

brief, and must leave open many important questions.

The investigations have been carried on under my direction by Dr. A. Libbertz and Stabsarzt Dr. E. Pfuhl, and are still in progress. Patients were placed at my disposal by Professor Brieger, from his polyclinic; Dr. W. Levy, from his private surgical clinic; Geheimrath Drs. Fräntzel and Oberstabsarzt Kohler, from the Charite Hospital; and Geheimrath v. Bergmann, from the surgical clinic of the University. I wish to express my thanks to these gentlemen.

As regards the origin and the preparation of the remedy, I am unable to make any statement, as my research is not yet concluded. I reserve this for a future communication.*

The remedy is a brownish, transparent liquid, which does not require special care to prevent decomposition. For use, this fluid must be more or less diluted, and the dilutions are liable to undergo decomposition if prepared with distilled water. As bacterial growths soon develop in them they become turbid, and are then unfit for use. To prevent this, the diluted liquid must be sterilized by heat and preserved under a cotton-wool stopper, or, more conveniently, prepared with a one half per cent. solution of phenol.

It would seem, however, that the effect is weakened both by frequent heating and by mixture with phenol solution, and I have therefore always made use of a freshly-prepared solution. Introduced into the stomach the remedy has no effect. In order to obtain a reliable effect it must be injected subcutaneously, and for this purpose we have exclusively used the small syringe suggested by me for bacteriological work. It is furnished with a small India-rubber ball and has no piston. This syringe can easily be kept aseptic by the use of absolute alcohol, and to this we attribute the fact that not a single abscess has been observed in the course of more than a thousand subcutaneous injections.

The place chosen for the injection, after several trials of other places was the skin of the back between the shoulder-blades and the lumbar region, because here the injection led to the least local reaction—generally none at all, and was almost painless. As regards the effect of the remedy on the human patient, it was clear from the beginning of the research that in one very important particular the human being reacts to the remedy differently from the animal generally used in experiments, namely, the guinea-pig. A new proof for the experimenter of the all-important law that experiment on animals is not conclusive, for the

human patient proved extraordinarily more sensitive than the guinea-pig. As regards the effect of the remedy, a healthy guinea-pig will bear a subcutaneous injection of 2 cubic centimetres, and even more, of the liquid without being sensibly affected; but in the case of a full-grown healthy man 0.25 cubic centimetre suffices to produce an intense effect. Calculated by the body-weight, one-fifteen-thousandth part of the quantity which has no appreciable effect on the guinea-pig acts powerfully on the human being.

The symptoms arising from an injection of 0.25 cubic centimetre I have observed after an injection made in my own upper-arm. They were briefly as follows: three to four hours after the injection there came on pain in the limbs, fatigue, inclination to cough, difficulty of breathing, which speedily increased in the fifth hour, and were unusually violent. A chill followed, which lasted almost an hour. At the same time there were nausea, vomiting, and a rise of body temperature to 39.6° C.

After twelve hours all these symptoms abated, the temperature fell, and on the next day it was normal. A feeling of fatigue and pain in the limbs continued for a few days, and for exactly the same period of time the site of injection remained slightly painful and red. The smallest quantity of the remedy which will affect the healthy human being is about 0.01 cubic centimetre, equal to 1 cubic centimetre of the one-hundredth dilution. As has been proved by numerous experiments, when this dose is used reaction in most people shows itself only by slight pains in the limbs and transient fatigue. A few showed a rise of temperature to about 38° C.

Although the effect of the remedy in equal doses is very different in animals and in human beings, if calculated by body weight, in some other respects, there is much similarity in the symptoms produced, the most important of these resemblances being the specific action of the remedy on the tuberculous process, the varieties of which I will not here describe. I will make no further reference to its effects on animals, but I will at once turn to its extraordinary action on tuberculosis in human beings. The healthy human being reacts either not at all, or scarcely at all, as we have seen when 0.01 cubic centimetre is used. The same holds good with regard to patients suffering from diseases other than tuberculosis, as repeated experiments have proved; but the case is very different when the disease is *tuberculosis*. A dose of 0.01 cubic centimetre injected subcutaneously into tuberculous patients causes a severe general reaction as well as a local one.

I gave children aged from two to six years one-tenth of this dose, that is to say, 0.001 cubic centimetre—very delicate children only 0.0005 cubic centimetre—and obtained powerful, but in no way dangerous reaction. The general reaction consists

*Doctors wishing to make investigations with the remedy at present, can obtain it from Dr. A. Libbertz, Lüneburger Strasse, 28, Berlin, N. W., who has undertaken the preparation of the remedy with my own and Dr. Pfuhl's co-operation, but I must remark that the quantity prepared at present is but small, and that larger quantities will not be obtainable for some weeks.