

of importance influencing it is the fly curve, which in its turn also depends largely upon the rains. Close aggregation necessitated by the rainy months and early cold season may also help as subsidiary factors in determining the period of maximum prevalence.

A considerable number of cases of long continuous fever, in certain aspects simulating enteric but differing from it in having slight leucocytosis, rapid pulse even from the very beginning and repeated negative Widal, come up for diagnosis towards the decline of the enteric season and during the lag period. There are reasons to suspect that some of these cases may be of typhus and in any event it is essential to work out their cause. Very recently it was decided to do the Weil-Felix reaction on all the Widal negative specimens to elucidate this point. The macroscopic procedure was adopted as in the Widal test, employing the OX19 and the OXK strains of *B. proteus* kindly supplied by Prof. Kingsbury of Kuala Lumpur. Alcoholic suspensions from plain agar prepared as described in *The System of Bacteriology* (Medical Research Council) was used as antigen. Formalized (0.2 per cent) broth cultures were also included in the test but they were found to be much less sensitive than the alcoholic suspensions. Out of 20 sera tested so far one gave positive reaction against OXK in 1 in 640 and another in 1 in 320. Although the results cannot be considered to have clarified the issue on account of the small number of cases investigated, they point to the necessity of further investigation in this field. It is hoped to pursue this work as opportunities arise. In this connection it is interesting to note that when the writer was taking blood for culture from a suspected enteric patient a tick was noticed hanging from the left side of the chest. It was found on examination to be a hard tick and as the significance of a tick-bite in the causation of typhus was little appreciated at that time, nothing further was done. The patient had a sharp rise of temperature from the beginning, the characteristic temperature pulse correlation of typhoid was absent, he had slight leucocytosis instead of leucopenia and an enlarged spleen but no rash. The blood culture was negative and the Widal also twice negative. The temperature touched normal on the nineteenth day and he had an uninterrupted convalescence. The association of a tick in this case may have been fortuitous and in the absence of further confirmatory findings it can only be taken at best to be a case of suspected typhus. But it was this observation that suggested later the possibility of the existence of some form of the non-epidemic type of typhus in Vizagapatam.

I take this opportunity to express my thanks to Dr. A. Neave Kingsbury of Kuala Lumpur for the strain of proteus and for the Annual Reports of that Institute and to Dr. C. Ramamurti, Professor of Bacteriology in the Medical College, for his valuable suggestions.

## VACCINE TREATMENT OF TYPHOID

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### Introduction

As early as 1913 the workers Frankell, Ichikawa and Thirolix issued reports upon the successful treatment of typhoid fever by the intravenous injection of typhoid bacilli vaccines. Recently, non-specific protein shock therapy has been tried with benefit in many acute and chronic infective conditions. The question of treating typhoid fever with injection of proteins and specific and non-specific vaccines has been taken up by many clinicians and observations and reports are published from time to time in the literature. Price, in the *Lancet* for December 1934, quotes the results of Uroiste of Montevideo and Stejskal of Vienna. These workers used carefully-standardized triple typhoid vaccine intravenously, to produce the shock. Triple vaccine, by virtue of its specificity, produces a more defined and uniform reaction than other foreign proteins or non-specific vaccines. Being impressed by the successful results obtained by the above workers, we have treated, since June 1935, almost every case of typhoid fever which has come to the Krishnarajendra Hospital with triple vaccine.

The advantages of this method of treatment are:—

1. That it aborts the disease before the patient reaches the stage where there is danger of perforation or hæmorrhage, and before there is marked loss of weight, vitality and strength.
2. That it prevents relapses and sequelæ.
3. That it enables a more liberal diet to be given even during the pyrexial stage.

It has been claimed that these ideal results can be obtained when the patient comes for treatment early, preferably in the first week, or at any rate not later than the second week. Our observations also confirm this statement.

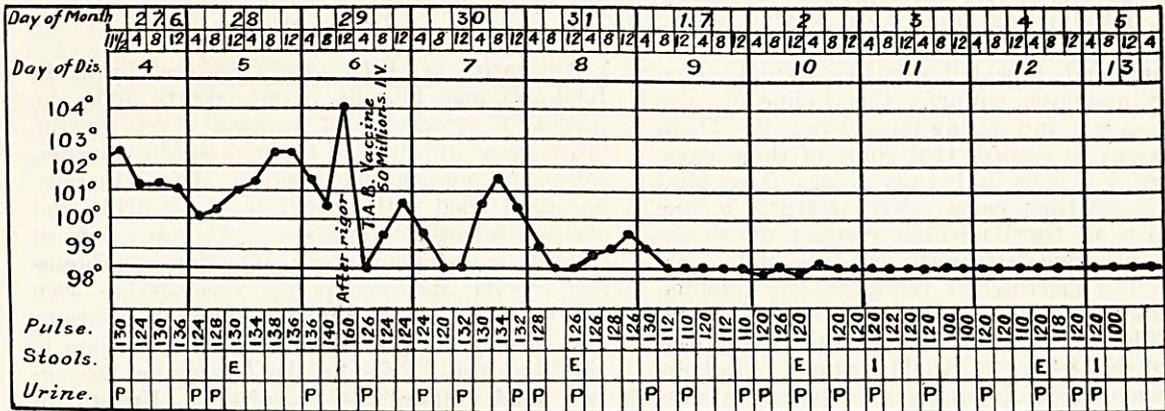
*Mode of administration.*—Administration of vaccine by the intravenous route is most effective in producing the required degree of shock. We have recorded as high as 84 per cent success in cases where intravenous triple vaccine was started in the first week of illness. On the other hand in late second week cases, when the patient is in a state of toxæmia with signs of toxic myocarditis, we hesitate to give triple vaccine intravenously for the obvious reason that the shock produced might be followed by unfavourable results. In such cases we prefer giving the vaccine intramuscularly; some respond well, others do not show much reaction. This explains the lower percentage of success in our series of second week cases. Thus triple

vaccine given intramuscularly has its own advantage and it is not too much to infer from our case reports that it prevents complications

patient and brings about a modification in the range of temperature, though it may not cut short the course of the fever in all cases.

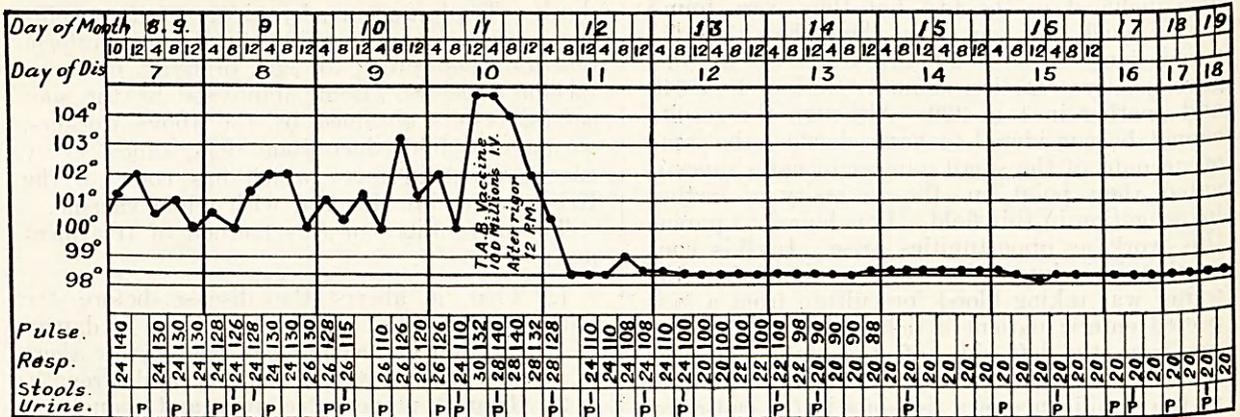
CASE NO 1.

Name... Venkata.Subba. Age... 6 years.



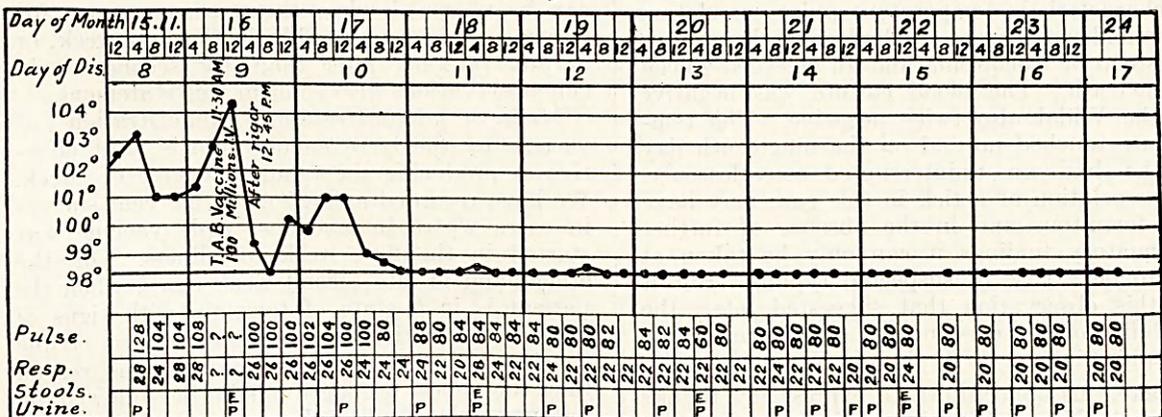
CASE NO 2.

Name... Agnes Mary. Age... 16 years.



CASE NO 3.

Name... Rukmini. Age... 14 years.



both early and late, clears the toxæmic condition quickly, improves the general condition of the

Dosage.—The average adult dose given in our series of cases varied from 50 to 100 million

organisms intravenously and 100 to 200 million organisms intramuscularly. Estimating that the potency of a given batch of vaccine had diminished, we gave 300 million organisms intramuscularly to two different cases without untoward effect though the temperature shot up to 106°F. The dose usually employed in children between eight and twelve years of age is 50 million organisms intravenously. The dose and the route of administration have to be determined in each case by taking into consideration the degree of toxæmia, the day of the disease, the condition of the myocardium, the temperature, the age and the general condition of the patient.

*Reaction.*—Typhoid vaccine injection is generally followed in about half an hour by a severe rigor which lasts for about twenty minutes to an hour, and it may be necessary to treat this condition by hot drinks, blankets, hot-water bottles, etc. As the chill subsides there is a definite rise of temperature which reaches its maximum in about two to four hours. This reaction temperature may vary from 102°F. to 104°F. In our series of cases 106°F. was the maximum temperature following the intravenous injection of 300 million organisms in the triple vaccine. Temperature elevation persists for twelve to twenty-four hours after which it usually drops abruptly, and is accompanied by profuse sweating. It should be remembered that the patient has to be carefully watched during this stage of reaction. Some observers have noticed a state of depression during this period; the temperature falling below normal, the volume of the pulse being reduced considerably and becoming rapid. Under such circumstances fifty cubic centimetres of a 50 per cent glucose solution given intravenously with 1/30th grain of strychnine are advocated to combat the collapse. In our series of fifty-five cases we have had no occasion to resort to this measure.

One striking feature that is observed in almost all cases treated with the triple typhoid vaccine is the remarkable change in the general appearance of the patient. Within twenty-four to forty-eight hours the patient has a clear face, cheerful look and bright eyes. The tongue becomes moist and clean, appetite returns, and above all the patient himself expresses a feeling of well-being and freshness. This is in marked contrast to an average typhoid patient, with dull eyes, heavy look, flushed cheeks, dry-coated tongue, headache and low muttering delirium.

#### Laboratory findings

(1) We find in cases so treated there is definite leucocytosis. According to Stejskal, this is a sign of good response and means an improvement in the condition of the patient.

(2) The blood and stool cultures become rapidly negative.

(3) The agglutination test becomes strongly positive if formerly negative, and stronger if it had been weakly positive.

(4) The anti-bodies appear much earlier and also are more active.

In this connection it seems probable that the danger of the spread of infection through carriers is also lessened.

This report is based on the observations of fifty-five cases treated with triple typhoid vaccine from June 1935 to December 1935. The diagnosis in all cases reported in this paper was confirmed by blood culture or Widal test, and in some instances by both, before commencing treatment. A few case reports, illustrating the typical reaction that follows intravenous or intramuscular triple typhoid vaccine, are appended.

*Case 1.*—A child, aged 6 years, was admitted on 27th July with a history of continuous fever for five days. Blood was sent on the 28th for culture and showed a positive growth of typhoid and paratyphoid A. Fifty million organisms of triple vaccine were given on the 29th. The temperature shot up to 104°F., then dropped to normal the same evening, but showed a little rise the next day. It returned to normal on the 31st of July and there was no further rise. The patient was discharged on the 12th day of the disease.

*Case 2.*—A female patient, aged 16 years, was admitted to the hospital on 8th September at 8 p.m. with a history of continuous fever for seven days. The blood was sent for a Widal test on the 10th September and found to be positive in all dilutions. One hundred million organisms of triple typhoid vaccine were given intravenously on the 11th at 11-30 a.m. This was followed by a rigor at 12 noon, the temperature reaching its maximum of 105°F. at 4 o'clock that afternoon. By 8 o'clock the next morning the temperature had dropped to normal and remained normal for the rest of her stay in the hospital.

*Case 3.*—A girl of 18 years was admitted to the hospital on 15th November with a history of continuous fever for eight days and a temperature ranging between 101°F. and 103°F. On the same day the blood was sent for a Widal test and was found to be positive in all dilutions. On 16th November, 100 million organisms of triple typhoid vaccine were given intravenously at 11-30 a.m. and at 11-45 she had a severe rigor, the temperature rising to 104°F. by 12 noon. It dropped to normal on the same night at 8 o'clock. The next day (the 17th) there was a slight rise to about 100°F., but the temperature returned to normal that evening, and there was no subsequent rise. The patient remarked the day after her injection, 'Thank you Doctor, I am all right now. When shall I go home?' Such a sense of well-being is rarely found in the usual run of patients ill with enteric fever in the second week of the disease!

From the above case reports it will be seen that within 36 hours of giving the vaccine treatment it was possible to declare these patients well on the way to recovery, as shown by the absence of temperature and rapid return to normal health. To complete the course of treatment it is advisable to give a second injection of the vaccine intravenously followed by one or two intramuscular doses at intervals of two or three days. When no definite leucocytosis results from the triple vaccine injections other proteins such as milk or omnadin are recommended.

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## SODIUM MANDELATE IN THE TREATMENT OF *BACILLUS COLI* INFECTION

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In Bengal, coliform infection frequently occurs after abortion in women. Ordinarily, *Bacillus coli* escape from the large intestine, their normal habitat, in diseases of the bowels in which the natural immunity is disturbed by removal of mucus and damage to the mucous membrane of the intestinal wall, by dysentery or diarrhoea, or by violent purgatives. The lymphoid tissues of the small intestines and lymphoid glands round the ileo-colic veins afford further protection against coliform infection. The urinary tract is specially liable to be

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Statistics of cases treated with triple typhoid vaccine from July to December 1935

Week	Number of cases treated	Number of cases which responded	Percentage of successful results
Early ..	7	6	84
First ..	14	10	70
Second ..	27	13	42
Third ..	7	All cases ran their usual course with no complication.	..

**Conclusion.**—The intravenous route in selected cases yields the best results. In the majority of our successful cases, one intravenous injection has been sufficient to bring down the temperature; rarely two were required. The earlier the case the better is the response to this mode of treatment. Even in the *mofussil*, where laboratory equipment is inadequate, this mode of treatment can be carried out as it is usually possible to diagnose a case as typhoid even before the second week by the clinical signs and symptoms alone, particularly when there is an epidemic, and with certainty if there is a case of continuous fever in a house in which there has already been a case of typhoid.

The vaccine employed was obtained from the Public Health Laboratory, Bangalore. We thank Dr. Natarajan, the Director, for his promptness in sending supplies. We also wish to express our thanks to Dr. J. F. Robinson, the medical officer of the Krishnarajendra Hospital, Mysore, for his help in the preparation of this paper. It was he who urged our adoption of the vaccine treatment and the administration of liberal diet in typhoid fever, based upon his successful experience of twenty years with this method.

attacked by *B. coli*, resulting in pyelitis or cystitis, if by any means the natural immunity of the intestinal walls is removed. The frequency of coliform infection after the puerperium, miscarriages and abortions may be due either to direct infection of the uterus through the vagina, or to urinary stasis on account of pressure of the gravid uterus on the urinary passages. Less frequently *B. coli* escapes into the blood stream from sensitized intestines, either directly or through the lymphatics, the gall-bladder and urinary bladder are then secondarily affected.

Cholecystic troubles are also more frequent in females than in males in this country and a large proportion of them are due to coliform infection. Interference with the drainage of the gall-bladder is an important factor in favouring its infection.

The habits and peculiar condition of women make them more liable to disorders of the bowels. Chronic constipation, visceroptosis, colitis and chronic diarrhoea remove the natural barrier to passage of *B. coli* from the large intestine to the interior of the body, as suggested by Besredka. The presence of a septic focus or septic foci in some part of the body is also a predisposing factor to coliform infection, hence a considerable number of cases give a history of some trouble such as chronic appendicitis, cholecystitis, or salpingitis.

**Diagnosis.**—In many cases more than one culture of urine is necessary to obtain positive results, and better results are obtained if the sample of urine is collected during the actual attack of rigor at the onset of fever.

**Treatment.**—The treatment of *B. coli* infection was formerly confined to strong alkalis and urinary and biliary antiseptics. Of the latter, various preparations, such as hexamine, hexylresorcinol, urotropine and pyridium, were largely employed, but the results were not always satisfactory. The alkalis are sometimes effective in reducing the temperature, but the effect is usually temporary. Any drug producing a strong acid reaction of the contents of the bladder hinders the growth of the organism. Acid sodium phosphate, which is usually given with hexamine in coliform infections, favours not only the production of the antiseptic formaldehyde in the system, but directly hinders the growth by increasing hydrogen-ion concentration of the urine. It was also found that to make hexylresorcinol effective the urine should not be made alkaline. The success of Helmholtz and Clark's ketogenic diet was attributed, however, to the special action of 1- $\beta$ -oxybutyric acid as well as the reduced pH value. The drawback of these treatments is that they take a long time to produce the desired results and frequently are ineffective.

The introduction of mandelic acid in the treatment of coliform infection of the urinary tract has been a great advance as no more than