till after the fifth and eighth days. From this table all cases have, of course, been excluded which ran an afebrile course throughout, and also those dying during the treatment. The figures, therefore, rather understate the result, since in the antitoxic series the mortality is much less, and therefore the number of recoveries of severe cases with more prolonged temperature is greater.

EFFECT OF ANTITOXIN ON OTHER SYMPTOMS.

Paralysis was observed only in 23 of the 178 cases during the time they were in the hospital; but it occurred after leaving the hospital in several children who attended later as out-patients, and probably in others who were not seen again; so that it is impossible to say in what proportion of cases it was produced; but it is probable that in these cases, as in other recorded series, the frequency of paralysis has not been reduced by the antitoxin treatment.

As to the effect on the duration of membrane in the throat, albuminuria and other symptoms, it is impossible to speak definitely, as no exact particulars as to these facts can be obtained for the pre-antitoxin years, and so no comparisons can be instituted; but it is a matter of ordinary clinical observation that the duration of visible membrane is much shorter in the antitoxin cases; and also that it is extremely rare to observe any spread of the membrane either locally in the throat or to previously unaffected parts such as the nose and larynx, after twenty-four hours from the time of injecting the serum.

BAD EFFECTS OF ANTITOXIN.

In 49 of the 178 cases rashes were observed. The rash was urticarial in 19 cases, erythematous or scarlatiniform in 16, papular or morbilliform in 14. In 8 cases it appeared between the second and fifth day, in 25 between the sixth and tenth, and in 16 between the eleventh and fifteenth. In most cases the rash caused no disturbance or uneasiness except some itching; but in 13 cases there was a rise of temperature, and in four cases more or less severe joint pains with some synovial effusion, affecting only the larger joints, especially the hip, knee, and shoulder. In 3 of these cases with joint pains the temperature reached 104°. In 1 case an abscess formed at the seat of injection. This must have been due to some fault in the technique of the injection and not to the serum; as the serum then in use was at once examined bacteriologically with a negative result both at the laboratories of the Royal Colleges of Physicians and Surgeons and by us. No other bad symptom was seen, which could be ascribed to the antitoxin.

CONCLUSIONS.

1. The great reduction seen both in our total and tracheotomy mortality can be only due to the treatment with antitoxic serum, for the examination of the cases reveals no other factor capable of producing this result.

2. The full benefit of antitoxin was not obtained until fairly large doses (on an average between 7,000 and 8,000 normal units) were employed; the mortality then fell from 28 per cent. in the first antitoxin year to 17.7 and 17 per cent. in the next two years. Each case of diphtheria should have an initial dose of not less than 6,000 normal units.

3. Since antitoxin has but little effect on the mortality when given after the fourth day, it should be administered as soon as the patient is seen without waiting for the bacteriological diagnosis, and the full dose should be given immediately in one injection, not in divided doses on successive days.

4. Not only does antitoxin reduce the mortality, but it also distinctly lessens the severity of the disease in cases which recover. This is best shown by the effect on the duration of the fever, which in our series lasted only four days in a very much larger proportion of antitoxin than of pre-antitoxin cases.

5. The effect of antitoxin is chiefly seen in its specific action of the diphtheritic membrane, as shown by the cessation of its spread and more rapid clearance, and also by the greatly-lessened mortality of such cases in which the chief danger is from extension of membrane, the mortality of tracheotomy cases especially being reduced from 65.5 to 26.4 per cent., a greater reduction than seen in the other cases.

REFERENCE.

¹ BRITISH MEDICAL JOURNAL, 1898, vol. i, p. 1455.

FURTHER NOTE ON BILE AS AN ANTIDOTE TO VENOMS AND DISEASE-TOXINS.

By T. R. FRASER, M.D., F.R.S., F.R.C.P.E.,
Professor of Materia Medica and Clinical Medicine, University of Edinburgh.

I HAVE already shown that the bile of several animals possesses antidotal properties against serpents' venom and against the toxins of such diseases as diphtheria and tetanus, and that the bile of venomous, or more correctly of nocuous serpents is specially powerful as an antidote against the venom of serpents.¹ The experiments have been extended, with the result that further proof of these propositions has been obtained.

Taking, in the first place, the dry Indian cobra venom, whose minimum lethal dose for rabbits is slightly less than 0.0024 g. per kilo., in a series of *in vitro* experiments a definition has been obtained of the smallest quantity of the dry bile of several serpents, nocuous and innocuous, and of a number of higher animals, to render non-lethal 0.0025 g. per kilo. of this venom, when solutions of each were mixed together and left in contact for ten minutes. The quantity of each bile required per kilo. of animal was approximately:

Crotalus bile...	0.0005 gramme	Indian python bile	0.005 gramme
African cobra bile...	0.001 "	Grass snake bile	0.0065 "
Pseudechis bile	0.002 "	Rabbits' bile	0.0075 "
Puff adder bile	0.003 "	Human bile...	0.015 "
Daboia bile	0.003 "	Ox bile	0.02 "
Indian cobra bile	0.004 "	Pig's bile	0.02 "

Corresponding results have been obtained with the venom of several other species of serpents.

The most important results are that the bile of nocuous or venomous serpents is the most powerful antidote to venom, and is closely followed in efficiency by the bile of innocuous serpents, while the bile of animals having no venom-producing glands—as man and the ox, pig, and rabbit—while definitely antidotal, is less so than the bile of innocuous serpents, and much less so than the bile of nocuous or venomous serpents. It is remarkable to find that the bile of one species of venomous serpent may actually be a more powerful antidote against the venom of another species than is the bile produced by this species, and that there is no direct correspondence between the toxic activity of the venom produced by a serpent and the antidotal power of the bile of that serpent.

Extending these experiments to the toxins of disease, it was found, in the case of a specimen of diphtheria toxin whose minimum lethal dose for rabbits was 0.05 c.cm. per kilo., that a dose of 0.1 c.cm. per kilo. could be rendered non-lethal by:

Daboia bile	0.025 g. per kilo.	Ox bile	0.1 g. per kilo.
Rabbits' bile	0.02 "	Human bile...	0.15 "

When tetanus toxin, tested, however, in guinea-pigs, was similarly examined, in a dose of it exceeding the minimum lethal considerably more than in the experiments with serpents' bile and with diphtheria toxin, the results were that the smallest quantity of bile able to prevent death from occurring was with:

Daboia bile	0.005 g. per kilo.	Human bile...	0.15 g. per kilo.
Rabbits' bile	0.005 "		

The biles tested against toxins have been comparatively few in number, because the deterioration which rapidly occurs in the strength of toxins prevents a large number of consecutive experiments from being made with the same specimen. With the exception of human bile, all the biles were taken from the gall bladder. The bile, therefore, of the venomous serpents examined has also more antidotal power against the toxins of disease than the bile of the majority of non-venomous animals. It is noteworthy that among the non-venomous animals, the rabbit should produce a bile definitely superior to the others in antidotal quality against not only toxins but also venoms.

As disease toxins and venoms are excreted from the blood into the intestinal canal, the antidotal bile which they must there be brought into contact with, constitutes a potent means of defence of the body by rendering the toxins and venoms inert before they can be absorbed from the intestines into the blood. The therapeutic importance of remedies that are able to increase the hepatic secretion is thus indicated. Although

not yet experimentally demonstrated, it may be inferred, almost as a corollary from the above, that poisons generated in the intestinal canal will also be rendered inert by bile. Traditional belief is clearly in favour of the view that certain forms of disordered health are produced by deterioration in the functions of the liver. Many of these disorders are now referred to auto-intoxication, and the advantage of cholagogue treatment thus finds an intelligible explanation.

While all the biles examined are antidotal against both toxins and venoms, it is shown that the bile produced by an animal in whose body venom is present is much more antidotal against venoms than against toxins. It is thus indicated that a special antidotal constituent, additional to the ordinary constituents, is present in the bile of an animal whose body contains a poison of the nature of the venoms or toxins. In all probability this constituent is antivenin or antivenene, which has been eliminated from the blood into the bile, and which in an infective disease would thus reinforce the antidotal qualities common to the normal bile of all animals. This, no doubt, is the explanation of the favourable results which have been obtained by Koch and others in the treatment of rinderpest with the bile of animals which have been infected with the micro-organisms, and consequently with the toxin, of that disease.

As in the case of *in vitro* and other experiments with antivenene and venom, the experiments with bile afford strong evidence in favour of the view, which in opposition to prevailing views I had ventured several years ago to suggest, that the antidotal or curative effects of antivenene and of disease antitoxins are of a chemical or physical, and not of a biological, nature.

REFERENCE.

¹ *Proc. Roy. Soc. of Edinburgh*, xxi, 1897, 457-565; *BRITISH MEDICAL JOURNAL*, September 4th, 1897, p. 595.

MEMORANDA:

MEDICAL, SURGICAL, OBSTETRICAL, THERAPEUTICAL, PATHOLOGICAL, ETC.

INTESTINAL OBSTRUCTION DUE TO INDURATION OF THE GREAT OMENTUM.

A MAN, aged 66, came under observation in June, 1895, suffering from ulceration of the left leg. The lower half in nearly the whole circumference was a discharging ulcer with three sinuses leading to a thickened tibia. In addition to this lesion he had a scar on the forehead very suggestive of a healed gumma, with exfoliation of the outer table of the frontal bone. A nasal intonation of the voice was present without apparent cause in the soft palate or nose. In addition there was a marked condition of knock-knee on the left side, with considerable enlargement of the internal condyle of the femur. The case was regarded as one of tertiary syphilis. During the succeeding two years he had occasional attacks of vomiting, which easily yielded to treatment, and the condition of his leg improved but never entirely healed up till just previous to his last illness, when the ulcer was replaced by a firm white scar with cessation of discharge from the sinuses. For some months previous to his death he was subject to constipation.

On December 17th, 1897, he commenced to vomit, and had pain in the epigastric region. His bowels were relieved by an enema, and under treatment the stomach became less irritable, and some amount of nourishment was subsequently retained with occasional vomiting. The vomit was not faecal. Lying across the abdomen from right lower to left upper regions was an ill-defined fixed resistance, best felt on the left side just above the umbilicus, at which spot the fingers below and to the left could define an edge on a level with a transverse division of the rectus muscle giving the impression of a tumour, while at no other point could the limits of it be differentiated. There was no fluid in nor distension of the abdomen.

On December 25th, in spite of his illness, he obtained a small portion of currant cake which he retained. No change in condition occurred till ten days later when with renewed

vomiting the currants were returned undigested, the vomit having a faintly faecal odour. As there had been no relief from the bowels for seven days an enema was administered with practically no result. From this date everything taken by the mouth was immediately returned, and although fed by nutrient enemata his condition did not improve. On January 11th it was obvious that he had peritonitis, and death ensued on the following day.

A *post-mortem* examination revealed the presence of free non-faecal fluid in the peritoneal cavity with a few flakes of lymph here and there. The large intestine was empty, the small containing a little faecal matter. The ill-defined resistance proved to be the great omentum, very much indurated, surrounding the transverse colon. Contraction had occurred to such an extent that the lumen of the gut for a length of 6 inches or more would just admit a fine penholder. The stomach was closely attached to this, but there was no abnormality nor disease of it. The pylorus, pancreas, and liver appeared natural.

I am indebted to Dr. C. P. White, Pathologist to the General Hospital, Birmingham, for examining the specimen, and he reports, "Microscopical examination shows great increase of fibrous tissue which stains extremely badly, and here and there a few nodules of granulation tissue. The colon wall contains a large excess of fibrous tissue, and there is some hypertrophy of the muscular coat."

The absence of evidence of malignant disease after death, and the lesions present during life would suggest a syphilitic origin of the induration of the omentum.

Herne Bay.

T. ARMSTRONG BOWES, M.D. Cantab.

TETANUS NEONATORUM.

ON July 2nd Mrs. H., wife of an engine driver, was delivered of a healthy female child after a short and easy labour. I was not present at the birth, but saw the infant shortly after delivery. On the fourth day I was sent for to examine the baby, who was reported as being "strongly convulsed." The aspect of the child was very striking; marked risus sardonius, the lower jaw was protruded and tightly fixed so as to limit the introduction of even my little finger; the spasm of the body was opisthotonic, it extended to all the limbs, and was much aggravated by handling. I directed my attention to the umbilical wound, and found that the cord had separated, leaving an angry inflamed surface, but with no appearance of enlarged veins diverging as described by Gowers. The infant died from exhaustion twenty-four hours after my first visit in spite of the free use of sedatives such as chloral, belladonna, and bromide of potassium.

The most interesting point in the case was the fact that the umbilical stump had been dressed by the "wise woman" with a raisin, which I learnt is a usual vulgar application in this district. One would be tempted to attribute this untoward infection to the seemingly harmless dressing sanctioned by traditional custom, and an opinion that the germs were present in the dried fruit is strengthened when we recall the process used for drying grapes in Southern Italy, Sicily, and other vine-bearing countries. Tetanus is very frequent in Italy, the soil often laden with the bacilli; so the chain of evidence is complete enough to afford a warning.

We could hardly suggest the adoption of Baccelli's injections of carbolic acid for such tender patients, and the lean results of the serum cure do not warrant a general reliance in the antitoxin. One thing we can do, and that is see to the asepsis of the cord and its stump from the first day, and discountenance the fallacious teachings of legendary handy-woman-craft.

Maidstone.

A. DILLON CARBERY.

A NOTE ON GLYCERINATED CALF LYMPH.

IN April of the present year I purchased glycerinated calf lymph in capillary tubes from four different sources, and tested them by a series of surface plate cultures with the following results:

Specimen 1.—From 12 to 20 colonies of staphylococcus, streptococcus, and bacilli (nature undetermined).

Specimen 2.—From 20 to 25 colonies of staphylococci, bacilli, and penicillium glaucum.

Specimen 3.—From 4 to 6 colonies of staphylococcus and yeast¹

Specimen 4.—Four colonies of staphylococcus and bacilli