

   Duration of vomiting ----------

3. Stool: Colour ---------- Consistancy---------

4. Have you had any treatment since onset of symptoms? YES/NO.

   If yes what treatment? (if known).

5. If infant: Breastfeeding? YES/NO ----------

   If female: Are you breastfeeding? YES/NO.------

6. Is there any one at your home who has had diarrhoea during the last eight weeks YES/NO. ----------

B. DURING HOSPITALISATION:

8. Antibiotics used and duration.

   1. ----------

   2. ----------

   3. ----------

9. Severity of dehydration: mild/moderate/severe (clinical assessment).

10. Total amount of fluid and type.

    i) Normal saline---------- Route ----------

    ii) Half strength Darrows------ Route ----------

iii) Hartmann solution ---------- Route ----------

iv) Ringer lactate solution --------- Route ---------

v) *5%/10% Dextrose ----------Route----------

Delete as necessary)

vi) Oralite ----------

11. Discharged positive/negative for v. cholerae

12. Remarks ----------

Appendix C.

II. QUESTIONAIRE FOR CARRIERS:

1. Name ---------- Age ---------- Sex---------

2. Serial No. ---------- Residence----------

3. Healthy/convalscent (delete as applicable)

4. (i) If convalascent, date of discharge----------

IP. No. ----------

(ii) If still admitted, date symptoms ceased--------

5. If child: Breastfeeding? ----------

6. If female: Breastfeeding? ----------

7. If Healthy carrier ----------

i. Household contact? YES/NO

ii. When contact had symptoms. ----------

8. Follow up cultures for V.cholerae.

Date	Positive (+) Negative (-)

APPENDIX D.

KEY: H=HEALTHY
C=CONVALESCENT
B/F:BREASTFEEDING
HHC=HOUSEHOLD CONTA
TX= TREATED
Y = YES
N = NO
D = DURATION(DAYS)C
POSITIVITY FOR
V. CHOLERAE.

SERIAL NO.	INITIALS	AGE	SEX	H/C	B/F	HHC	TX	D.
1.	B.G.	22	M	H	N	Y	Y	1
2.	M.G.	45	M	C	N	N	Y	2
3.	F.M.	43	F	C	N	N	Y	1
4.	T.M.	34	M	C	N	N	Y	1
5.	M.W.	65	F	C	N	N	Y	1
6.	J.K.	12	M	C	N	N	Y	1
7.	T.M.	4	F	C	N	Y	Y	2
8.	W.N.	13	F	H	N	Y	Y	2
9.	K.M.	63	M	H	N	N	Y	2
10.	I.N.	4	M	H	N	N	Y	2
11.	W.M.	4	F	H	N	Y	Y	2
12.	M.M.	50	M	H	N	Y	Y	2
13.	A.M.	45	M	H	N	Y	Y	2
14.	M.M.	4	M	H	N	Y	Y	2
15.	P.N.	22	F	H	N	N	Y	2
16.	M.K.	0.7	M	H	Y	Y	Y	2
17.	L.W.	25	F	H	N	N	Y	2
18.	W.G.	50	F	H	N	Y	Y	2
19.	F.M.	34	M	H	N	Y	Y	1
20.	N.W.	9	F	H	N	Y	Y	1
21.	J.W.	25	F	H	N	Y	Y	2
22.	N.W.	45	M	H	N	N	Y	2
23.	W.G.	6	F	H	N	Y	Y	2
24.	S.M.	12	M	H	N	Y	Y	2
25.	K.K.	7	M	H	N	Y	Y	2
26.	W.M.	6	F	H	N	Y	Y	2
27.	B.N.	35	M	H	N	Y	Y	2
28.	J.M.	35	M	H	N	Y	Y	2

SERIAL NO.	INITIAL	AGE	SEX	H/C	B/F	HHC	TX	D.
29	F.W.	9	F	H	N	Y	Y	1
30	J.N.	5	M	H	N	Y	Y	1
31	S.M.	32	M	H	N	Y	Y	2
32	J.M.	31	F	H	N	Y	Y	1
33	E.W.	21	F	H	N	N	Y	2
34	D.M.	37	M	H	N	Y	Y	2
35	F.M.	47	M	H	N	Y	Y	1
36	J.K.	27	F	H	N	Y	Y	2
37	I.W.	7	M	H	N	N	Y	3

APPENDIX E: PATIENTS' DATA

KEY TO ABBREVIATIONS

D= DURATION OF DIARRHOEA/VOMITING IN HOURS

S= STOOL CONSISTENCY/COLOUR

W= WATERY

D/K=DONT'T KNOW

TX= PRE ADMISSION TREATMENT (DRUGS) ANTIBIOTIC

Y= YES Mg= Milligram gm= Gram

Y= NO.

B/F= BREASTFEEDING

HHC= KNOWN OR HOUSEHOLD CONTACT

RW = RICE WATER. G= GREENISH B= BROWNISH YW=YELLOWISH

R_x= TREATMENT IN HOSPITAL.

T_1= Tetracycline 1 gram (gm) stat then 0.5gm 6 hourly

T_2= Tetracycline 2gm stat then 0.5gm 6 hourly.

T_o= Tetracycline 1gm stat.

T_3= Tetracycline 2gm stat.

T_4= Tetracycline 0.5gm stat then 0.25gm 6 hourly

T_5= Tetracycline 0.25gm stat then 125 gm 6 hourly

DH= Severity of dehydration (at admission).

+= Mild

++= Moderate

+++= Severe

IV= IV. Fluid therapy (In hospital).

N= Normal saline

H.S.D.=Half strength darrows solution

5% D.W.= 5% Dextrose solution

SP= COTRIMOXAZOLE II BD.

C.= CHLORAMPHENICOL 50mg 6 hourly

-= NO DATA AVAILABLE

C_1= CHLORAMPHENICOL 125mg 6 hourly

C_2= Chloramphenicol 250mg 6 hourly.

SERIAL NO.	INITIALS	AGE	SEX	D	S
1.	D.A	70	F	14/14	W/DK
2.	M.M	13	M	6/6	RW
3.	A.O	22	M	7/7	WB
4.	P.A	25	M	24/24	W/YW
5.	T.O	16	M	48/0	W/B
6.	G.O	12	M	24/0	RW
7.	C.O.	5	M	36/36	W/YW
8.	W.O	50	F	24/24	W/G
9.	P.A	20	M	48/48	RW
10.	D.A	60	M	24/24	W/DK
11.	G.O	4	M	24/24	W/DK
12.	0.0	60	F	96/96	W/DK
13.	M.N	65	F	24/24	RW
14.	L.O	26	F	12/0	R.W
15.	C.O	11	M	8/8	R.W
16.	J.A	10	F	4/4	R.W
17.	M.A	14	F	9/9	R.W
18.	O.O	1	M	24/24	R.W
19.	S.A	25	M	48/48	W/RW
20.	E.A	30	F	96/96	R.W
21.	J.A	5	F	24/24	R.W
22.	D.A	26	M	96/24	R.W
23.	P.A	9	M	10/0	R.W

APPENDIX E:

DATA ON PATIENTS

TX	B/F	HHC	R	DH	IV
N	N	N	T_1	++	N/HSD/5½ DW
T_o	N	N	T_1	++	0/2.41/1.0
T_3	N	N	T_1	+++	5.5/2.5/0
Y/DK	N	Y	T_2	+++	1.0/7.0/0
T_3	N	Y	T_2	+++	1.0/3.5/0
T_3	N	Y	T_1	++	1.0/35/0
Y/DK	N	Y	T_1	++	0/3.5/0
N	N	N	T_2	++	0/2.5/0
N	N	N	T_2	++	0/2.5/0
N	N	N	T_1	+++	0/6.0/2.0
N	N	N	T_2	++	0/6.0/0
N	N	N	T_2	++	0/6.0/0
N	N	N	T_1	+++	0/2.0/0
N	N	N	T_2	+++	2.0/0.5/0
N	N	N	T_4	++	0/2.0/0
N	N	N	T_4	++	0.5/4.0/1.0
N	N	N	T_4	++	0/4.0/0
N	N	N	T_5	++	0/4.4/0
N	N	N	T_2	+	0/0/0
Y/DK	N	N	T_1	++	0.5/1.0/1.0
Y/DK	N	N	S.P	++	0/1.0/0.5
N	N	N	C	+	1.0/3.5/0
N	N	N	T_4	++	

24	M.A	20	F	24/24	R.W	N
25	B.O.	8	M	14/14	R.W	N
26	C.O	35	M	-	R.W	-
27	F.M	43	F	144/96	W/DK	Y/DK
28	W.M.	40	F	96/24	W/YW	N
29	G.W	12	M	24/12	W/DK	N
30	J.W	30	F	96/48	W/YW	Y/DK
31	M.N	40	M	72/0	W/YW	Y/DK
32	J.K	19	M	6/0	W/DK	N
33	J.W.	30	F	72/0	R.W	Y/DK
34	E.W	7	F	72/0	W/B	N
35	G.N	65	M	48/0	W/YW	N
36	E.N	11	F	6/0	R.W	T_3
37	A.K	65	M	7/7	R.W	N
38	W.M	55	F	12/12	R.W	T_3
39	J.G	11	M	72/0	R.W	T_3
40	A.M	25	M	10/24	R.W	Y/DK
41	S.M	35	M	72/24	R.W	N
42	P.M	17	M	5/5	R.W	N
43	R.N	60	M	7/7	R.W	N
44	M.M	27	M	10/10	R.W	N
45	P.W	3	F	6/6	R.W	N
46	D.G	80	M	120/120	R.W	N
47	L.M	50	F	60/60	R.W	N

N	N	T_2	+++	1.5/6.5/1.0
N	Y	T_4	++	0/5.5/0
–	–	T_2	+++	FATAL.
N	N	T_2	++	0/0/0
N	N	T_2	++	1.5/0.1/3.5
N	N	T_2	+++	0/0/1.0
N	N	T_2	+	0/0/0
N	N	T_2	++	0/0/0
N	N	T_2	++	0/0/0
N	N	T_4	+	0/0/0
N	Y	T_4	+	0/0/0
N	N	T_2	+	0/0/0
N	N	T_4	+	1.0/0/0
N	N	T_2	+++	3.0/2.0/2.0
N	N	T_2	+++	1.5/2.0/1.5
N	N	T_4	+	0/1.5/0.5
N	N	T_2	++	1.0/1.0/0
N	N	T_2	+	0/1.0/0
N	N	T_2	+++	3.5/1.5/0
N	N	T_2	+++	1.5/5.5/1.0
N	N	C_1	++	0/1.5/0
N	N	C_1	+	0/3.0/1.0
N	N	C_2	+	0/2.0/0
N	N	C	++	0/2.0/2.5

48	E.W	40	F	D/K	R.W	N	N	N	C	+++	FATAL
49	P.W	13	F	7/0	R.W	N	N	N	T_4T_2	++	0/1.0/0
50	M.O	65	F	4/0	W/DK	N	N	N	T_1	++	0/5.0/0

REFERENCES:

1. Manson's tropical diseases 18th Edition. 1982 pages 360 - 371 Bailliere Tindal.

2. Zeinser's Textbook of Bacteriology 9th Edition 1948 page 494 Appleton - century crofts. Inc.

3. Health and Disease in Kenya. East African Literature Bureaul974 Nairobi, Dar-es-salaam, Kampala .

4. A. Huq. Influence of water temperature solinity and PH on survival and growth of toxigenic vibrio cholerae serovar Ol associated with live copepods in Laboratory Microcosms. Appl & Environ. Microbiol. 1984 48 (2) 420-4

5. V. Radojcic. Cholera el tor vibrios and atypical forms isolated during cholera in Kenya in 1971. E. Afr. Med. Jnl. 1973: 50 696

6. J.M. Johnston et al cholera on a Gulf coast oil rig. N. Eng/jnl. Med. 1983 309 523-6

7. Sinclair G.S. Et al Determination of the mode of transmission of cholera in leboura. S. Afr. med/Jnl. 1982 62 753-5.

8. Baine W.B. et al.
Epidemiology of cholera in Italy
Lancet 1974 2 1370-4

9. Mhalu F.S. et al
Hospital outbreak of cholera transmitted through close person contact
Lancet 1984 2 82 - 4

10. Mngola, E.N.
Cholera epidemic in Kenya
E. Afr. Med. jnl. 1972 49 151

11. Cox P.S. Vibrio cholera in Kenya
East Afr. Med. jnl. 1972 49 440.

12. Roberts J.M.D.
Cholera detection and surveillance in Kenya
E. Afr. Med. Jnl. 1972 49 159

13. Ministry of Health, Kenya: Division of Communicable disease control and research

14. Palmer, D.L. et al
Comparison of sucrose and glucose in the oral electrolyte therapy of cholera and other severe diarrhoeas.
N. Engl. Jnl. Med. 1977 297 1107 - 10.

15. Current Therapy 1981
W.B. Saunders Company
Page 14 - 19

16. M.J. Dapont et al
Development of plasmid mediated resistance in V. cholerae during treatment with Trimethoprim - Sulphamethoxazole.
Antimicrob. agents & chemother.
1985 27 (2) 280 - 1

17. Kobari K. et al.
Evaluation of various antimicrobial drugs for the treatment of cholera.
Bull. WHO 1967 37 810 - 1

18. Wallace C.K. et al.
Antibiotic drugs in cholera
Ann. Int. Med. 1968 69 166 - 7

19. Cash R.A. et al.
Trimethoprim - Sulphamethoxable in clinical cholera: Comparison with Tetracycline.
Jnl. Infect. dis. 1973 128 (Suppl) 749 - 53.

20. Charagozloo et al
A comparative trial of Tetracycline, Chloramphen and Trimethoprim - Sulphamethoxazole in eradicat of Vibrio cholerae.
Br. Med. Jnl. 1970 iv 281 - 2.

21. R.I. Glass et al.
Plasmid borne multiple drug resistance in vibrio cholerae serogroup 01 biotype el tor evidence for a point source outbreak in Bangladesh
Jnl. Infect. dis. 1983 147 (2) 204 - 9.

22. Mhalu F.S. et al.
Rapid emergence of El tor vibrio cholerae Resistant to antimicrobial agents during the first six months of fourth cholera epidemic in Tanzania
Lancet 1979 1 345 - 7

23. K.J. Towner et al (lett)
Resistant vibrion-cholerae el tor in Tanzania
Lancet 1979 2 147-8

24. R.I. Glass et al
Emergence of multiply antibiotic resistant V.cholerae in Bangladesh
Jnl. Infect dis. 1980. 142 6 939-42

25. Mazumdar D.N. et al
Minocycline, Tetracycline and furazolidine in the treatment of cholera.
Ind. Jnl. Med. Res. 1977 66 917-921.

26. Wallace C.K. et al
Optimal antibiotic therapy in cholera.
Bull WHO. 1968 39 239-245.

27. Uylangco et al.
Observations on 285 cases of cholera el tor treated with various antibiotics.
Bull. W.H.O. 1967 812 - 4.

28. Kobari K. et al
Evaluation of various antimicrobial drugs for the treatment of cholera.
Bull. WHO. 1967 37 810 - 811.

29. Kobari K. et al.
Observations on cholera treated orally and intravenously with antibiotics with particular reference to the number of vibrious excreted in stool.
Bull. WHO. 1967 37 751 - 762.

30. Seigel M.I. et al.
Fatal non-ol vibrio cholerae septicaemia in chronic lymphocytic leukaemia.
Gastroenterology 1982 83 1130 - 1

31. Onyemelukwe G.C. et al.
Endotoxaemia in el tor vibrio cholerae
Tans. Roy. Soc. Trop. Med. 1982 76 590.

32. R.I. Glass et al
Protection against cholera in breastfeed
Children by antibodies in breastmilk.
New. Engl. jnl. Med. 1983 308 1389 - 1392

33. Gunn. R.A. et al.
Breastfeeding as a risk factor for cholera
in infants
Lancet 1979 2 730-2.

34. Palmer D.L. et al
Nutritional status: a determinant of severity
of diarrhoea in patients with cholera.
J. infect. dis. 1976 134 8 - 14.

35. De. S.
Oral glucose - electrolyte solution in the
treatment of cholera and other diarrhoeas.
jnl. Indian. Med. Assoc. 1975 65 230 -2

36. Gill G.V.
Biochemical treatment of cholera
Lancet 1976 1 915.

37. Frost W.H.
Cholera: Synopsis of clinical aspects and
Principles of treatment.
Canad. Med. Assoc. jnl. 1976 115 401 - 3

38. Hirshom N et al: Decrease in stool output during intestinal perfusion with glucose containing solutions
N. Eng. Med. jnl. 1968 297 176 - 181.

39. Pierce N.F. et al.
Oral maintainance of water - electrolyte and acid - base balance in cholera.
A. preliminary report.
Ind. jnl. Med. Res. 1968: 56. 640 - 5

40. Pierce N.F. et al.
Replacement of water and electrolyte Losses. in cholera by an oral glucose - electrolyte solution.
Ann. Int. Med. 1969 70 1173 - 81.

41. Chaudri. et al.
A. composite rehydration fluid in treatment of cholera.
jnl. Ind. Med. Assoc. 1968 51 290 - 1.

42. R. Sinha et al.
Role of carriers in the epidemiology of cholera in calcutta,
Ind. jnl. Med. Res. 1968 56 964 - 978.

43. R. Sinha et al
Cholera carriers studies in calcutta 1968 - 7
Bull. W.H.O. 1967 37 89

44. Bryceson A.D.
Role of carriers in maintainance of infection.
Ind. jnl. Pub. Hith. 1977. 199 109 - 114.

45. Pal. S.C. et al.
Studies on cholera carriers in Delhi
Ind. jnl. Med. Pes. 1973: 61 495 - 502

46. Dizon J.J. et al.
Studies on cholera carriers
Bull. W.H.O. 1967 37 737 - 743.

47. Sinha R.
Cholera carriers in calcutta (lett.)
Lancet 1969 1 1162 - 3.

48. Azurin J.C. et al
A long term carrier of cholera: cholera Dolores.
Bull. W.H.O. 1967 37 745 - 9.

49. Greenough et al.
Tetracycline in the treatment of cholera
Lancet 1964 i 355 - 7

50. Ericsson. H.M. et al.
Antibiotic sensitivity testing
Acta pathol. Microb. Scand. Sect. B. Supp. 217 pg

51. Wallace C.K.
Oral Tetracycline therapy in cholera
Trans. Roy. Soc. Trop. Med. & Hyg. 1965
59 621 - 7.

52. T.P. Pesigan et al.
Drug sensitivity of isolates from cholera El tor patients in san Lazaro Hospital, Manila.
Bull. WHO. 1967 37 814.

53. Cary S.G. and Blair E.B. (1964)
New transport medium for shipment of clinical specimens.
J. Bacteriol 88 96 - 8

54. Manual of clinical microbiology 2nd Edition (C) 1974
Edited by Lennette E.H. et al.
American Society for Microbiology
Washington D.C. Page 239 - 244.

55. Guentzel M.N. et al.
Protection of Sucling mice from experimental cholera by maternal immunization: comparison of the efficacy of whole cell, ribosomal derived and enterotoxin immunogens infection & immunity 1974: 10 167 - 172.

56. Arap Siongok (Dr) T.K. Director, D.C.D.C., Ministry of Health.

57. Mechanisms of disease and immunity in cholera: A review J. Inf. dis. 1977 136 Suppl. P. 105-112.

58. Baine W.B. et al.
Epidemiology of cholera in Italy.
Lancet 1974 2 1370 - 4.