If adopted, the operative technique devised by Carrel appears to offer the best chance of success. In old-standing cases of traumatic arterio-venous aneurysms, or aneurysmal varices Matas's arteriorrhaphy or the Matas-Bickham operation may be adopted.

A consideration of the wounds of arteries by bullets of small calibre and their treatment shows that progress in this branch of military surgery has taken the direction of increased conservatism and expectancy. In this it is no exception to that observed in every other chapter of the subject. Non-interference in fractures has become almost the general rule, operations on joints have decreased in number almost to a vanishing point, injuries to the nerves are seldom the subjects of primary treatment, and we have seen that those of the vessels come into the same category. Still more striking is the expectant attitude maintained by the surgeon in the case of wounds traversing the great body cavities, in all of which primary operations have become progressively fewer.

REFERENCES.

- ¹Mühsam, *Centralbl. f. Chir.*, 1913, No. 28 Beilage, p. 104; 45 thoracic, 13 contour; 22 skull, majority contour. ²Frisch, *Centralbl. f. Chir.*, 1913, No. 28, Beil. 107. ³Kikuzi, *Beitr. z. klin. Chir.*, Bd. 1, p. 21. ⁴Report on the Surgical Cases noted in the South African War, 1899-1902, 1905. ⁵*Deutsche Zeitschr. f. Chir.*, Band 85, 1906, p. 577. ⁶Loc. cit. ⁷Brentano, *Arch. f. klin. Chir.*, vol. lxxx, 1906, p. 395. ⁸*Surq. Exp. in S. Africa*, p. 117. ⁹*Lancet*, vol. ii, 1913, p. 1248. ¹⁰A. Kohler, *Arch. f. klin. Chir.*, vol. i, p. 333, 1906. ¹¹*Beiträge zur klin. Chir.*, Bd. 1, 1906, p. 1. ¹²Saigo, *Deutsche Zeitschr. f. Chir.*, vol. 85, 1906, p. 577. ¹³*Arch. f. klin. Chir.*, Bd. 77, p. 590, 1905. ¹⁴*Deutsche Zeitschr. f. Chir.*, Bd. 123, 1911, p. 1. ¹⁵*Arch. f. klin. Chir.*, Bd. 79, p. 515. ¹⁶Von Mantouffell, *Arch. f. klin. Chir.*, Bd. 81, p. 1.

TYPHOID-PARATYPHOID VACCINATION WITH MIXED VACCINES.

By ALDO CASTELLANI, M.D.,

DIRECTOR, GOVERNMENT CLINIC FOR TROPICAL DISEASES, COLOMBO, CEYLON.

CONSIDERING the fairly frequent occurrence of paratyphoid A and paratyphoid B in tropical regions, at least in Ceylon and India, I have for several years advocated the use of a mixed vaccine, namely, typhoid + paratyphoid A + paratyphoid B, instead of the usual simple typhoid vaccine.¹

My belief in the possibility of producing an efficient mixed vaccine was based on the experiments I carried out in Bonn, working under Professor Kruse during 1901 and 1902. I demonstrated then² that by inoculating an animal with two different bacteria at the same time, the blood produced agglutinins and immune bodies for both, and that provided a sufficient minimum quantity had been inoculated, the amount of agglutinins and immune bodies for each germ was about the same as in the animals inoculated with one germ only. I demonstrated that even inoculating a rabbit with three different micro-organisms (*B. typhosus* + *B. pseudo-dysentericus*, No. 1 (Kruse) + strain of *B. coli communis*), the amount of agglutinins and protective bodies elaborated for each germ was nearly the same as in animals respectively inoculated with one germ only. During the course of these experiments I was able to confirm the fact that when the immunization is obtained by a single inoculation, provided the minimum dose sufficient to obtain the maximum immunization be given, the amount of agglutinins and immune bodies elaborated by the inoculated animals is not in proportion to the amount of cultures injected. A series of rabbits inoculated with 2 c.cm. of typhoid cultures will give the same average agglutination limit and the same amount of immune bodies as a series of rabbits inoculated with 4 c.cm.

Since 1905 I have experimented with several mixed vaccines in man, of which the principal are (1) a typhoid + paratyphoid A + paratyphoid B vaccine, and (2) a typhoid + dysentery (Kruse-Shiga) + dysentery (Flexner) vaccine. I will limit my remarks to (1), but I may be allowed to note that anyone wishing to experiment with mixed dysentery vaccines should be careful always to use peptone-water cultures, as broth cultures of dysentery give rise to an extremely painful infiltration at the point of inoculation.

Method of Preparation of the Mixed Typhoid-Paratyphoid Vaccine.

The mixed vaccines as prepared by me are either dead vaccines, the cultures being killed in the usual way by

heating at 53° C., or live attenuated vaccines got by heating the cultures at 50° C., for an hour. During recent years I have used rather extensively both the dead mixed vaccine and the live attenuated one.

At first I used to prepare the vaccine in the following manner: Several tubes containing 10 c.cm. of broth each were inoculated with two loopfuls of an agar culture of typhoid forty-eight hours old, other tubes with two loopfuls of paratyphoid B, and others with two loopfuls of paratyphoid A. All the strains I used were non-virulent but rich in antigen, as shown by animal experiments. The inoculated tubes were kept for twenty-four hours in the incubator at 35° C. These cultures were then heated in a water bath at 55° C. (dead vaccine) or 50° C. (live attenuated vaccine) for an hour; they were then mixed together in certain proportions in sterile Petri dishes—two tubes (20 c.cm.) of typhoid, one tube (10 c.cm.) of paratyphoid B, and one tube (10 c.cm.) of paratyphoid A. The mixed vaccine consisted, then, of two parts typhoid, one part paratyphoid A, and one part paratyphoid B. I used to give 10 minims of the mixed vaccine at the first inoculation, and 20 or more at the second and third. At the present time the vaccine is standardized by counting the germs before mixing. The mixed vaccine I use at the present time contains per cubic centimetre 500 million typhoid, 250 million paratyphoid B, and 250 million paratyphoid A, and is prepared either from broth cultures or emulsions in physiological salt solution. A little lysol (0.2 per cent.) is added.

Dose and Method of Vaccination.

As already stated, the mixed vaccine I now use—either the dead one obtained by heating cultures at 53° C. or the attenuated live one prepared by heating cultures at 50° C. for an hour—contains per cubic centimetre 500 million typhoid, 250 million paratyphoid A, and 250 million paratyphoid B. I give 0.6 c.cm. the first time, and double the dose a week later, and, whenever possible, a third dose two weeks from the first. In some cases, however, I give only ½ c.cm. the first time, and 1 c.cm. the second. Very thin, delicate individuals and young women receive a little less. Children between 8 and 15 get a quarter to half the adult dose. The inoculation of the mixed vaccine is followed by a local and general reaction which, as a rule, is not distinctly severer than after the inoculation of simple typhoid vaccine. Three or four hours after inoculation the region on the arm where the injection has been made becomes painful and red, and fever may supervene, which does not last longer, as a rule, than twenty-four to thirty-six hours, and does not in most cases incapacitate one for work.

As I do not believe that the immunization given by bacterial inoculation lasts in man very long, I generally advise people to be vaccinated once every two years, or even once a year.

Innocuity of the Mixed Typhoid-Paratyphoid Vaccine.

The mixed vaccine, either the dead one or the attenuated live one, is innocuous, as proved by several thousand inoculations done to date in Ceylon. Professor Browning, the Director of the Ceylon Government Chemical Institute, has to date received 35 inoculations of mixed live vaccine at one or two weeks' intervals, in addition to 29 inoculations of simple typhoid live vaccine. He has always remained in very good health.

Remarks on the Immunization Obtained in Man by the Mixed Vaccine.

Lack of time prevented my studying the amount of all protective substances produced in inoculated individuals; the investigation, therefore, has been limited to studying comparatively the amount of agglutinins produced in some individuals inoculated with mixed and simple vaccines.

Two natives, D. and F., were inoculated with mixed (dead) vaccine, 0.6 c.cm. the first time; 1.2 c.cm. after a week.

One native, P., was inoculated with simple typhoid vaccine (dead), 0.6 c.cm. the first time; 1.2 c.cm. after a week.

One native, S., was inoculated with simple paratyphoid A vaccine (dead), 0.6 c.cm. the first time; 1.2 c.cm. after a week.

One native, A., was inoculated with simple paratyphoid B vaccine (dead), 0.6 c.cm. the first time; 1.2 c.cm. after a week.

Two natives, A. E. de S. and D. G., were inoculated with 0.6 c.cm. mixed live (attenuated) vaccine, and with 1.2 c.cm. after a week.

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

ALBERT E. MORISON, F.R.C.S. EDIN.,
SUNDERLAND.

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