choroidal degeneration which seemed of doubtful traumatic origin. These have remained constant since the patient came under observation.

Left Eye.—Pupil circular, 3 mm. in diameter, larger than right. Reaction to accommodation and convergence sluggish, but doubtful to light. At the outer margin and slightly above horizontal meridian the iris is detached from its ciliary border for 2 mm., and shows an identical semilunar-shaped opening to the right eye. Optic disc somewhat paler than normal, with ill-defined margins. Surrounding retina shows some effusion. Red reflex present through openings in both irides, but equator of lens not visible.

He was not conscious of any increased illumination through the secondary pupils. There was no evidence of any hyphaemia when he came under observation. X-ray examination and Wassermann reaction gave negative results.

The fields were markedly contracted, especially for red and green.

The diplopia was not constant, and could not be elicited in examination by the ordinary methods. He stated that it was present at times when lying down in bed and described the one image as being lower than the other. Beyond this it was difficult to obtain information which could be considered reliable, but the evidence pointed to the eccentric pupil accounting for the condition.

The amblyopia, seemingly due to commotio retinae and functional disturbance, improved with rest and treatment, his general condition benefited, and his view of life became considerably more cheerful and intelligent.

Vision now: R. = $\frac{1}{2}$ c. disc $\frac{1}{2}$. L. = $\frac{1}{2}$ c. disc $\frac{1}{2}$.

The fields were taken on admission and twice since, and show no material improvement. This corresponds with Lister's observations on similar cases.

Monocular diplopia can now be elicited in both eyes, but it does not inconvenience him.

I cannot discover any recorded case of a similar binocular condition of the irides, traumatic or congenital. Parsons states that multiple dialyses occur, but presumably means of the same eye. Fuchs states that "he never saw them as a result of injury."

The peripheral zone of the iris adjacent to its ciliary attachment where it lacks the support of the lens behind, and is backed only by the zonule of Zinn, is admittedly the weakest, and the usual situation of these injuries.

The detachment in the left upper angle of each eye would be explained by a blow from the left and above. The head was probably held down in the act of running forward, or automatically ducked on hearing the scream of the shell, as in the case of bullets whistling above.

In the absence of other injuries

to the eyeballs the detachments were most probably due to sharp impacts through the upper lids, from lumps of mud and clay from the left front. This explanation would readily fit in with Arlt's explanation of the condition, which says: "The cornea being momentarily flattened, the circle described by the corneo-scleral border and the ciliary body, with which it is firmly united, is extended, whilst the sphincter iridis is contracted, the serrated connexion of the iris with the ciliary body is torn to a greater or less extent, and a second communication is formed between the anterior and posterior chambers."

I am indebted to Mr. Stroud Hosford for his opinion on the case, and the kind use of one of his beds.

Chart 1.—Fields: w, White; r, Red; g, Green. Size of object 5 mm. (June 14th, 1915.)

THE PROPHYLAXIS OF TETANUS:

A SUMMARY.

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IN the BRITISH MEDICAL JOURNAL, October 10th, 1914, a short and necessarily incomplete account of the use of tetanus antitoxin was given.

Since then many cases of tetanus have occurred, and many papers have been written on the subject, and a consideration of them should show us where our knowledge has made progress, and where it has been found wanting.

Owing, doubtless, to the exigencies of the times in which we are living, the writers, while expressing definite opinions, have given usually incomplete details of the results upon which their conclusions were based. This want of precision has tended to confusion, and has prevented in many instances the separation of those wounded who had a prophylactic injection of serum from those who had none. The value of the communications is thereby lessened, but in spite of this it is hoped that this further summary of the literature on the prophylaxis of tetanus may prove of interest and of use to those whose duties have not allowed them much time for reading during the past year.

PROPHYLAXIS.

In the *Memorandum on the Treatment of Wounds in War* (July, 1915) there are the following statements:

The prophylactic use of tetanus antitoxin is a proceeding of well established value.

Since, in the first two months of the war, more cases of tetanus occurred than had been anticipated either by ourselves or our Allies, it was decided to direct that a preventive dose of

serum should be given to every wounded man. The results have been excellent, and in the last six months there have been only 36 cases of the disease among those who received a preventive dose of serum within twenty-four hours of being wounded.

The preventive dose of 500 U.S.A. units should be given subcutaneously at a distance from the wound at the earliest possible moment. In severe wounds medical officers not infrequently give 1,500 units; there is no objection to this, but at the same time there is no evidence that the smaller dose is insufficient if given promptly.

Such has been the experience of the British army. Do the reports from other countries confirm it? Walther (1914) records that the action of prophylactic injections has been clear, although they could not in some cases be made until five to eight days after the wound. All the wounded in three wards and ten seriously wounded in another ward received each 10 c.cm. of antitetanic serum. Only one case had tetanus, and this came on the day after the injection—that is, before the serum could have produced its full effect. All the other cases of tetanus were observed among the wounded of three other wards in which prophylactic injections could not be given.

Hartmann (1914) at Besançon and Bourg met with 43 cases of tetanus among 3,373 wounded, and states that at neither of these places did a case occur among the men who had received an injection of antitoxin. He is of opinion that if a prophylactic dose of serum were given in all cases and repeated six to seven days later in anfractuous wounds tetanus would disappear as a complication of wounds.

Hufnagel (1914) reports that among 2,193 cases received into a hospital at Namur between September 11th and November 30th, 1914, there were 27 cases of tetanus. After October 15th every case had a prophylactic injection of 20 (Behring) units = 800 U.S.A. units, and among the

1,195 men admitted after that date (presumably October 15th) there was not a single case of tetanus, though many were severely wounded.

Madelung (1914), speaking of Strassburg where up to October 31st, 1914, there were 15,134 wounded with 101 deaths from tetanus, mentions that no case of tetanus occurred in those who were injected prophylactically before admission into hospital, but that tetanus occurred in some cases though they were received shortly after being wounded and on admission had a prophylactic injection of serum.

Bazy (1915) relates that 200 wounded had to be divided into two lots—each 100 containing cases of about the same degree of severity. The one half had prophylactic injections of serum, and among them there occurred one case of tetanus which developed the day after the injection. Among the other 100 who had no serum, there were 18 cases of tetanus. There were 10,896 wounded with 129 cases of tetanus, of whom 70 per cent. died. One case was admitted into hospital on October 8th, 1914, and had serum the same day. Tetanus began on December 12th and ended fatally on December 18th.

Gasch (1915) describes the usual routine treatment of the hospital with which he was connected as consisting of a prophylactic injection of 20 Behring units in every case of dirty wounds, thorough opening up of the wound and keeping it open. After this treatment there was not a case of tetanus among 700 cases. One case, among a series of 65, was not injected because of the apparent innocency of a wound of the great toe. He developed tetanus and died.

According to Nivière (1915), 14,100 soldiers were admitted into the nineteen hospitals in Vichy between August 17th, 1914, and November 16th, 1914. There were 61 cases of tetanus, and none of them had had a prophylactic injection of serum.

Heile (1915), when reporting his experience of 12 cases of tetanus, mentions that there was no case of tetanus among the wounded who had had a preventive injection. Five severely wounded soldiers were admitted from the same field of battle, and four of them had a prophylactic dose. The fifth man did not seem to be so badly wounded as the others, and so the serum was not given. In his case tetanus appeared on the seventh day, and ended fatally. Ritter (1915) had no more cases of tetanus after prophylaxis with serum was instituted.

Teutschländer (1915) mentions that tetanus bacilli were cultivated from the secretions of the wounds of three soldiers, each of whom had had a prophylactic dose of serum. Except that one man had a slight transient, painless contraction of the sole of the wounded foot, there were no symptoms or signs of tetanus at any time. Notwithstanding vigorous local disinfection, tetanus bacilli, virulent for mice, were cultivated from the wounds several weeks later.

From September 23rd to October 1st, 1914, Goldscheider (1915) had 14 cases of tetanus (one or two a day). Then 500 wounded were admitted in three days and each of them received 20 (Behring) units (= 800 U.S.A. units). Among these there were 4 cases of tetanus, each of whom either showed premonitory signs of the disease when injected or developed it within forty-eight hours. One died of sepsis, one died from the severity of a wound of the lung, and the other two were mild cases. No other case of tetanus occurred, and up to November 5th 1,427 wounded were admitted.

Now Hinterstoisser states (1915) that in the Franco-Prussian war there were, among 95,000 German wounded, 350 cases of tetanus = 0.36 per cent., and F. Stricker (1914) that in the battles of Colomby, Mars la Tour, and Gravelotte, with 29,340 wounded, there were 62 (= 0.21 per cent.) cases of tetanus, and in the battle of Spichern among 3,482 wounded there occurred 20 (= 0.57 per cent.) cases of tetanus.

How does this compare with the incidence in the present war?

If we put together the figures given in the various papers, we get an approximate idea of the percentage of wounded soldiers who have developed tetanus. It is only approximate, as it is impossible to ascertain exactly how much, if any, overlapping there is. It must also be remembered that some of the wounded had received a prophylactic injection.

Percentage of Wounded Developing Tetanus.

	No. of Wounded.	Cases of Tetanus.	Percentage.
Bazy	10,896	129	1.18
Walther	456	20	4.30
Hartmann	3,373	43	1.30
Gasch	700	1	0.14
Hufnagel	2,193	27	1.23
Schoute	242	3	1.20
Nivière	14,100	61	0.43
Goldscheider	1,427	4	0.28
Madelung	15,134	101*	0.66
Hinterstoisser	800	13	1.60
L. Simon	700	8	1.14
Joly	1,798	21	1.60
Siemon (German	1,500	26	1.74
Siemon (French	600	2	0.33
Forestier	74	5	6.75
Arzt	26,600	65	0.24
Eunicke	3,000	10	0.33
	83,593	539	0.65

* Deaths.

Hinterstoisser (loc. cit.) also mentions that on the western front during two months of 1914 there occurred among 27,677 German wounded (Madelung's 15,134 may possibly be included in these figures) 174 cases of tetanus = 0.62 per cent. He quotes further:

	Number Wounded.	Cases of Tetanus.
Crimean war	12,094 (English) ...	19 = 0.15%*
American Civil War	217,000 ...	505 = 0.2%
Russo-Turkish War..	51,700 (Russian) ...	66 = 0.12%

We thus see that the incidence of tetanus in the present war has been greater than would have been anticipated from previous experience.

The figures available with regard to the wounded who received prophylactic injections are very small.

Wounded who received Prophylactic Injections.

	No. of Injected.	Cases of Tetanus.	Percentage.
Bazy	100	1*	1
Gasch	70	0	
Hufnagel	1,195	0	
Heile	4	0	
Teutschländer	3†	0	
Goldscheider	500	4*	0.8
Dudgeon, Gardner, and Bawtree ...	9	0	
	1,881	5	0.25

* It is questionable whether these cases should be included (cf. Bazy, Goldscheider, above), but even if they are, the incidence rate among the injected is less than half the total incidence.

† In all these cases tetanus bacilli were found in the secretions of the wounds.

Very much stress cannot be laid upon these figures, but from the "experiential evidence," as it has been termed, quoted above it may be gathered that the surgeons of the armies on the western front have found tetanus antitoxin of extremely great value when used prophylactically.

Thus the estimate of its value formed before the war has been confirmed by the further experience gained from its use during the severe test of active service.

PROPHYLACTIC DOSE.

The next point to be considered is the number of U.S.A. units of antitoxin which should be given as a prophylactic dose. It is necessary to specify the kind of unit referred

to, as the German unit is much larger than the American—1 German unit = 40 U.S.A. units. The unitage of French serum is not given, and one can only presume an average unitage from the results of tests of samples. V. Behring (1915) tested a sample of French serum and found that it contained 40 U.S.A. units per c.cm. Rosenau and Anderson (1908) estimated the strength of two samples to be 40 U.S.A. units and 66 U.S.A. units respectively. The writer tested a market sample, and found the titre to be more than 50 and not quite 100 U.S.A. units per c.cm. We may therefore assume that the usual prophylactic dose of 10 c.cm. of Pasteur Institute serum is equal to some 600 U.S.A. units.

Doses Recommended by Several Writers.

v. Behring (Nov., 1914)	800 U.S.A. units, and repeat if wound not healed, as the preventive injection may merely postpone the tetanus.
v. Behring (Feb., 1915)	800 U.S.A. units, but if the serum can be given immediately the wound is received 500 U.S.A. units may be enough.
Goldscheider ...	800 U.S.A. units.
Kümmel ...	800 U.S.A. units. Must be repeated in some cases.
Grundmann ...	800-4,000 U.S.A. units, and repeat every two weeks.
Weintraud ...	800 U.S.A. units.
Hufnagel ...	800 U.S.A. units.
Casch ...	800 U.S.A. units.
Aschoff ...	4,000 U.S.A. units, and 800 units eight days later.
Walther ...	10 c.cm. = about 600 U.S.A. units.
Bazy ...	10 c.cm. = about 600 U.S.A. units. Thinks that in some cases 2 or 3 c.cm. might be enough.
English army ...	500 U.S.A. units. No evidence that this dose is too small.
Jochmann ...	800 U.S.A. units.
Ennicke ...	800 U.S.A. units, and repeat twice at weekly intervals.

Here, again, war experience confirms the pre-war conclusion, and it may be accepted that from 500 to 1,000 U.S.A. units of tetanus antitoxin is a sufficiently large prophylactic dose for the *great majority* of injuries, provided it is given early.

ANOMALOUS CASES.

Cases have, however, occurred, and, no doubt, will occur again, in which the injection of from 1,500 to 4,000 U.S.A. units appears to have had only a comparatively limited effect, if any, in preventing the onset of an attack. In some of these cases the interval between the injection and the onset of the disease was too short to allow of the development of the full effect of the antitoxin. As an instance, a case recorded by L. Simon (1909) may be mentioned. A boy aged 5 years, weighing 45 lb., was run over on the evening of August 31st, and brought to the hospital shortly after the accident. It was found that he had a compound fracture of the right leg with a very dirty wound. Amputation at the knee was performed. There was also a compound fracture of the left toe, which was cleaned and dressed. At the same time 20 Behring units, = U.S.A. units, of tetanus antitoxin were injected into the right thigh. At 11 a.m. on September 1st (eighteen hours after the injury) symptoms of tetanus appeared. The attack was moderately severe, and ended in recovery. In the same paper Simon gives details of another case (a boy aged 12 years, run over), in which tetanus developed nineteen hours after the injury. In such cases serum given subcutaneously has no chance of exerting its full effect. But there are some cases in which the seeming failure of a prophylactic injection of antitoxin must be left unexplained until we possess fuller knowledge of the subject. The most remarkable is that recorded by v. Behring (1914):

His assistant H. Sch. was infected:

- (1) In 1895, through the nasal mucous membrane when he was preparing dried tetanus toxin.
- (2) In 1898, by inhaling dried powdered tetanus toxin; in this attack there was early tetanus of the diaphragm.
- (3) In 1902, at 9 a.m. on Sunday, November 9th, owing to a litre flask of bouillon culture of tetanus breaking in his right hand, and pieces of glass penetrating deep into the palm. The same afternoon very careful antiseptic treatment was given to the hand, and a plentiful amount of antitoxin was injected into the right arm. On the fourth day there were suspicious of tetanus, and on November 13th there was obvious tetanus

which, in spite of further injections of serum, increased in severity, so that on the sixteenth, as a last resort, the chief nerve trunks in the right axilla were exposed, and as much as possible of Behring's strongest serum was injected into each of them; the result was excellent. The tetanus ceased to progress, and the case gradually but slowly went on to recovery. The use of the right arm was not perfect for a long time.

It is most unfortunate that Behring does not say how many units of antitoxin were given or where it was injected in the earlier stages of the case. He, however, concludes that very shortly after the injury the intra-muscular nerve endings had taken up and fixed a minimal lethal dose of the toxin. This, however, is a questionable statement; for if so much of the toxin was absorbed so soon on the 9th, then the lethal dose had not all passed up to the central nervous system by the 16th—that is, in seven days—a rate of travel which is somewhat slow according to experimental evidence (*cf.* Marie and Morax, 1902; Permin, 1913). v. Behring would not, we presume, have given a smaller dose of antitoxin than 20 Behring units, = 800 U.S.A. units, but whatever the dose was the immunity due to it did not last longer than four days.

Duration of Passive Immunity.

The duration of the passive immunity conferred by a dose of antitoxin is a question which has been the subject of investigation but is still unsettled.

In this connexion I may refer to an experiment performed by Meyer and Ransom (1902), though it had a different object in view.

They injected into the left sciatic nerve of a dog about 2.1 U.S.A. units of tetanus antitoxin, and immediately afterwards an equivalent amount of toxin subcutaneously, half being injected into the right fore-leg and half into the left hind-leg. On the third day the right fore-leg was tetanic but the left hind-leg was free. On the seventh day there were signs of commencing tetanus in the left hind-leg, and on the eleventh day it was distinctly involved.

In this case the passive immunity conferred on the left hind-leg by an amount of antitoxin sufficient to neutralize all the toxin injected began to pass off in one week. Ruediger (1913) showed from his experiments that the subcutaneous injection of 1,500 U.S.A. units of antitetanic horse serum into the horse confers a passive immunity lasting from six to eight weeks, and that 250 U.S.A. units of similar tetanus antitoxin injected into guinea-pigs protects them for four weeks against a dose of tetanus toxin in each case fatal to the control animals. If we take the blood volume of an ordinary horse to be about 30,000 c.cm., and that of a guinea-pig of 500 grams to be 50 c.cm., then the amount of antitoxin injected was $\frac{1}{60}$ U.S.A. unit per cubic centimetre and 5 U.S.A. units per cubic centimetre respectively. These quantities bring out the difference in the duration of the effect of a homologous and of a heterologous serum. Calculating from the guinea-pig figures, according to body weight only, a man weighing 70 kilos would require some 35,000 U.S.A. units of antitoxin to protect him for a month against a fatal dose of tetanus toxin.

Levin (1909), from experiments made with diphtheria antitoxin, concludes that there is no difference in the rate of absorption of a homologous and of a heterologous serum, but that the former appears to remain about three weeks in the circulation, while the latter has almost all disappeared at the end of a week. He states that of two animals of the same weight receiving the same amount of antitoxin, one may show 50 per cent. higher concentration of antitoxin in its blood than the other (*cf.* Park and Biggs, 1912-13); that if 10, 20, or 40 c.cm. of heterologous serum be injected into a rabbit, practically all has disappeared at the end of about six days, whether it was given intravenously, intramuscularly, or subcutaneously; also that if it is wished to keep the antibody concentration at a certain height for some time, a series of relatively small doses must be given, and not one very large dose.

L. Simon (1914, *loc. cit.*) mentions the following case:

In a shell wound of the arm, because there was some twitching of the arm and face, 300 (presumably Behring) units = 12,000 U.S.A. units, of tetanus antitoxin were given intravenously. As all the symptoms subsided, it was concluded that the assumption of tetanus was a mistake. Thirteen days later the symptoms of tetanus returned in a more severe form, and so another 300 units were given intravenously under chloroform anaesthesia. On recovery from the narcosis the patient became suddenly cyanosed, had a rigor and a temperature of 40.9° C., but the pulse kept good and the respiration was

normal. After this partial shock had subsided there was no return of the tetanic symptoms. Three days later (seventeenth day after the first injection) 100 units were injected intravenously. The patient became totally unconscious for half an hour, there was marbling of the body, the pulse was scarcely perceptible, and the temperature rose to 40.1° C., but the respiration was fairly normal. Recovery was rapid and complete.

Then we have Rowan's (1910) "run over" case:

There was compound comminuted fracture of both bones of the leg, in which five hours after the accident 1,500 U.S.A. units of tetanus antitoxin were given subcutaneously. On the twenty-fifth day after the accident there were "premonitory symptoms" of tetanus, and death occurred on the fourth day of the attack.

In Simon's case we have 12,000 U.S.A. units protecting for only thirteen days, while in Rowan's case 1,500 U.S.A. units conferred immunity for over three weeks.

These results are conflicting, and when considered in conjunction with the general experience that 500 to 1,000 U.S.A. units is a good prophylactic dose make plain the existence just here of a gap in our knowledge which we should endeavour to fill up by taking every advantage of the present opportunity of studying the disease.

The fact that these large doses failed to protect completely, and the experience of the British army that "there is no evidence to show that 500 U.S.A. units is too small a dose" tend to confirm Levin's conclusions that it is better to give a series of small doses rather than one large one. If the dose of 500 units is repeated at the end of a week and of a fortnight after the receipt of the wound we should not use any more serum, and we should probably get a more prolonged immunity than by giving the 1,500 units which some surgeons seem to prefer.

VERY LATE DEVELOPMENT OF TETANUS.

Other cases which are puzzling are those in which tetanus develops very late. One such case is reported by Don (1915). A man was wounded in the shoulder on December 21st, 1914, and received a prophylactic injection (number of units not mentioned) on December 23rd. On March 2nd, 1915, tetanus developed. Tetanus bacilli were found in the pus. Were these tetanus bacilli present from the date of the wound or did infection occur at a later period?

Köhler (1915) and also Grundmann (1915) both suggest that some cases of tetanus arise after admission into hospital, owing to the infection being conveyed from one wounded man to another—most probably by the patients themselves. In 3 cases Teutschländer (1915, loc. cit.) found virulent tetanus bacilli on the secretions of wounds which had been received several weeks previously, and Dudgeon, Gardner, and Bawtree (1915) state that—

"A wounded man may be acting as a carrier of tetanus bacilli for at least two months after the date of the wound, and without any reason on clinical grounds to suggest that these bacteria are present in the tissues."

They cultivated tetanus bacilli from two cases neither of whom had had a prophylactic injection of antitoxin. One of these developed the disease and recovered, whilst the other escaped scot-free.

As suggesting possible sources of late infection, two cases of tetanus recorded by Kirmisson (1914) are not without interest.

The first was that of a girl of 17½ years, who was being treated for dorsal scoliosis. A plaster corset was put on on February 10th, and layers of felt were slipped in underneath the plaster on February 14th and 21st, and on March 7th and 21st. On April 1st there was trismus. The corset was immediately taken off, and a little eschar was found on a right costal projection. Death occurred forty-eight hours later.

The second case was that of a girl of 19½ years, who under similar conditions developed acute tetanus, and died in forty-eight hours.

Kirmisson suspected the felt, and his suspicions were proved to be correct as tetanus bacilli were isolated from it.

Another way in which infection may be brought about is that to which Jacobsthal (1914) has called attention. After meeting with tetanus in two cases in which the East Indian fibre known as Pengawar Djambi had been used to dress the wounds, he examined seven specimens of this fibre, and found tetanus bacilli present in three of them.

Further, it appears that the surgeon may be the cause of the development of tetanus by the use of procedures

which under ordinary conditions would be quite harmless but which are not safe owing to certain peculiarities of the tetanus bacillus. These "vagaries," as they may be called, are well brought out by the results of the laboratory studies of the bacillus carried out by Francis (1914). Eleven vaccine viruses, ten of which contained *B. welchii*, were artificially contaminated with tetanus spores and injected subcutaneously on the back of 26 mice and on the abdomen of 26 guinea-pigs. All the guinea-pigs contracted tetanus after an average incubation period of four days and all died; 17 of the mice had tetanus—average incubation period eight days—and died. The remaining 9 mice showed no signs of tetanus, but each of these 9 mice had a mate which had an injection of the same amount of the same material and each mate, with one exception, developed tetanus from which it died. After forty-five days, in the case of 6 of these mice, and after sixty-six days in the case of the other 3, they were all injected subcutaneously on the back with a twenty-four-hour old agar culture of staphylococcus and all promptly contracted fatal tetanus. Scrapings from the site of inoculation in each instance contained over 500 mouse minimal lethal doses of tetanus toxin.

Again, 93 glycerinated vaccine viruses artificially contaminated with tetanus spores were inoculated in 1 c.cm. amounts beneath the skin of the abdomen of 93 guinea-pigs weighing about 250 grams each. Seventy-seven died of tetanus, 4 had tetanus but recovered, while 12 manifested no symptoms whatever of tetanus. He showed that tetanus spores may remain in the tissues of the guinea-pig for about four weeks, and at the end of that time may be activated by injections of quinine or of staphylococci. White mice will harbour tetanus spores in the subcutaneous tissues for at least four months, at the end of which time the spores may be activated by staphylococci but not by quinine, and at the site of inoculation there may be produced as much as 10,000 mouse minimal lethal doses of tetanus toxin. Further, Francis mixed 0.5 c.cm. of glycerinated vaccine virus with 0.5 c.cm. of a rich suspension of tetanus spores and used the mixture to vaccinate five monkeys, each in five places on the back. There was a good "take" at every insertion, but none of the animals contracted tetanus. In the case of one monkey a portion of the "crust" was removed on the fourteenth day and injected beneath the skin of two guinea-pigs, both of which developed tetanus. This experiment was repeated in the case of three other monkeys with the same result. He then vaccinated a monkey with plain virus, and on the fifth day, when there was a good "take," he rubbed tetanus spores well into the "take." The animal never showed a sign of tetanus.

It would be interesting to compare Francis's animal figures with figures obtained from wounded men, but it cannot as yet be done. The only figures the writer has come across are those of Fleming (1915), who examined bacteriologically 127 wounds within seven days of infliction, and found tetanus bacilli to be present in 22 of them. It is not stated whether the bacilli were identified by microscopical examination only or by cultivation. Unfortunately he does not state how many of the men developed the disease.

The demonstration by Francis that injections of staphylococci may reactivate quiescent tetanus spores and give rise to a fatal tetanus is of great importance when considered in connexion with the experience of C. J. Bond (1915), who states that there are reasons for thinking that cases are occurring in which some slight surgical interference has relighted a violent local reaction in the neighbourhood of a recently healed wound. "I have records of cases in which after all incisions and sinuses round a compound fracture involving the elbow-joint or hip or other joint had completely healed, even simple passive movement of the joint under an anaesthetic has lighted up a violent reaction, the reappearance of the old sepsis and the formation of local abscesses, although no incision was made, nor any solution of skin surface produced."

Confirmation is afforded by Bérard and Lumière (1915), who have encountered a number of cases of tetanus following some operation or trauma affecting a wounded soldier who had had a prophylactic dose of serum, and had long recovered apparently from his wound.

Goldscheider, too, suggests that a case recorded by him

was possibly due to too early and prolonged active movement after a wound had healed.

The case was that of a soldier who received a flesh wound of the left thigh on October 4th, 1914. A dressing was applied by a comrade, and he was admitted into hospital on October 7th. He had no prophylactic injection, and the progress of the wound was normal. On October 30th he was discharged as fit for active service, and he walked 22 kilometres that day, and 5 kilometres the next day with the object of regaining his regiment. On the night of October 31st–November 1st he had pains in the left leg and trouble in eating. He missed his regiment, and had to retrace his steps some distance. The symptoms increased, he was readmitted into hospital, and he died of tetanus on November 7th.

The studies of Francis and the experience of Bond, of Bérard and Lumière, and of Goldscheider point out a line along which we may conduct our investigation into the causation of these cases of late development of tetanus.

OPERATION.

As regards operating in cases of tetanus the opinion before the war was against doing so, and nothing has occurred since to change that opinion. This is not to be wondered at considering that it has been shown by:

1. Bolton and Fisch (1902), that toxin makes its appearance in the blood of the horse several days before any symptoms of tetanus are to be observed, and that it gradually increases until about two days before the symptoms become noticeable, and then it suddenly diminishes and may in some cases even disappear. The amount of toxin varies in different cases. In one instance the serum from a diphtheria antitoxin horse about two days before the symptoms of tetanus appeared was sufficiently toxic to kill a guinea-pig in a dose of 0.1 c.cm.

2. Madsen (1908), that five days before the appearance of tetanic symptoms in a horse there was in the filtered serum enough tetanus toxin in:

5 c.cm. to kill a guinea-pig in 8 days	
8 " " " " 3 1/2 "	
10 " " " " 3 1/2 "	

Serum obtained shortly before the horse's death, on the same day that the symptoms were noticed, killed a guinea-pig in a dose of 4 c.cm.

Nivière (1915) mentions that in 8 cases which had been operated on tetanus developed, in 2 within twelve hours, in 4 within twenty-four hours, and in 2 within forty-eight hours after the operation.

Cobb (1914) reports a case of severe shell wound of the left arm in which amputation of the arm was performed two days after the injury at the base hospital in France. He was admitted into hospital in England on the seventh day with wounds very septic and large sloughs. These latter were cut away, the whole area swabbed with H₂O₂, and a prophylactic dose of antitetanic serum given. Next day there were twitchings in the shoulder, and later in the day the patient developed well-marked trismus. The attack progressed rapidly, and ended fatally on the third day of the disease—the tenth from the receipt of the wound.

As another example, Esau's (1910) case may be cited. A boy of 14 years of age received a pistol shot wound of the left hand. The wound was opened up and cleaned on the third day after the injury. On the seventh day there were slight contractures of the flexors of the left hand, but they passed away, and serum was not given. On the following days the contractures recurred more frequently. They could be overcome with slight force, but this gave pain, and they returned again at once. Not the slightest trouble with the jaws. On the fifteenth day after the injury the wound was opened up again, and some foreign bodies removed. Next day (sixteenth) there was general tetanus, which became moderately severe, but ended in recovery.

It is imperative, therefore, when an operation is proposed in wounded who may have been infected with the tetanus bacillus, to bear in mind that there may be toxin circulating in the body. A large prophylactic injection is consequently necessary, and it should be given in such a way as to ensure that there is no free toxin in the blood at the time of the operation and for some time after. Subcutaneous injections, except as supplementary agents, are out of the question here because of the slow rate of absorption. If the injection be given intramuscularly, then the operation should not take place for several hours. An intravenous injection permits of the operation being performed at once, and as it bears upon the question it is

of interest to note a statement of Behring's (1915) to the effect that the amount of antitoxin present in 1 c.cm. of blood a few minutes after an intravenous injection of antitoxin remains constant for nearly sixty minutes.

An intravenous injection of serum always raises the question of the possibility of anaphylactic trouble ensuing. E. E. Irons (1915) gives an instance of this and a description of the precautionary measures which were taken. The patient had a prophylactic dose of 1,500 U.S.A. units after a punctured wound of the heel. Ten days later tetanus set in. While arrangements were being made for his admission to hospital 1,500 U.S.A. units were given subcutaneously. This was followed by a moderate urticaria. Eight hours later, on arrival at the hospital, 5 c.cm. of serum were injected intravenously on the assumption that sufficient time had elapsed since the previous dose, which had been followed by an immediate cutaneous reaction, to render him insensitive to further serum. However, an immediate severe serum reaction occurred after this second dose—urticaria, rapid respiration, and rapid pulse. "The severity of the tetanus made us feel that unless something further could be done he would surely die of tetanus. We prepared a 10 per cent. solution of antitetanic serum in NaCl solution, and injected 10 c.cm. intravenously very slowly, watching carefully the pulse, blood pressure, and respiration. There was no further reaction, and the full dose of 20,000 U.S.A. units was then given intravenously and 5,000 units intraspinally without a trace of serum reaction." Surgical treatment of the wound and sufficient sedatives to control spasms completed the treatment. The patient recovered.

CONCLUSIONS.

The experience gained during the first year of the war has confirmed the opinion that from 500 to 1,000 U.S.A. units of tetanus antitoxin is a sufficiently large prophylactic dose for the majority of cases, and that it is advisable, in severe wounds, to repeat the dose once or twice at intervals of a week. Occasionally cases occur in which antitoxin appears to have little preventive effect. These cases should be recorded with minute details, so that our knowledge of them may be increased and an explanation of their occurrence obtained. Those cases of tetanus which develop some weeks after the receipt of an injury may be due to the reactivation of a quiescent focus by too early or two energetic active or passive movement.

NOTE.—It has been assumed that, in all articles published in German, when the expression "A.E." (Antitoxin Einheit) is used it means a "Behring unit."

BIBLIOGRAPHY.

- Arzt, 1914: *Wien. klin. Woch.*, December 27th, 1914, p. 1633; abstract in *Journ. Amer. Med. Assoc.*, February 6th, 1915, p. 551.
 Aschoff, 1915: *Deut. med. Woch.*, April 8th, 1915, p. 456.
 Bazy, 1915: *Presse médicale*, Paris, February 4th, 1915.
 v. Behring, 1914: *Deut. med. Woch.*, October 8th, 1914, and November 12th, 1914.
 v. Behring, 1915: *Berl. klin. Woch.*, February 8th, 1915, p. 121.
 Bérard and Lumière, 1915: *Bull. de l'Acad. Méd., Paris*, August 31st, 1915; abstract in *Journ. Amer. Med. Assoc.*, October 16th, 1915.
 Bolton and Fisch, 1902: *Trans. Assoc. Amer. Phys.*, xvii, pp. 462–7, cited by Rosenau and Anderson.
 Bond, 1915: *BRITISH MEDICAL JOURNAL*, September 25th, 1915, p. 467.
 Cobb, 1914: *BRITISH MEDICAL JOURNAL*, November 14th, 1914, p. 856.
 Don, 1915: *Lancet*, June 12th, 1915, p. 1233.
 Dudgeon, Gardner, and Bawtree, 1915: *Lancet*, June 12th, 1915.
 Esau, 1910: *Deut. med. Woch.*, p. 705.
 Eunicke, 1914: *Muench. med. Woch.*, October 27th, 1914, p. 2147.
 Francis, August, 1914: *Bull. 95, Hyg. Lab., U.S. Public Health Service*.
 Fleming, 1915: *Lancet*, September 18th, 1915, p. 638.
 Forestier, 1914: *BRITISH MEDICAL JOURNAL*, November 14th, 1914, p. 854.
 Gasch, 1915: *Deut. med. Woch.*, March 11th, 1915, p. 330.
 Goldscheider, 1915: *Berl. klin. Woch.*, March 15th, 1915.
 Grundmann, 1915: *Berl. klin. Woch.*, February 22nd, 1915.
 Hartmann, 1914: *Bull. de l'Acad. Méd., Paris*, December 8th, 1914.
 Hufnagel, 1914: *Deut. med. Woch.*, December 17th, 1914, p. 2102.
 Helle, 1915: *Berl. klin. Woch.*, February 15th, 1915.
 Hinterstrasser, 1915: *Wien. klin. Woch.*, February 18th, 1915.
 Irons, 1915: *Journ. Amer. Med. Assoc.*, May 8th, 1915.
 Jacobsthal, 1914: *Muench. med. Woch.*, October 13th, 1914, p. 2079.
 Jochemann, 1914: *Deut. med. Woch.*, October 22nd, 1914, p. 1881.
 Joly, 1915: *Bull. de l'Acad. Méd., Paris*, January 26th, 1915.
 Kimmel, 1915: *Muench. med. Woch.*, April 20th, 1915, p. 570.
 Krimmison, 1914: *Bull. de l'Acad. Méd., Paris*, lxxviii; abstract in *Journ. Amer. Med. Assoc.*, July 4th, 1914, p. 44.
 Kohler, 1915: Abstract in *Berl. klin. Woch.*, February 8th, 1915, p. 137.
 Levin, 1909: *Zeitsch. für Immunitätsfor.*, 1, orig., pp. 3–27.
 Madeluna, 1914: *Muench. med. Woch.*, December 29th, 1914, p. 2441.
 Madsen, 1908: *Centralbl. f. Bakt.*, 1, orig., xlvii, p. 276.
 Marie and Morax, 1902: *Annal. Inst. Past.*, xvi, p. 818.
 Meyer and Ransom, 1903: *Archiv f. Experim. Path. u. Pharm.*, xlix, pp. 367–416.
 Nivière, 1915: *Bull. de l'Acad. Méd. Paris*, March 30th, 1915, p. 409.

- Park and Biggs, 1912-13: Collected Studies, Bureau of Laboratories, Health Department, City of New York.
 Permin, 1913: Communications de l'Institut sérothérapique de l'Etat Danois.
 Ritter, 1915: *Muench. med. Woch.*, April 23th, 1915.
 Rosenau and Anderson, 1908: *Bull. Hyg. Lab., U.S. Public Health Service*.
 Rowan, 1910: *Journ. Amer. Med. Assoc.*, February 12th, 1910, p. 533.
 Ruediger, 1913: *Philippine Journ. Science*, viii, Sec. B, pp. 138-142.
 Schoute, 1915: Abstract in BRITISH MEDICAL JOURNAL, January 2nd, 1915, p. 45.
 Siemon, 1914: *Muench. med. Woch.*, December 1st, 1914.
 Simon, 1909: *Muench. med. Woch.*, p. 2264.
 Simon, 1914: *Muench. med. Woch.*, November 10th, 1914.
 Stricker, 1914: *Deut. med. Woch.*, December 24th, 1914, p. 247.
 Teutschländer, 1915: *Deut. med. Woch.*, May 13th, 1915.
 Walther, 1914: *Presse médicale, Paris*, October 8th, 1914.
 Weintraud, 1914: *Bert. klin. Woch.*, October 19th, 1914.

THE CONTROL OF "DIPHTHERIA-BACILLUS CARRYING"; AND THE JASMIN OIL METHOD.

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The revelation of the unsuspected evil of "carriers" arose from a study of the longer and less direct route followed by the dissemination of typhoid, although the recrudescence of diphtheria epidemics at schools had long been identified with a readmission of pupils certified (after an adequate convalescence) as clinically cured. The notion that these were minor relapses after the cure continued to be held for a while after the first observation (by Kayser in 1906) of the spread of typhoid by a "cured-typhoid" bacillus carrier. Since then we have recognized the more subtle and possibly frequent danger from the "typhoid-intact" carrier; and it is now admitted that diphtheria also may have its "cured-diphtheria" and its "diphtheria-intact" carrier, both needing their local internal sanitation, though with a less remote and extensive seat of infection than in typhoid.

That result does not appear to have been achieved. This late publication of suggestions originated and practised long before the "carrier" period has been occasioned by a recent inquiry by a correspondent (BRITISH MEDICAL JOURNAL, 1915, vol. ii, p. 459) for a reliable method of curing diphtheria carriers. My first paper in 1897 (BRITISH MEDICAL JOURNAL, vol. ii, p. 1564), in conjunction with my then house-physician, Dr. W. A. Hubert, was mainly concerned with tracheotomy dangers—namely, to safeguard the patient against the dangerous suppression of his cough mechanism inflicted for the sake of an air-way; and to help him, less through antiseptics than by the expectoration of the infective material and by a recovery of some of the impaired ventilation and circulation of the lung. It also referred, however, to my antecedent treatment for several years. This contained potentially all the clinical work that followed: practically the "spreading oil-film method" as a mechanical substitute for the impractical principle of corrosive antiseptics, which is inapplicable to the healthy membrane of the carrier. It is to be regretted that that effort should have passed unnoticed in this country; although in France some reference has subsequently been published to an intranasal instillation of oil which, perhaps, may still be in vogue. Owing to that oversight, and to the lack of systematic institutional opportunities for any test by results, I now offer this method only as a tentative proposition for the purpose of disinfecting carriers. Yet it has not lacked clinical evidence for its feasibility and for its benefits, under active infection.

I had realized the desirability of forestalling any extensive secondary sinus infection, and if possible of suppressing it gradually during treatment, whilst at the same time mitigating the severity of the local trouble. Eventually instructions were given for a systematic toilet at least twice daily in all my cases of diphtheria from the beginning of and throughout their hospital treatment. Antitoxin, which came in as the supreme agent for the clinical cure, did not displace that hygienic indication. I may mention, in illustration of the cleansing power of oil, the benefit derived three weeks ago by an adult patient with bilateral pulmonary phthisis, operated on last February for polypi and still suffering from them, but now unfit for surgical interference. The discomfort was greatly relieved by the first application, and, within three or four days, the

severe foetor from which he had suffered for years was completely suppressed. In this instance, however, I had followed up the oil supply with an insufflation of boracic powder, immediately.

The original disinfecting purpose led me to take within the systematic scope of the method practically all the infections (including influenza, whooping-cough, mumps, tonsillitis, etc.) which own an ori-nasal origin or extension. Meanwhile the mechanical "oil-film by water carriage" disclosed its ability to reach beyond the feebly moistened glottis and to give relief to an inflamed tracheal or bronchial membrane; though its greatest benefaction is in easing the acute catarrhal upper nasal obstructions, as well as all the acute and chronic catarrhal affections of the naso-pharynx, fauces, and upper larynx.

The method itself has hardly varied from its original form, except for the discarding of carbolic acid (1 in 60) and the substitution of jasmin oil, which is exceptional among flavoured oils in its freedom from the irritating effect of any added essential oil. The mechanism of the method is simple, but needs judgement. It is not free from the influence of the psychical factor, which the sense of relief usually cures provided this is not marred by inexperience in the patient or the nurse. The main idea is still the original one of utilizing to the full the downward action of the cilia, and to sweep the mucous membrane with a continuous moving film. The supply must therefore be from above, not as in spraying, douching or syringing from below. Though introduced at the nostril the oil is collected in the upper fossae. The rapidity of the radiating spread of the film by surface tensions is great in proportion to the moisture of the surface and to the fluidity of the oil. Our main concern is its after movement practically independent in time from the first, and practically uninfluenced in its direction by those evenly centrifugal radiations, which broadly coincide with it in one hemisector of the field whilst contrary to it in the other. Whether "up or down," the cilia work the transportation towards the external orifice. From a charged frontal sinus it moves downwards, the same way as the massive discharge from blowing the nose, and also backwards. But in the trachea any "descending" film would be moved upwards, the same way as if it arose from an intratracheal injection. The film is, of course, a passing show, easily broken up by absorption. Its full value is in its frequent renewal with adequate charges.

The simple implements are an eggcup to hold a small supply and a penfller to convey the oil into the nose—namely, for an adult, a charge nearly half filling the tube. The patient reclines on a bed or flat couch with a narrow bolster, and spreads a towel well up to the chin or higher. The essential is to throw the head well back behind the bolster and to maintain it there for half, or the whole of a minute after charging both nostrils. The oil must not be rushed up or run in, but instilled drop by drop. The other essential is the complete lateral movement of the head to the right for a while and then to the left, to favour the irrigation of the sinuses, as that small supply cannot fill them. As the head is gradually levelled the oil is felt to trickle down the back of the naso-pharynx. This is the only unpleasant sensation. But that surplus is not considerable. It may be swallowed; or better, by refraining from swallowing, it may be allowed to find its own way down the larynx and trachea. It is better to have assistance, but most of my patients succeed in their unaided performance on the strength of these simple directions. I believe—but must leave the decision to those with larger opportunities—that this method, with the addition of the insufflation, if duly persevered with, is the most likely one to rid a carrier of his influenza or of his diphtheria bacillus.

BIBLIOGRAPHY.

- BRITISH MEDICAL JOURNAL, 1897, vol. ii, p. 1564. Ibid., 1898, vol. i, p. 1381. Ibid., 1899, vol. i, p. 342. *Lancet*, 1899, vol. i, p. 377. Ibid., 1899, vol. ii, p. 780. Ibid., I. A. Grimes, 1899, vol. ii, p. 409. Ibid., 1899, vol. ii, p. 1808. Ibid., 1909, vol. i, p. 33.

THE *Medical Record* states that out of 600 applicants for the United States Navy examined recently in Boston only 30 were accepted, the remainder being rejected as physically below the normal or mentally or morally unfitted for the service. From this, Rear Admiral Albert Ross draws the conclusion that America must make its rapidly degenerating citizens into men before they can be made sailors or soldiers.