

COMPARISON OF CLINICAL EXPRESSION OF DIARRHOEA AMONG FIELD TRIAL PATIENTS

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Introduction

In the wake of search for a new and more effective preventive measure against cholera than the killed bacterial vaccine in current use, a cholera toxoid vaccine was put on trial at our Matlab Project. The detailed report of this trial is being reported by Dr. George Curlin.

In considering the effectiveness of the toxoid vaccine, its ability to reduce clinical severity without altering attack rate, has to be considered.

In this report, attempt has been made for a clinical comparison between patients of toxoid group and placebo group, who were received at our Matlab Field Hospital with cholera, during cholera epidemic following toxoid vaccination in 1974.

The purpose of this comparison was to observe the effect of toxoid on clinical severity using clinical parameters.

Materials and Methods

On arrival at Matlab hospital patients were first categorized by the attending physician as either an Out-patient or Admission case, according to his clinical assessment of the patient's condition. An admission case was hospitalized immediately for necessary fluid replacement, antibiotic therapy and other routine hospital procedures. On the other hand, an Out-patient case was kept in a separate block for observation for a period varying from 4-12 hours, since on arrival they had doubtful or no clinical dehydration. During this observation period these cases were watched frequently for their purging rate, stool volume and subsequent development of dehydration necessitating admission for routine therapy. In the event that these patients did not purge an appreciable volume of stool, they were discharged after the necessary observation period with a 3-day course of

tetracycline for use at home.

Patients of both categories had rectal swabs taken for culture for vibrios and blood samples collected for serum solid estimation before any treatment was started. All admission cases were kept in the hospital until their diarrhoea stopped. During their hospital stay they were weighed daily including weight on admission, intake and output measurements at 8-hourly intervals as routine hospital procedure.

Culture reports, vaccine status of all admission patients were collected later and matched with their respective data of serum solids, stool volume, duration of purging, admission weight and discharge weight.

Data regarding OPD patients are limited to culture reports and serum solid values only, due to insufficient clinical data about purging.

A data from total of 160 Admission and 50 Out-patient cases with proven cholera from among the toxoid field trial volunteers were analysed.

Results

Among admission cases 65 were males and 95 were females, whereas 29 males and 21 females comprise the OPD cases. Age and sex distribution is shown on table 1. 48% of admission cases (77) and 52% of OPD cases (26) received toxoid immunization whereas 52% of admission cases (83) and 48% of OPD cases (24) received placebo immunization.

Slide 2 shows the serum solids of Out-patient and hospitalized cases on arrival. Over all the hospitalized group showed slightly higher values than Out-patients. Adults were also more dehydrated on admission than children as indicated by serum solids on admission. The lack of a striking difference between OPD and Hospitalized patients may relate to the El Tor biotype which produced an overall milder disease.

The next graph compares the serum solid values among toxoid and placebo immunized group of hospitalized cases. No

significant difference is shown between toxoid and placebo immunized groups. But overall the mean values are higher in toxoid group, implying that patients in toxoid group had relatively more dehydration upon arrival at hospital.

Table 4 compares the first full eight hour stool volume in the two vaccine groups. Here also, practically no difference is noted between toxoid and placebo groups. But it may be noted here that patients of 15 years over age group had more stool volume in first 8-hour period, both in placebo and toxoid patients than the patients in other two age groups. This is due to our failure to calculate stool rates on a per kilogram basis since adults produce more stool than children because of their bigger body size.

Table 5 shows total stool volume in toxoid and placebo groups. Here also a repetition of findings of table 4 is noted with the difference that 15 over age group shows little higher mean values in placebo immunized group than in toxoid group. This is probably due to accumulation of a more heterogenous group of cases in the placebo immunized cases as is shown by the bigger range difference.

Table 6 shows duration of diarrhoea among hospitalized cases. No differences were noted between toxoid and placebo groups. Moreover it can be seen that overall duration did not exceed four 8-hour periods which is commonly expected in antibiotic treated cholera patients.

Table 7 compares the difference between admission and discharge weight calculated as percent of discharge weight, which is an indirect indicator of dehydration status on admission. No practical difference is noted between the two groups of cases; but whatever difference is there tends to confirm results of table 3.

Discussion

The results of the comparison of parameters between toxoid and placebo immunized groups clearly indicates that toxoid vaccine has no discernable effect on clinical severity of cholera. It also indicates the epidemic was a clinically milder one as is suggested by lower than expected values of serum solids in both OPD and hospitalized groups of patients.

Comment

This comparative study suggests that the efficacy of cholera toxoid vaccine as a potent preventive weapon against diarrhoeal morbidity of cholera is yet to be proved.

TABLE I

CASES ANALYSED: AGE AND SEX DISTRIBUTION

Age	ADMISSION				OPD						MALE & FEMALE					
	Male		Female				Male		Female				Adm.		OPD	
	Tox.	Pl.	Tox.	Pl.	Total	%	Tox.	Pl.	Tox.	Pl.	Total	%	Tox.	Pl.	Tox.	Pl.
1-4	9	6	3	6	24	15	6	10	8	1	25	50	12	12	14	11
5-14	26	24	19	27	96	60	7	6	4	3	20	40	45	51	11	9
15+			20	20	40	25			1	4	5	10	20	20	1	4
Total	35	30	42	53	160	100	13	16	13	8	50	100	77	83	26	24

ADMISSION SERUM SOLIDS OF HOSPITALIZED AND OUT-PATIENT CHOLERA PATIENTS
BY AGE GROUP
(Mean $\pm$ 1 Std. Error of Mean)

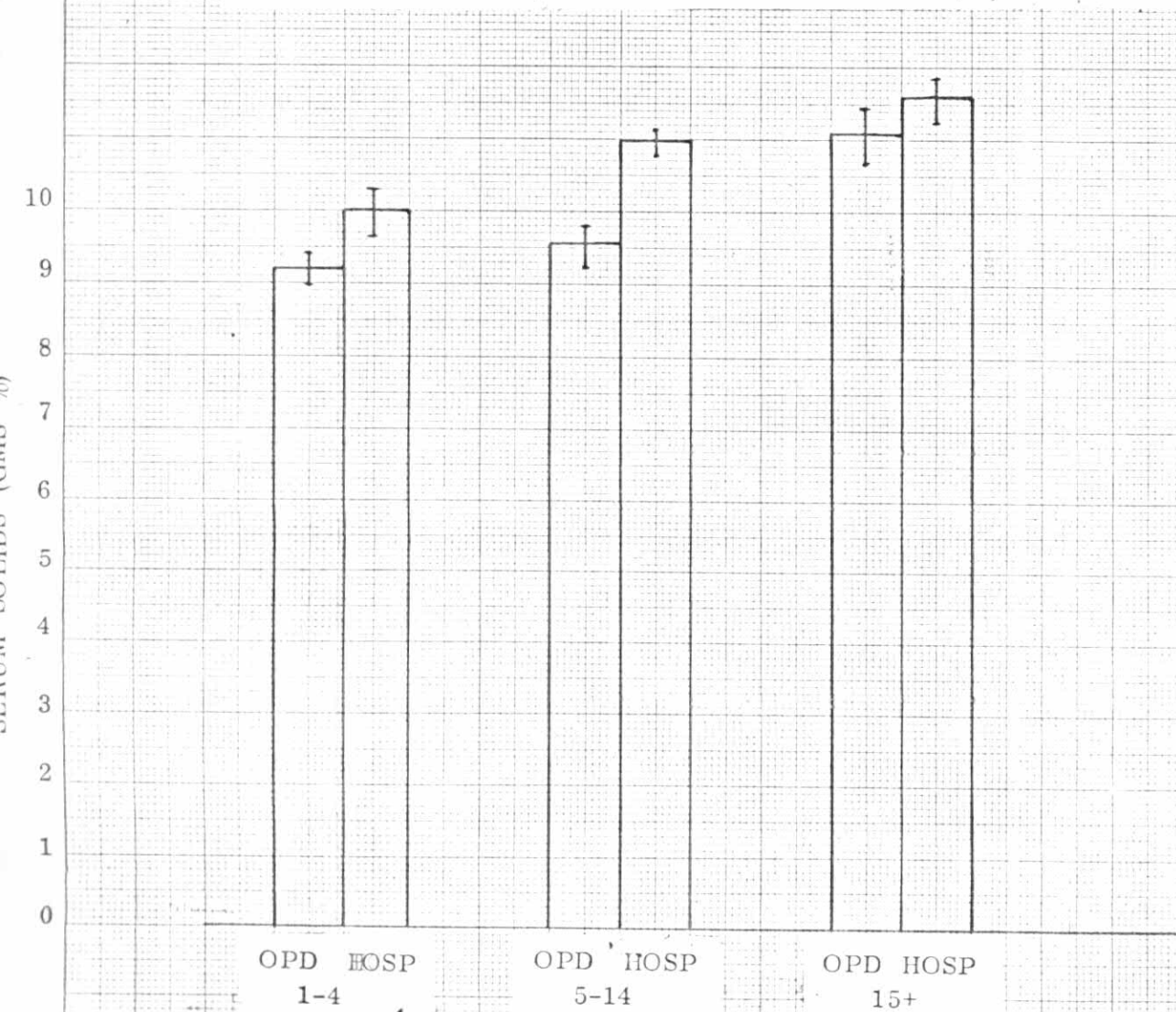
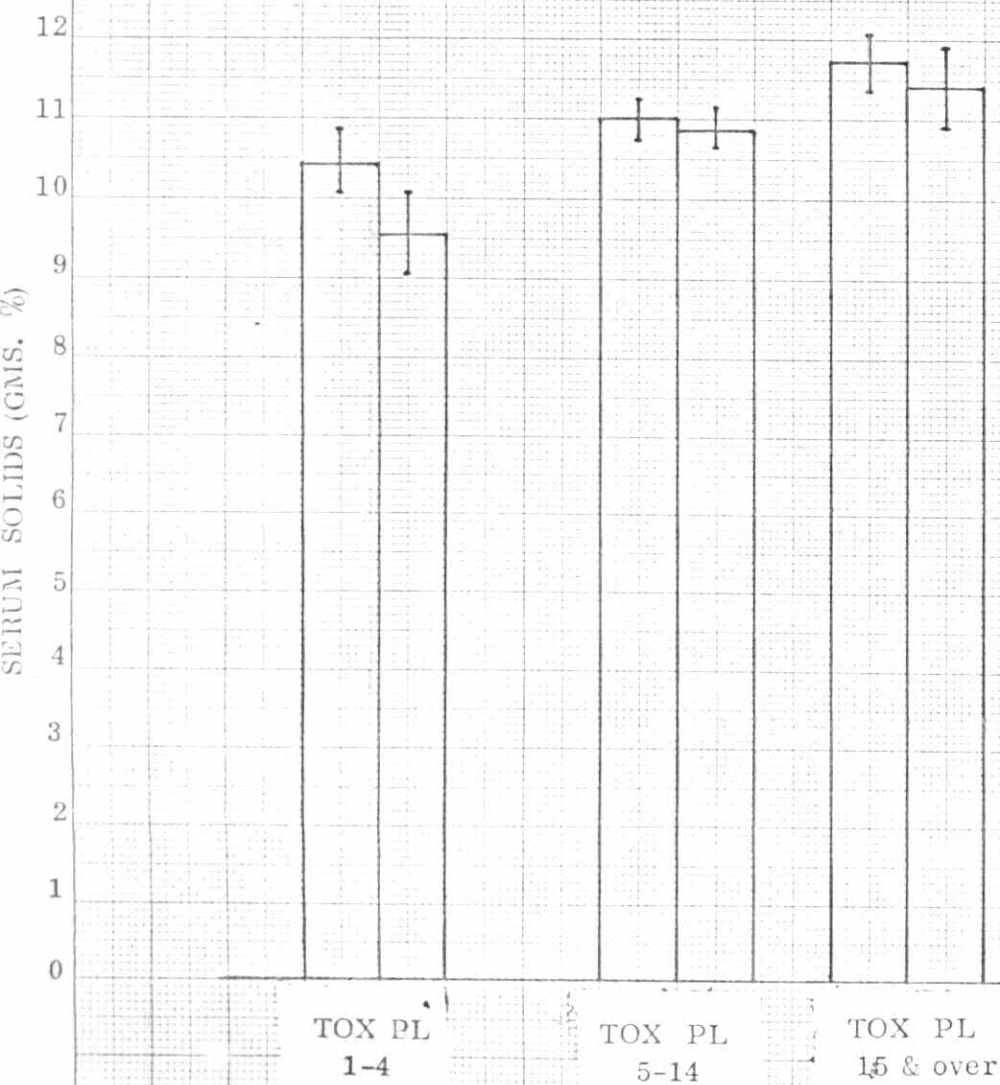
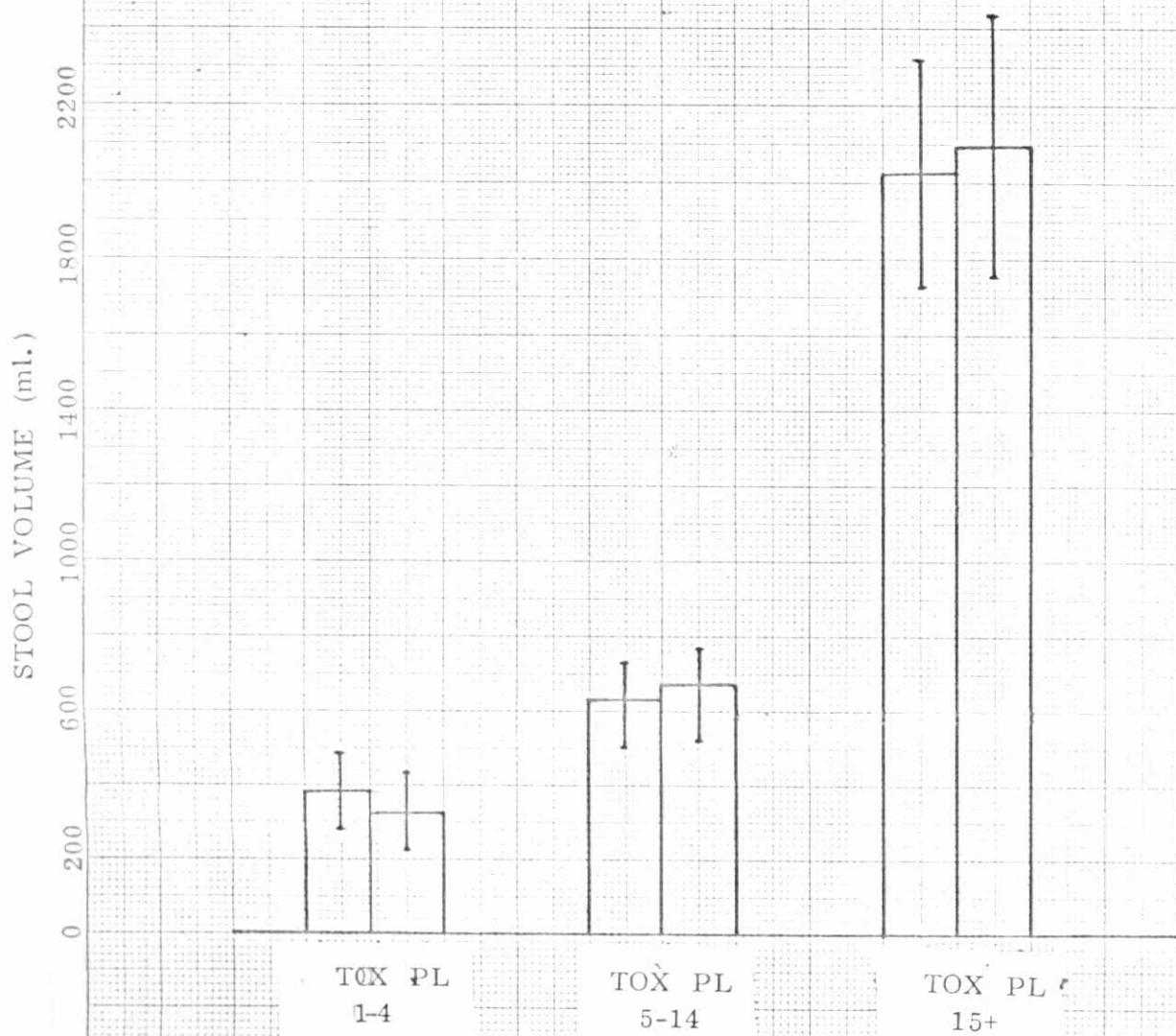


TABLE III

ADMISSION SERUM SOLIDS OF HOSPITALIZED CHOLERA CASES BY AGE-GROUP AND VACCINE STATUS

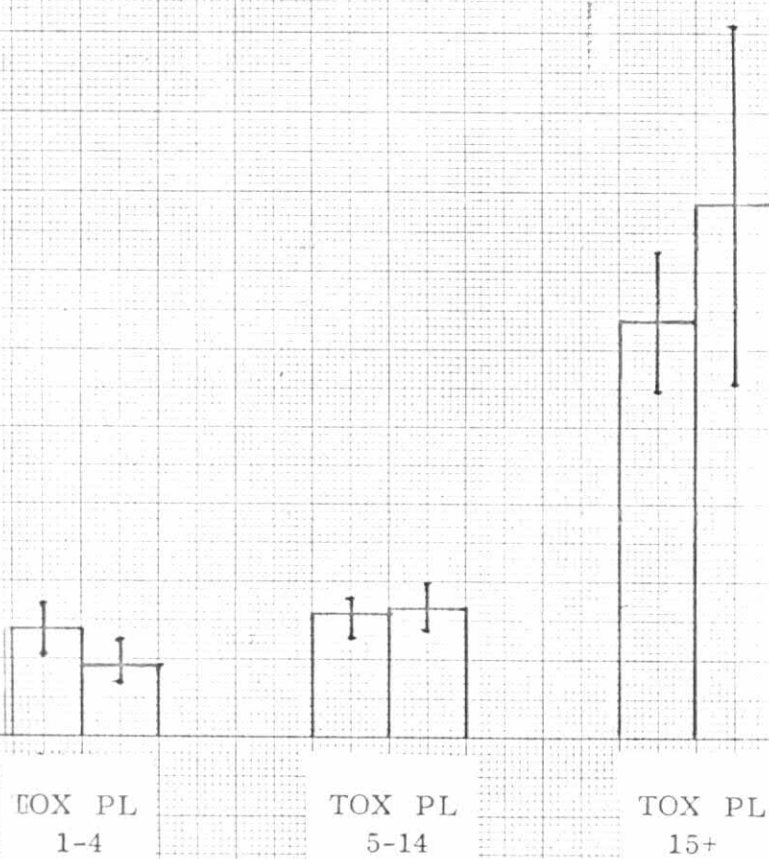
(Mean $\pm$ 1 Standard Error of Mean)

VOLUME OF STOOL OF HOSPITALIZED PATIENTS DURING FIRST FULL
EIGHT HOURS COLLECTION PERIOD BY AGE GROUP AND VACCINE STATUS



TOTAL VOLUME OF STOOL OF HOSPITALIZED CASES AGE GROUP AND
BY VACCINE STATUS

STOOL VOLUME IN LITRES



DURATION OF DIARRHEA IN NUMBER OF 8-HOUR COLLECTION PERIODS
HOSPITALIZED CHOLERA PATIENTS BY AGE GROUP AND VACCINE STATUS
(Mean $\pm$ 1 Std. Error of Mean)

NUMBER OF EIGHT-HOUR PERIODS

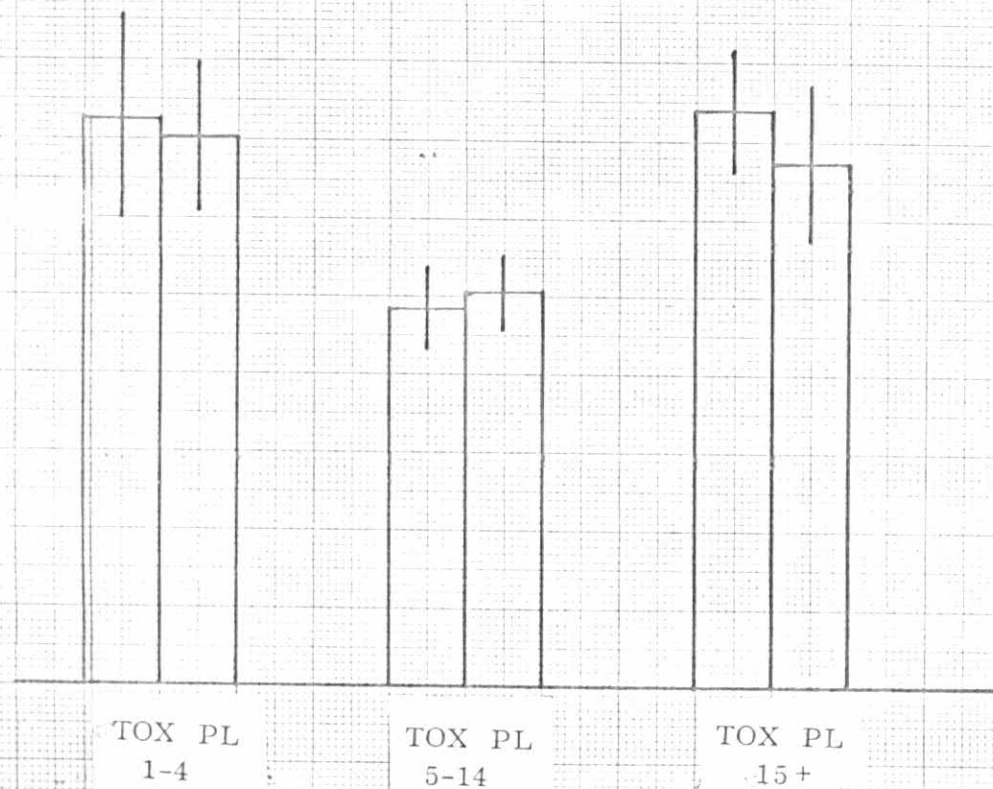
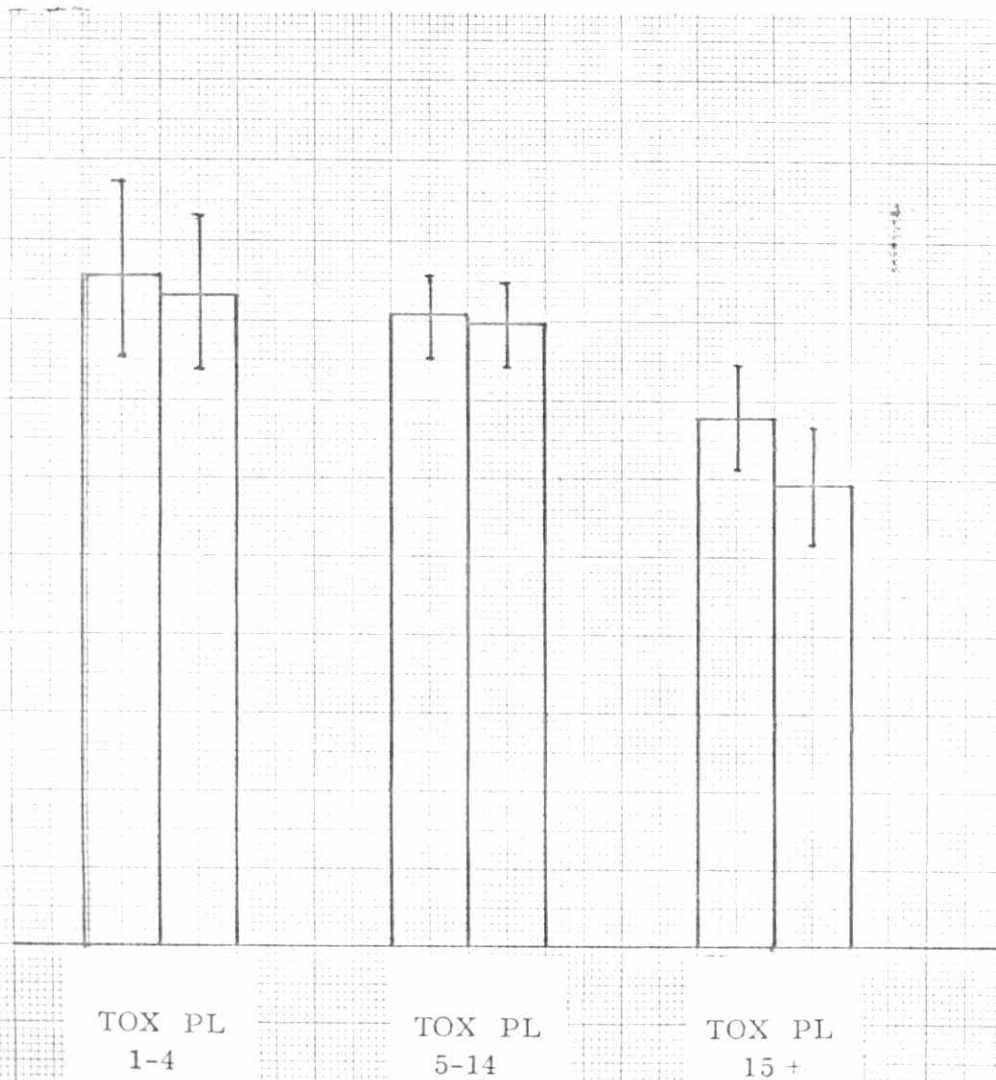


TABLE VII

CHANGE IN WEIGHT AS PERCENT OF DISCHARGE WEIGHT FOLLOWING
REHYDRATION BY AGE GROUP AND VACCINE STATUS

WEIGHT CHANGE (% of Discharge weight)



PROCEEDINGS OF THE 9TH MEETING OF THE SCIENTIFIC
REVIEW AND TECHNICAL ADVISORY COMMITTEE OF
THE CHOLERA RESEARCH LABORATORY

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and

REPORTS OF THE COLLABORATIVE STUDIES BETWEEN CENTER
FOR MEDICAL RESEARCH AND CHOLERA RESEARCH
LABORATORY

For the
YEAR 1974

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