for colour-blindness and its photophobia, improving the vision and reducing the nystagmus.

The contact glass is also valuable for serpentine ulceration of the cornea, progressive abscesses, and other forms of keratitis, especially if the concavity of the glass is smeared with a disinfectant ointment. Other conditions for which it is useful include neuroparalytic keratitis, some forms of sclerotic keratitis, acne rosacea of the conjunctiva and cornea, spring catarrh, trachoma, pemphigus, xeroderma pigmentosa, hay-fever, kerato-iritis, dystrophia marginalis, and lagophthalmic keratitis. Cases of primary iritis also do well with contact glasses, and even tuberculous, syphilitic, rheumatic, diabetic, gouty, and infective cases are suitable.

There is no fear of causing glaucoma by the use of these glasses, although anxiety is sometimes aroused when the patient sees rainbow colours round an open light. This is due to misfit of the glass with the cornea, or the use of hard or distilled water, and can be obviated by appropriate fitting and the use of physiological saline. Patients who have had a plastic operation on the cornea should wear contact glasses to keep the implanted piece in position when the lids sweep over it.

Contact glasses are indicated for the treatment of squint, and one eye can be corrected by itself if desired. There are also occupational indications for this form of correction; architects, seamen, pilots, chemists, actors, and engineers should try it; so also should sportsmen such as ski-runners, bicyclists, swimmers, motorists, gymnasts, sailors, tennis players, and those who hunt.

Finally, there is the cosmetic indication; women who have pale grey or blue eyes can have them darkened to any desired degree by contact glasses.

Illustrative Cases.

CASE 1.—A man, aged 42, had lightning cataract with vision in the right eye of 6/8 with a + 14 lens and in the left eye of 6/6 with a + 16 lens. With a coloured contact glass 2/6 he obtained 6/6 vision.

CASE 2 was totally colour-blind and shunned the light, but with 50 per cent. coloured contact glasses 2/8 he could open his eyes in a bright light.

CASE 3.—A girl, aged 8, had 6/18 vision in both eyes with a — 8 lens in the right eye and a — 7 in the left. With a contact glass of 2/9·5 in the right eye and 2/10 in the left she obtained 6/8 vision. She has worn her glasses daily since October, 1929, taking them out at night, and could not now do without them.

CASE 4.—A seaman, aged 25, had a vision of 6/6 with a — 3 lens and lost his berth in consequence. With contact glasses he has normal vision and is fit for sea again.

CASE 5.—A gamekeeper, aged 29, had a vision of 6/60 in the right eye and 3/60 in his left eye. With contact glasses 2/8 in the right eye and 2/85 in the left eye he has 6/8 vision, and he wears the glasses daily without discomfort.

CASE 6.—An orchestral conductor, 56 years old, is presbyopic, but by the aid of contact glasses he obtains the necessary field of vision at a distance of 80 cm. which is necessary for his work. He cannot wear spectacles, but with contact glasses has already conducted ten important concerts.

CASE 7.—A girl of 16 has 6/60 vision in the left eye, improved by a — 2 spectacle lens to 6/36. She is astigmatic; the right eye is normal. Since December, 1929, she has worn a contact glass 3/86 on the left eye, which gives her 6/8 vision and makes her very comfortable. Her parents are delighted with her increased happiness and the abandonment of the ugly spectacles.

CASE 8.—A married woman, aged 35, a concert singer, suffers from myopia and astigmatism. She obtains 6/8 vision with a correction in the right eye of sphere — 3 and cylinder — 2, and in the left eye with a sphere — 6 and a cylinder — 2. With contact glasses 81 in the right and 86 in the left she gets the same or slightly better correction. At first she could hardly bear the glasses for an hour, but now she keeps them in as long as she wants to, and once she even fell asleep in them.

CASE 9.—A spinster, aged 20, has myopia with a little astigmatism. With spectacles (cylinder — 1, sphere — 6) she has 6/6 vision, which she also obtains with contact glasses of 9. At first she wore the glasses for an hour only, but after some days she became accustomed to them.

CASE 10.—A man of 30 has a normal right eye but the left has trachoma, pannus, and myopia, produced by keratoconus in the middle of the cornea. He can distinguish fingers at a distance of 2 ft. When he first wore a contact glass of 76 he felt very uncomfortable, and his eyelashes seemed to scratch the cornea. In time, however, the cornea grew clearer and in a few months he had a vision of 1/10 and was able to wear the glasses continuously for a fortnight.

It will, I think, be seen that contact glasses are likely to prove increasingly useful in ophthalmic work.

ANTIGENIC PROPERTIES OF DIPHTHERIA TOXOID-ANTITOXIN FLOCCULES.

BY ROBERT SWYER, M.R.C.S. ENG., D.P.H.,

SENIOR ASSISTANT MEDICAL OFFICER, NORTH-WESTERN FEVER HOSPITAL, LONDON COUNTY COUNCIL.

DURING the past few years several new forms of diphtheria prophylactic have been introduced. The object of workers in this field is to produce one which is safe, efficient, rapid in action, and free from non-specific poisonous materials, which—as is well known from the experience gained with the older forms of prophylactic—are apt to cause unpleasant local reactions, especially in adults. While many of the properties of diphtheria prophylactic can be studied and compared in laboratory animals, certain others, such as the liability to cause reactions on injection, can only be investigated in human beings, and the important question of the activity of prophylactics in producing rapid immunity must also eventually be investigated in human beings.

Through the courtesy of Dr. R. A. O'Brien, Director of the Wellcome Physiological Research Laboratories, I have had the opportunity, during the past two years, of studying the form of prophylactic known as "toxoid-antitoxin floccules" (T.A.F.) in a series of 87 nurses at the North-Western Fever Hospital. Attention has been specially directed toward the production of immunity as shown by the Schick reaction, the rate of production of the Schick-negative state and the degree of local and general reactions produced by the injections.

From the nature of their preparation, the floccules used would be expected to cause less reaction than the older forms of prophylactic. The preparation used in this work consists of a suspension in saline of the washed precipitate produced from mixtures of diphtheria toxoid and diphtheria antitoxin.

The first recorded observations on the antigenic activity of the precipitate produced by the interaction of diphtheria toxin and antitoxin were made by Park and his colleagues [1] in 1924. They showed that a "T.A. solution of precipitate from mixing toxin and antitoxin" immunised guinea-pigs. Sordelli and Serpa [2] in 1925 centrifuged the precipitate produced in an over-neutralised mixture of toxin and antitoxin and found that the precipitate and supernatant fluid had apparently equal immunising value. Hartley [3] investigated the antigenic properties of the washed precipitates produced in over-neutralised, neutral, and under-neutralised mixtures of toxin and antitoxin and showed that the immunising value

of the first was low, that the precipitate from neutral mixtures was non-toxic but of high immunising value, while the precipitate from under-neutralised mixtures, though toxic in relatively large doses, was a remarkably active antigen. Hartley showed that these washed precipitates contained less than 1 per cent. of the total nitrogen present in the mixtures from which they separate, and suggested that, working on these lines, a relatively pure antigen—free, at least, from the non-specific material frequently the cause of local reactions—becomes a possibility. Hartley's results were confirmed by Glenny, Pope, Waddington, and Wallace,[4] and Glenny and Pope [5] showed that the precipitates from mixtures of toxoid and antitoxin are as good antigens as those prepared from toxin and antitoxin.

The substitution of toxoid for toxin permits the preparation of floccules entirely devoid of all risk, and this form of diphtheria prophylactic—toxoid-antitoxin floccules—has been used in the present work. O'Brien [6] states that the preparation seems to be free from liability to cause local reactions in human beings and quotes a series of 56 subjects immunised by Okell and Parish, 45 of whom became Schick-negative when tested from one to five months later, after one, two, or three doses of toxoid-antitoxin floccules. Dudley [7] states that the toxoid-antitoxin floccule preparation introduced by Glenny and Pope in 1927 is a better immuniser than ordinary toxoid, and records that the painful local and constitutional reactions, observed by no means infrequently when the older forms of antigen are used, entirely disappear when these floccules are used as immunising antigens.

In Germany, toxin-antitoxin floccules prepared by Schmidt have been used to a considerable extent in recent years. Schmidt and Scholz [8] in 1925 reported that toxin-antitoxin floccules immunised rabbits, and from these results, and those obtained on man, expressed the view that toxin-antitoxin floccules constitute the best antigen yet available for the active immunisation of man. They state that the injection is painless, that the local reaction produced is trifling or absent altogether, and that the antigenic value is high. Eberhard,[9] using toxin-antitoxin floccule preparations supplied by Schmidt, reported promising results, and stated, inter alia, that a single injection suffices for the immunisation of human beings. Soldin [10] makes the same claim, but other workers in Germany, while in general agreement regarding the absence of local reaction following injection, advocate the use of more than one dose of prophylactic.

Method and Results of Investigation.

As a preliminary to commencing the use of toxoid-antitoxin floccules in ordinary immunising doses a small series of cases were first given one subcutaneous injection of 0·25 c.cm. Since the members of this small group remained entirely free from troublesome reaction, ordinary doses of 1 c.cm. were thereafter employed. All new nurses, numbering 211, were Schick-tested within a few days of taking up duty in the hospital. Reactions were read seven days later, when 87 proved to be positive and were at once given a dose of the prophylactic. The number of doses given and the intervals between consecutive inoculations varied at different periods of the work, but the majority (42) received three doses of 1 c.cm. each at intervals of a fortnight; eight received three doses at weekly intervals; four had two doses at fortnightly intervals, while one who was only weakly positive received one dose only and a fortnight later was found to be Schick-negative. Four of those who were still Schick-positive eight weeks or more after the commencement of immunisation received more than three doses, the intervals between doses varying from one to three weeks. Of these four, two had six doses, one five, and one four. Whenever possible a re-test was performed four weeks after the last inoculation—i.e., from six to eight weeks after the commencement of immunisation. Those proving still positive were re-tested at intervals of four weeks until they became Schick-negative.

Unfortunately, owing to various causes such as absence on leave, transfer to other institutions, illness or leaving the service, it was impossible to carry out this programme in all the 87 positive reactors. Thus 19 were not re-tested after their course of immunisation. Of the remaining 68, 64 eventually became negative and four left the hospital while still positive. In one of these immunisation was abandoned after the first inoculation owing to a severe reaction. Another, who was still positive ten weeks after the last of three inoculations, refused a second re-test. Of the remaining two, one, who was positive four weeks after the last of three fortnightly doses, received a further three doses and was still positive when she left hospital 29 weeks after the commencement of immunisation. The other was positive six weeks after the last of three weekly inoculations, received a further 1 c.cm., and was still positive five weeks later, when she was given a fifth dose. She was still positive five weeks and 14 weeks later—or 34 weeks after the commencement of immunisation—when she, also, left hospital.

In only two, therefore, of 86 nurses did a full-controlled course of inoculations certainly fail to convert the Schick reaction from positive to negative.

Table I. includes only those cases who received a single course of immunising injections and were then re-tested at intervals until immunity was established as shown by a negative Schick reaction. The particulars of the four subjects who received more than a single course of the prophylactic and finally became immune are as follows.

All four were first given a course of three inoculations; subsequent re-tests being positive, one was given one more dose and became negative 14 weeks from the commencement of immunisation; another had two extra doses and became negative in 20 weeks. The remaining two had a second course of three injections, becoming negative in 16 and 29 weeks respectively. Comparing these results with those shown in Table I., it does not appear that the extra doses of prophylactic have materially shortened the time required for immunisation.

Table I. gives some indication of the period required to establish immunity, but it must be remembered that, owing to the reasons already mentioned, some of the subjects were not re-tested at the scheduled times and therefore the actual time taken to immunise may have been less than that shown. For example, in the series which had three fortnightly inoculations, the one who was Schick-negative 25 weeks after the last dose only had the one re-test. Similar conditions obtained in several of the other long cases. An important fact brought out in this series is that, if three doses of 1 c.cm. each are given at intervals of a fortnight, one may expect nearly one-half of the cases to be immune four weeks later and 90 per cent. to be immune in nine weeks.

The small series who received only two inoculations were not specially selected cases, but were taken in rotation at the end of the investigation when an attempt was being made to discover if two doses were sufficient; results coming in since the Tables were compiled have not quite borne out the good impression that was based on the original small series.

The comparatively poor results shown in the series who had three doses at weekly intervals may be attributable to the fact that this series contained several long cases who were not re-tested early enough.

Precise details of the length of time elapsing between courses of immunisation and the proved establishment of immunity are scanty in the literature. Kelleher,[11] in his report of immunisation work in a series of 224 boys on the training ship *Exmouth*, found that the average time dating from the first immunising dose was 2·9 months. The antigen used by Kelleher was the older T.A.M., but the average age of his cases was probably five or six years below that of the hospital nurses.

TABLE I.—(*55 Cases*).

Inoculations—Number ..	1	2	3	3
Interval between ..	—	2 weeks.	1 week.	2 weeks.
Immunising time from final inoculations.	Number and percentage Schick-negative.			
Weeks.	%	%	%	%
2	1 (100)	1 (25)	—	—
3	—	—	—	1 (2·4)
4	—	1 (50)	1 (12·5)	19 (47·6)
5	—	1 (75)	—	6 (61·9)
6	—	—	1 (25)	3 (69)
7	—	—	—	1 (71·4)
8	—	1 (100)	—	2 (76·2)
9	—	—	1 (37·5)	6 (90·5)
13	—	—	—	1 (92·8)
15	—	—	—	1 (95·2)
19	—	—	1 (50)	—
20	—	—	2 (75)	—
21	—	—	1 (87·5)	—
25	—	—	1 (100)	1 (97·6)
28	—	—	—	1 (100)
Total cases..	1	4	8	42

REACTIONS ON INOCULATION.

This matter is of considerable importance both to the individual inoculated and to a hospital administration. I have, therefore, kept careful records of all reactions, and the results are shown in Table II.

TABLE II.

Local.		General.		Combined local and general.		Total.
Slight.	Mod.	Slight malaise	Mod. malaise with vomiting.	Slight local and slight general.	Slight local with mod. malaise and vomiting.	
12	1	5	2	2	3	25

The reactions were, generally speaking, either completely absent or very slight, although in one case in my series it was necessary to abandon immunisation on this account. The comparative absence of reactions is all the more striking when it is realised that all the subjects were of adult age, for it is well known that, whereas with the older prophylactics reactions were uncommon in children, the reverse was the rule in adults. A local reaction was classified as slight if there was no more than a little redness or tenderness at the site of inoculation. The one noted as moderate had redness and swelling, involving one-third of the upper arm and lasting about three days. In four of the five cases in which vomiting occurred, it was after the second injection. The one case in which immunisation was abandoned was 27 years of age and, as might have been expected, a combined pseudo and positive reactor. She showed marked redness, pain, and swelling of the upper arm, vesiculation around the site of inoculation, and considerable malaise after the first inoculation. No further dose was therefore given.

DIPHTHERIA DURING THE COURSE OF IMMUNISATION.

Four nurses developed undoubted faucial diphtheria before immunisation was complete and negative Schick reactions obtained.

CASE 1.—The onset was on the thirteenth day after her second inoculation—i.e., the day before the third dose was due. The Schick reaction was still positive 15 weeks after the onset of her attack, when she received a further 1 c.cm. of prophylactic. A second re-test four weeks later proved negative.

CASE 2.—The onset in this case was five weeks after the last of three fortnightly inoculations, when she was still Schick-positive. No further doses were given, but the Schick reaction was negative eight weeks later. She remained a nasal and faucial carrier for six weeks.

CASE 3.—This nurse received only two fortnightly doses of prophylactic and developed faucial diphtheria six weeks after the second. She became Schick-negative three weeks later.

CASE 4.—In this instance an attack of faucial diphtheria occurred 12 weeks after the last of four doses. The antitoxin content of the blood was then estimated and found to be less than 1/50 of a unit per c.cm.

None of these cases had any reaction, either local or general, after the injections, and the attack of diphtheria was mild and uncomplicated in every instance. The mildness of these cases helps to dispose of the negative phase bogy.

It must be borne in mind that these cases all occurred in newly joined nurses who had come from country districts where the natural immunity is low and that, once in the hospital, they were continuously liable to heavy doses of infection.

Conclusions.

The preparation of diphtheria toxoid-antitoxin floccules used in this work is an efficient and rapidly immunising antigen which definitely protects against diphtheria. Its use in adults is not commonly followed by unpleasant reactions and, with rare exceptions, in the few instances when these do occur they are of a trifling character. A preliminary small injection of the prophylactic is unnecessary, and the best results are obtained by giving a course of three inoculations of 1 c.cm. each with an interval of two weeks between doses.

I would like to acknowledge my indebtedness to Dr. R. A. O'Brien, of the Wellcome Research Laboratories, for his kindness in supplying the prophylactic; to Dr. P. Hartley, of the National Institute for Medical Research, for kind help in regard to the literature of the subject; and to Dr. A. Joe, medical superintendent of the North-Western Hospital, for valuable suggestions.

REFERENCES.

1. Park, W. H., Banzhaf, E. J., Zingher, A., and Schoder, M. C.: Amer. Jour. Pub. Health, 1924, xiv., 1047.
2. Sordelli, A., and Serpa, R.: Comptes rend. Soc. de biol., 1925, xcii., 824.
3. Hartley, P.: Brit. Jour. Exp. Path., 1925, vi., 112, and 1926, vii., 55.
4. Glenny, A. T., Pope, C. G., Waddington, H., and Wallace, U.: Jour. Path. and Bact., 1926, xxix., 31.
5. Glenny, and Pope: Ibid., 1927, xxx., 587.
6. O'Brien, R. A.: Brit. Med. Jour., 1928, ii., 434.
7. Dudley, S. F.: Quart. Jour. Med., 1929, xxii., 321.
8. Schmidt, H. and Scholz, W.: Arch. f. Hyg., 1925, xcvi., 251.
9. Eberhard, H. A.: Zeit. f. Hyg. u. Infect., 1926, cv., 614; Idem., Deut. med. Woch., 1928, liv., 91.
10. Soldin, M.: Münch. med. Woch., 1929, lxxvi., 1208.
11. Kelleher, W. H.: Annual Report Metropolitan Asylums Board, 1926–27, p. 199.