Initials.	Vaccine.		Limits of Agglutination.												
			Weeks after First Agglutination.												
			1	2	3	4	5	6	7	8	9	11	13	15	
D. ...	Mixed, dead ...	<i>B. typhosus</i> ...	o	1/400	1/200	1/200	1/300	1/80	1/80	1/80	1/60	1/40	1/20	1/20	
		<i>B. paratyphosus</i> A ...	o	1/60	1/60	1/60	1/100	1/60	1/80	1/60	1/60	1/60	1/20	1/20	
		<i>B. paratyphosus</i> B ...	o	1/20	1/40	1/20	1/60	1/20	1/20	1/20	1/20	1/20	1/20	1/20	
F. ...	Mixed, dead ...	<i>B. typhosus</i> ...	o	1/300	1/200	1/200	1/300	1/300	1/100	1/80	1/80	1/40	1/20	1/20	
		<i>B. paratyphosus</i> A ...	o	1/60	1/60	1/40	1/60	1/80	1/80	1/80	1/80	1/40	1/20	1/20	
		<i>B. paratyphosus</i> B ...	o	1/40	1/60	1/60	1/60	1/80	1/40	1/40	1/40	1/20	1/20	1/40	
P. ...	Typhoid, dead ...	<i>B. typhosus</i> ...	1/20	1/500	1/500	1/200	1/300	1/150	1/150	1/150	1/150	1/60	1/20	o	
		<i>B. paratyphosus</i> A ...	o	o	o	o	o	o	o	o	o	o	o	o	
		<i>B. paratyphosus</i> B ...	o	o	o	o	o	o	o	o	o	o	o	o	
S. ...	Paratyphoid A, dead ...	<i>B. typhosus</i> ...	1/20	1/80	1/20	1/40	1/60	1/80	1/60	1/60	1/40	1/40	1/20	o	
		<i>B. paratyphosus</i> A ...	o	o	o	o	o	o	o	o	o	o	o	o	
		<i>B. paratyphosus</i> B ...	o	o	o	o	o	o	o	o	o	o	o	o	
A. ...	Paratyphoid B, dead ...	<i>B. typhosus</i> ...	o	o	o	o	o	o	o	o	o	o	o	o	
		<i>B. paratyphosus</i> A ...	o	o	o	o	o	o	o	o	o	o	o	o	
		<i>B. paratyphosus</i> B ...	o	1/80	1/60	1/60	1/80	1/60	1/20	1/20	1/20	1/20	o	1/20	
A. E. de S.	Mixed, live ...	<i>B. typhosus</i> ...	1/20	1/300	1/500	1/200	1/200	1/100	1/100	1/80	1/60	1/20	1/20	o	
		<i>B. paratyphosus</i> A ...	o	1/40	1/40	1/20	1/40	1/20	1/20	1/20	1/20	1/20	o	o	
		<i>B. paratyphosus</i> B ...	o	1/40	1/40	1/20	1/40	1/20	o	o	o	o	o	o	
D. G.	Mixed, live ...	<i>B. typhosus</i> ...	o	1/500	1/300	1/200	1/200	1/100	—	—	—	—	1/60	1/20	
		<i>B. paratyphosus</i> A ...	o	1/60	1/40	1/40	1/40	1/40	—	—	—	—	1/40	1/20	
		<i>B. paratyphosus</i> B ...	o	1/20	1/60	1/60	1/60	1/20	—	—	—	—	1/40	1/20	
I. ...	Typhoid, live ...	<i>B. typhosus</i> ...	o	1/400	1/300	1/300	1/300	1/300	1/300	1/200	1/200	1/300	1/100	1/80	
		<i>B. paratyphosus</i> A ...	o	o	o	o	o	o	o	o	o	o	o	o	
		<i>B. paratyphosus</i> B ...	o	o	o	o	o	o	o	o	o	o	o	o	
W. ...	Paratyphoid A live ...	<i>B. typhosus</i> ...	o	o	o	o	o	o	o	o	o	o	o	o	
		<i>B. paratyphosus</i> A ...	o	1/100	1/80	1/60	1/60	1/80	1/80	1/60	1/60	1/60	1/60	1/60	
		<i>B. paratyphosus</i> B ...	o	o	o	o	o	o	o	o	o	o	o	1/60	
K. ...	Paratyphoid B, live ...	<i>B. typhosus</i> ...	o	o	o	o	o	o	o	o	o	o	o	—	
		<i>B. paratyphosus</i> A ...	o	o	o	o	o	o	o	o	o	o	o	—	
		<i>B. paratyphosus</i> B ...	o	1/20	1/80	1/80	1/60	1/20	1/20	1/20	o	o	o	—	

One native, I., was inoculated with 0.6 c.cm. live (attenuated) typhoid vaccine, and with 1.2 c.cm. after a week.

One native, K., was inoculated with 0.6 c.cm. live (attenuated) paratyphoid B vaccine, and with 1.2 c.cm. after a week.

All the inoculated persons were healthy young natives who volunteered for the experiment. They were inoculated on the same days, the first inoculation taking place on June 14th, 1913, and the second on June 21st. The blood of all the inoculated persons was investigated for the presence of agglutinins regularly once a week, and the results are collected in the accompanying table, for the compilation of which I am indebted to Mr. Burgess.

From the table it will be seen that the agglutinins seldom appear before the seventh day, and that individuals inoculated with a mixed typhoid+paratyphoid A+paratyphoid B vaccine produced agglutinins for all three germs, and that on the average the amount of agglutinins produced for each germ was not much smaller than in individuals inoculated with one germ only, although the latter had a much larger dose of the germ. As regards the length of time during which the agglutinins were present in the inoculated individuals, the results did not differ much; if anything, they were rather in favour of the mixed vaccines. Although, of course, one cannot gauge the actual immunization obtained by simply studying the agglutination, there can be no doubt that to a certain extent agglutination is a rough index for immunization.

It seems to me that these results are decidedly in favour of the advisability of using a mixed typhoid+paratyphoid A+paratyphoid B vaccine in countries where all three diseases are met with.

Conclusions.

1. The use of the mixed typhoid + paratyphoid A + paratyphoid B vaccine, either the dead or the "live" (attenuated) one, is harmless. As there is such a general objection to the use of live vaccines, I now recommend for routine use the mixed dead vaccine, which consists of an emulsion of typhoid and paratyphoid A and B bacilli, killed by heat (53° C.) and standardized, so that 1 c.cm. contains approximately 500 million typhoid bacilli and 250 million each of paratyphoid A and B.

2. The inoculation of such vaccine to human beings in the doses mentioned in this paper—namely, 0.6 c.cm. or

about 10 minims, the first time, and 1.2 c.cm., or about 20 minims, the second—induces a production of agglutinins for all three germs: *B. typhosus*, *B. paratyphosus* A, and *B. paratyphosus* B. The amount of agglutinins elaborated for each germ seems to be practically the same as in individuals respectively inoculated with typhoid vaccine only, paratyphoid B vaccine only, paratyphoid A vaccine only.

3. In countries where, besides typhoid, there occur paratyphoid A and paratyphoid B, a mixed vaccine should, in my opinion, be used instead of the simple typhoid vaccine. This has been done in Ceylon for the last five years with good results.

I desire to express my indebtedness to Mr. Burgess Assistant Bacteriologist, for the very valuable assistance rendered.

REFERENCES.

¹ Notes on the subject of mixed vaccines may be found in my earlier publications in the *Centr. für Bakteriologie* (1909) and in the *Transactions of the Bombay Medical Congress* (1909), in the *Ceylon Medical Reports*, and in various recent publications. ² *Zeit. für Hygiene*, 1902.

TYPHOID CHOLECYSTITIS.

BY

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It has been known for a long time that the gall bladder is a common focus of infection in so-called typhoid carriers, and the presence of the *B. typhosus* has been demonstrated in this viscous seventeen years after exposure to typhoid infection. It has also been shown that the *B. typhosus* is found in the gall bladder in many cases of gall stone. In a large proportion of cases in which death has occurred from typhoid fever the organism has been found in bile taken from the gall bladder. During epidemics of typhoid fever, so-called "relapses," with abdominal symptoms and prolonged illness, have been shown to be due to infection of the gall bladder by this organism. Even in patients who are not known to be suffering from typhoid but are under observation for some other ailment, the correct diagnosis may only be made by the discovery of a positive Widal's reaction. The symptoms do not always refer to the gall bladder, but careful examination will not often

fail to discover cholecystitis. The chief symptoms are a feeling of malaise and sickness, with a slight evening rise of temperature (99.5° to 101°), and occasional attacks of pain accompanied by rigidity of the abdominal muscles, not always localized to any special area in the abdomen. These attacks, if severe, recur with regularity every third or fourth day, are accompanied by vomiting and rise in temperature, and are followed as the temperature subsides by heavy night sweats. If during the attack or after the acute pain has passed away muscular rigidity is not pronounced, the gall bladder, sensitive to touch and more or less distended, can be felt. During the late South African war I saw many cases of obscure abdominal disease in men who had been exposed, as most of us were, to typhoid infection, in whom there was no suspicion of typhoid, but who presented symptoms such as these, and whose cases were diagnosed as appendicitis, renal calculus, gall stones, perforation of the intestine, etc. The following is an example:

CASE I.

During the height of the enteric epidemic among the troops in and around Bloemfontein an officer, aged 36, came under my care suffering from dysentery. He recovered slowly from this, and at the end of six weeks returned to duty, but never regained his full vigour and health. He again came under my care six months later, complaining of recurrent attacks of severe pain in the right hypochondrium. These came on every third or fourth day, were ushered in by a rigor and sickness, and the temperature rose to 102° to 103° . There was never jaundice. During each attack the gall bladder was very tender and could be distinctly felt. As the attack subsided the gall bladder became less evident, and profuse night sweats occurred. The blood gave a positive Widal's reaction. Under treatment the attacks of pain became less frequent and less severe, and after an illness of three months the patient was invalided home. His subsequent history is interesting. For two years he had attacks of a similar nature, but recurring at longer intervals and not so severe, but it was not until four years had elapsed that examination of the blood proved negative and that he became entirely free from his old symptoms.

I have recently seen two cases of a similar nature. They were of a less severe type, and occurred in patients one of whom was convalescing from typhoid fever, whilst the other, although exposed to infection, had shown no symptoms of the disease.

CASE II.

A. B., aged 19, seen with Dr. Muir, of Horden, was recovering from a mild attack of typhoid fever, but at the end of six weeks was still complaining of great weakness, night sweats, want of appetite, and the night temperature was about 100.5° . Nothing abnormal could be detected in the chest, the bowels were regular, and the urine healthy. On palpating the abdomen, as soon as my hand was passed into the right hypochondrium he winced and complained of tenderness. The fundus of the gall bladder could be felt and was sensitive to touch. A diagnosis of typhoid cholecystitis was made, and the treatment suggested was large quantities of liquid and 15 grain doses of sodium salicylate every four hours. The patient rapidly recovered and was able to return to work in the pit at the end of six weeks. He has remained well since.

CASE III.

This patient, seen in consultation on January 12th, 1912, was a woman aged 26, who had been confined six weeks previously of her second child. Labour was easy, but at the end of six weeks she was still confined to bed with malaise, night sweats, and occasional twinges of pain in "the pit of the stomach." The evening temperature varied between 99° and 100° . Three months previously she had been nursing a relative suffering from typhoid fever. Examination of the chest revealed nothing abnormal; the abdomen was flaccid and readily palpable until my hand was passed into the right hypochondrium, when on deep pressure she winced and exclaimed, "That's it." The fundus of the gall bladder could easily be felt, and this was the tender spot. Examination of the blood showed a positive Widal's reaction. The treatment adopted was similar to that in the previous case, and under it she rapidly improved till, at the end of a month, she was quite recovered, and has since continued to be in good health.

The next case I have to record is even more interesting. In it no history of exposure to typhoid infection could be elicited, but the symptoms were more severe and localized to the abdomen.

CASE IV.

E. G., aged 20, was suddenly seized while in bed on October 28th, 1911, with very severe pain in the right side. Except for occasional headaches, she had been in her usual health prior to this date. She vomited, but this brought no relief. A doctor diagnosed appendicitis and sent her into Monkwearmouth Hospital. The attack gradually passed off, but returned with similar symptoms, and as severely, in a few days. The temperature was above normal after each attack. During the

paroxysms of pain vomiting was frequent, and the whole abdomen was rigid and tender. On November 9th Dr. Bruce found a positive Widal's reaction present, and sent her as a case of typhoid fever to the Borough Sanatorium next day. On admission the temperature was 93.6° F., and the pulse 98. On the evening of November 11th she was again seized with pain, and the temperature rose to 99.6° , and the pulse was 90. On November 14th a more severe attack occurred; she vomited profusely, and the abdomen was then very tender and rigid all over; the temperature was 100.6° , and the pulse 120. This attack lasted for two days; the pain then gradually subsided, the symptoms disappeared, and she was able to take a little nourishment. On the morning of November 18th another attack came on, the most severe she had had, and Dr. Renney asked me to see her. I found her in great pain, vomiting everything taken, temperature 99.4° F., pulse 116. Her abdomen was so tender and hard that nothing could be felt, but she had not the very ill appearance of a case of peritonitis (due to perforation). She was removed the same day to the Royal Infirmary, and after poulticing the abdomen and administering hot saline enemata the pain gradually subsided, and on November 19th she was able to retain a little liquid nourishment. At 4 a.m. on November 21st I was sent for to operate. She was vomiting everything, the temperature was 101.4° F., the pulse 120, and the abdomen again rigid. Next day she had again recovered, and as the abdominal muscles were now flaccid my first opportunity of examining her satisfactorily came. As soon as her right side was palpated the muscles became rigid, but on deep pressure the fundus of the gall bladder could be felt very tender and distended. After this attack she was slightly jaundiced and bile appeared in the urine. She was treated with an effervescent mixture containing sodium salicylate. A much slighter attack came on on the evening of November 24th, sickness returned, the temperature was 99° F., and the pulse 120, but the symptoms rapidly passed off, and no further attack occurred. She was discharged from the infirmary on December 11th, and her doctor informs me she has since remained quite well.

These cases are of interest because I hope they will draw attention to a source of infection and a course of illness not generally recognized.

It is now generally believed that the cause of gall stones is an infective inflammation of the mucous lining of the gall bladder with the production of cholesterolin and that without a previous cholecystitis no cholelithiasis occurs. Also that organisms frequently form the nucleus of gall stones and when the inflammation of the gall bladder has subsided, the gall stones may remain quiescent unless some fresh infection occurs which lights up inflammation again. A tender and sensitive condition of the mucosa results and this causes expulsive efforts on the part of the muscular coats with painful spasms.

It is not so generally known that inflammation of the gall bladder without stones may produce the same symptoms and signs. It is important to bear in mind, as Case iv proves, that there may be no history of typhoid fever, no record of any exposure to infection, and yet typhoid cholecystitis may be the cause of a serious illness. It is also important to remember that the illness may be not only a source of danger to the patient, but that as typhoid carriers these people may be a menace to the community for several years. Unfortunately in many of them a definite clinical diagnosis cannot be arrived at, because Widal's reaction may be negative, and the cause of the cholecystitis can only be cleared up by operation and subsequent bacteriological examination. The condition has been diagnosed as gall stones, but on opening the gall bladder none are found, only an inflamed mucosa. Simple drainage (cholecystostomy) does not always cure; after it the symptoms subside for a time, but the drainage wound closes, attacks recur, and the only effectual cure may be removal of the gall bladder.

Puncture of the distended gall bladder with an exploring needle in these cases is a risky procedure. After the needle has been withdrawn leakage from the viscus may occur; and I can recall an instance of a patient who nearly died in my consulting-room of shock from this cause.

Medical treatment is simple, efficacious, and as a rule I have found it to act speedily. Large doses of sodium salicylate (15 to 30 grains) in an effervescent mixture until its physiological effect is produced, and abundant drinks, quickly cause disappearance of the symptoms, and recurrence is rare. The drug should be continued in smaller doses for a month after convalescence seems to be assured.

THE Congress of the United States has under consideration a bill providing for the allocation of a sum of £60,000 for the building of a Government hospital at Spartanburg for the treatment of pellagra.