this contamination from culture media these precautions may prove unnecessary. On the other hand, in the case of all those organisms which we have shown to be characterized by their ability in the living state to elaborate toxic derivatives from the media of artificial growth, these precautions cannot be neglected.

In conclusion, although it is premature to indicate the practical lines of direct immunity research opened up by these experiments, it is impossible to ignore the suggestions they offer as to the meaning of sensitization and the superiority of living vaccines over dead, as well as to the necessity for re-examination of the whole scheme of vaccine-therapy. And in the meanwhile, if they do no more than press home the necessity for fresh investigations into the true source and character of the natural antigens of disease they will faithfully have served their purpose.

NOTE.—Since this paper was placed in type two articles on experimental fever have appeared in a German periodical by Thiele and Embleton which might seem at first sight to affect some of the conclusions reached in this communication.⁹ In the articles referred to, the authors—as so many have done before them—have fallen victims to the very fallacies which Dr. Penfold and I have already exposed in the English journals.¹⁰ One of the fundamental errors, for example, in all study of experimental fever produced by injection is the assumption that water which is innocent of demonstrable infection at the time of injection must also be innocent of pyrogen, and that water collected direct from the condenser of a distilling apparatus in daily use and then filtered is necessarily pure water. In consequence, therefore, of failure to recognize this source of error these workers in many of their experiments unwittingly used impure water, as is clearly shown in their own protocols. This accident is alone sufficient to invalidate all the experiments and deductions based thereon, though there are other fallacies of almost equal importance which I have fully described elsewhere.

REFERENCES.

- ¹ Hort, E. C.: Autoxaemia and Infection, *Proc. Roy. Soc., B*, vol. lxxxii, 1910.
- ² Hort and Penfold: A Study of the Pyrogenetic Properties of *B. typhosus*, *BRITISH MEDICAL JOURNAL*, November 9th, 1912.
- ³ Hort and Penfold: Micro-organisms and their Relation to Fever, *Journ. of Hygiene*, vol. xii, No. 3, October 21st, 1912.
- ⁴ Hort and Penfold: Further Studies in Experimental Fever, *Proc. Roy. Soc. Med.*, 1912, vol. vi (Path. Sect.), pp. 76-84.
- ⁵ Emery: Immunity and Specific Therapy, 1909, p. 393. S. Martin, *Manual of Path.*, 1904, p. 77 et var.
- ⁶ Hort and Penfold: The Dangers of Saline Injections, *BRITISH MEDICAL JOURNAL*, December 16th, 1911, p. 1510.
- ⁷ Hort and Penfold: A Critical Study of Experimental Fever, *Proc. Roy. Soc., B*, vol. lxxxv, 1912, p. 175.
- ⁸ Hort: Normal and Immune Serum-Therapy, *BRITISH MEDICAL JOURNAL*, November, 1911.
- ⁹ *Zeitschrift für Immunitätsforschung*, 1913.
- ¹⁰ The Relation of Salvarsan Fever to other Forms of Injection Fever. *Proc. Roy. Soc. Med.*, 1912, vol. v (Path. Sect.), p. 137. Chart.

APYREXIAL TYPHOID.

BY

NORMAN FLOWER, M.A., M.B., B.Ch.Oxon.,

YEovil.

APYREXIAL typhoid, although known to exist, is of excessively rare occurrence, and may therefore readily pass unrecognized, particularly in the absence of an epidemic of the disease. Cases of this type have been described by Gerhardt and Dreschfeld, and of these brief mention is made by the latter in Allbutt's *System of Medicine*.

In typhoid fever we know that, in patients of over 40 years of age, the temperature curve is lower and less characteristic, but although cardiac, pulmonary, and renal complications are more common, splenic enlargement and rose rash are frequently absent. For these reasons, therefore, the diagnosis may be rendered more difficult. The case recorded below will serve to illustrate these points.

The patient was a woman aged 60, who had resided in the same house for more than thirty years, and during that period had never required medical assistance for more than minor ailments. A careful investigation into her previous history precluded all possibility of any previous attack of typhoid fever.

The present illness commenced in the first few days of September, with the usual feelings of malaise, and with gradually increasing diarrhoea. She took to her bed on September 8th.

When first seen, on September 10th, the patient was in an exhausted condition, with a dry, furred tongue and subnormal temperature. The outstanding feature of the case at the time was the exceedingly profuse diarrhoea, which persisted in spite of all the usual remedies. On September 12th (two days later) the patient began to wander, and sank into a semi-comatose state, in which she remained for the ensuing fourteen days. During this period the intestinal symptoms were unchanged, there was a moderate distension of the abdomen, but no spots or enlarged spleen were present then or later. Widal's reaction on September 16th was positive in every dilution. From the onset of the attack until September 25th (that is, the fourth week of the disease), when complete consciousness returned, the mouth and surface temperatures were invariably subnormal, and the rectal temperature, taken twice daily, never exceeded 99.4°. From September 26th to October 4th the mouth and rectal temperatures each reached their maximum of 99.6° and 100.4° respectively, after which they dropped again.

During the fourth week a further specimen of serum was obtained for the purpose of comparative agglutination reactions to *B. typhosus* and other allied organisms, with the following results:

- B. typhosus* agglutinated up to 1 in 2,000.
- B. paratyphosus B* agglutinated up to 1 in 200.
- B. paratyphosus A* agglutinated very slightly.
- B. enteritidis* (Gaertner) agglutinated not at all.

The patient ultimately made a good recovery, and without serious complications.

An investigation of the water-supply of the (isolated) dwelling revealed a privy in close proximity to the well, which constituted the sole supply of drinking water on the premises. This water, on examination by the county authority, proved to be contaminated with sewage.

In the light of all the bacteriological findings, I think there can be very little doubt that in this case there existed a true typhoid infection.

A SIMPLE AND RAPID METHOD FOR THE ADMINISTRATION OF SUBCUTANEOUS SALINES.

By E. MUSGRAVE WOODMAN, M.S., F.R.C.S.,

ASSISTANT SURGEON, GENERAL HOSPITAL, BIRMINGHAM.

THE administration of saline solution by the method of subcutaneous injection has many points in its favour and should by no means become obsolete. There is no method to equal it when the absorption of a large quantity of fluid is required.

In numerous cases of late years I have made use of an apparatus which, from its convenience and simplicity, has served to replace more cumbersome methods.

The only requisites are (1) a large silver cannula from a Southey's tube apparatus; (2) Southey's rubber tubing; (3) a small piece of glass tubing, narrow at one end to fit this tubing, and larger at the other (for this an ordinary clean fountain-pen filler does very well); (4) a large glass funnel connected to the glass tube by rubber. The various parts are joined together and the whole is sterilized by boiling.

The mode of introduction deserves special notice, for it differs considerably from the usual method. The anterior axillary fold is grasped firmly and drawn outwards. The trocar with its cannula is then passed into the skin in a direction vertical to the chest wall and is pushed steadily through the axillary fold so that its point emerges within the axilla. The trocar is then withdrawn and the cannula is pressed onwards into the axilla until its shoulder rests flush with the skin.

The fluid as it emerges from this cannula spirts in all directions and is poured out into three distinct plains, separated anatomically into watertight compartments by the deep fascial layers. Into the most superficial of these

G1, Glass funnel. R1, Large bore rubber tubing. G2, Glass tube. R2, Southey's rubber tubing. T, Trocar. C, Cannula.

fluid flows into the fatty tissue over the pectoral muscle and around the breast and extends upwards over the clavicle into the neck. Beneath this saline exudes into the pectoral muscles and is limited by the deep fascia on either side. Absorption is here rapid owing to the great vascularity of the part and to the pressure maintained by the fascial limitations. Lastly distension of the axillary space takes place and the normal concavity of the axilla is replaced by a rounded swelling.

Fluid is absorbed very rapidly when introduced in this way and two pints can be run into the tissues in twenty minutes, little trace of swelling being found. After an hour the cannula is left *in situ*, and the administration can be repeated as often as necessary.

This method has one disadvantage, and I think only one. The introduction is rather painful, but hardly more so than when the needle is merely inserted beneath the skin, while the pain resulting from distension is largely obviated. But in the majority of cases the patient is still under the influence of the anaesthetic when the administration is given or is so collapsed as to be insensitive to pain.

This objection is more than compensated for by the ease of introduction and rapidity of absorption of a large quantity of saline by means of a simple appliance which every practitioner has at his command.

ADRENALIN IN THE EMERGENCY TREATMENT OF NON-CORROSIVE POISONING BY THE MOUTH

(CYANIDE, STRYCHNINE, ACONITE, ETC.).

BY

JUDAH LEON JONA, D.Sc.ADEL., M.D., B.S.MELB.,
BEIT MEMORIAL FELLOW, LISTER INSTITUTE; FORMERLY ASSISTANT
LECTURER IN PHYSIOLOGY, UNIVERSITY OF MELBOURNE.

WHEN a chemical substance enters the stomach or bowel it must first be absorbed into the circulation before it can exert a general direct action on the body. One of the chief factors determining the rate of absorption of any substance introduced into any part of the gastro-intestinal tract is the vascularity of the part, and particularly of the lining membrane. Now if, after the introduction into the stomach of a poisonous chemical substance whose general toxic action depends partly upon the rate at which it enters the circulation, we are able to limit the rate of absorption of the drug—for example, by diminishing the blood supply to the mucosa of the stomach—time is provided for the preparation and adoption of methods to neutralize any possible action which would normally follow the introduction of the particular substance into the stomach, either by removing it altogether by means of a stomach tube and a stomach wash-out, or by inactivating it by means of a chemical antidote. Particularly valuable would such an agent be which would lower the rate of absorption into the circulation of a substance which, entering the blood in large quantity, would destroy the life of the individual, but which the body is able, by the exercise of special powers, to efficiently neutralize when it gains entry into the economy slowly. To such a category belong the cyanides. Theis⁸ and Buttrick¹ have demonstrated that when an animal has been killed by a lethal dose of KCN the amount of cyanide present in the organs diminishes on standing, while Lang⁴ and Grober⁵ have shown that when HCN is introduced into the diet of an animal the amount of cyanide in the stomach diminishes, while the amount of sulphocyanate in the saliva and urine is increased.

Intraperitoneal injection of adrenalin has been found by Exner² to diminish the rate of absorption of a poison, such as strychnine or potassium cyanide, when introduced into the stomach. This academical piece of work suggested the investigation of the effect of the introduction of adrenalin* into the stomach on the absorption of rapidly-acting poisons, such as cyanides, strychnine, and aconite, also introduced into the stomach, and whether such administration of adrenalin had any value in the practical

treatment of cases of accidental poisoning by these rapidly-acting drugs.

CYANIDES.

The hitherto generally recognized antidote in cases of cyanide poisoning has been that advocated by Professor C. J. Martin and Mr. J. A. O'Brien.⁵ Its principle is the formation in the gastro-intestine of Prussian blue, which is a practically innocuous substance, by the administration subsequent to the cyanide poisoning of ferrous sulphate and alkali. They proposed that 30 c.cm. (1 oz.) of ferrous sulphate solution of 23 per cent. strength, 30 c.cm. (1 oz.) of KOH (5 per cent. solution), and 2 grams (30 grains) of magnesia, the former two kept in hermetically sealed phials, be mixed and immediately taken. In their experiments on rabbits, using a lethal dose of 0.01 gram, given as 10 c.cm. of a 0.1 per cent. solution of KCN per kilogram of body weight, they found that death invariably ensued unless the antidote were administered within five minutes. Considering that the antidote consists of three separate ingredients, which must be mixed before use, the preparation of the antidote must occupy time and would probably take about two minutes, even if everything were at hand; so that if about three minutes were lost before discovering that cyanide had been accidentally taken, the patient's chances of recovery would be very small, for we may legitimately assume that the respite or "latent period" would only be a little if any longer in the human being than in the rabbit. Also, the ordinary medical man might not have the antidote ready at hand, and the value of some means of delaying the absorption of the poison from the gastro-intestine is apparent, and this is especially so in the case of poisoning by cyanide, whose action is so rapid.

Intraperitoneal injections of adrenalin having been found to diminish the rate of absorption of strychnine introduced into the stomach,² it was therefore decided to try and see if adrenalin administered by the mouth would have any effect in giving us more time to treat a case of cyanide poisoning. As a preliminary investigation, KCN solution, of strength varying from 1 per cent. to 5 per cent., was painted on various mucous membranes (conjunctiva, buccal mucous membrane, gastric mucosa) for five minutes, and then adrenalin (1 in 10,000) painted on, when blanching occurred in every case.

These experiments showed that adrenalin will still exert its vaso-constrictor action even after the arteriolar wall has been subjected to cyanide.

Further experiments showed that when adrenalin solution was administered (about 4 to 5 c.cm. 1 in 10,000 solution per kilogram body weight, the rabbit receiving the lethal dose of 0.01 gram KCN per kilogram body weight) either with or subsequently to the administration of the poison the animal's life was prolonged, and if the adrenalin solution were administered within five minutes of the poison, and Martin and O'Brien's antidote given, or the stomach washed out within four or five minutes subsequent to the administration of the adrenalin, the animal's life would be saved. Thus, the administration of adrenalin "on sight" would give a respite of some minutes during which the antidote could easily be prepared and administered or the stomach contents evacuated.

The results of a few of the more crucial experiments are appended. A number of experiments have been discarded because the rabbits did not tolerate the washing out of the stomach to which many were subjected. It may also be stated at the outset, that Martin and O'Brien⁵ found that if a dose of cyanide were going to prove fatal the rabbit always died within thirty minutes, so that we may take it that if we are able to tide a patient over the fatal thirty minute limit by any means at our disposal, then the patient will have a very fair chance of recovery. Of course, if it be borne in mind that the adrenalin only delays the absorption of the poison (principally by its vaso-constrictor action on the vessels of the mucosa), it will be recognized (as Experiment No. 4 shows) that those cases are practically hopeless in which a large dose of the poison has been taken and in which the amount of poison being absorbed through the mucosa even under maximal adrenalin influence exceeds the lethal limit, unless the chemical antidote be immediately given or the stomach immediately evacuated. The time relation here indicated (namely, that the pathological effect depends to a certain degree upon the amount of poison coming into contact with the tissues per unit of time), and the fact that the administration of

* Throughout this investigation adrenalin (P. D. and Co.) and hemisine (B. W. and Co.) were both used with the same effect.