the dementia which is the last scene in the history of many a once great mind. There may be difficulty in determining the extent of this at the commencement; questions of diagnosis and of mental responsibility may arise, but of the prognosis there can be no doubt. But one meets with a certain number of cases of mania, and more frequently of melancholia, in old people, many of whom recover in a surprising way.

The year before last I was asked to see an old lady of 75 years, whose mental and bodily strength had been failing, as her medical man had told me, for six months. She did not know where she was, though she was in her own house, where she had lived for many years, and she had all kinds of delusions. Being unmanageable there, she was removed to an asylum, and everyone supposed it to be the beginning of the end. She was in a somewhat acute state for some weeks, had hallucinations of sight and many delusions, and then gradually improved, became perfectly clear in her mind and memory, and went home to the old house in less than three months recovered.

Dr. Clouston gives the particulars of 203 cases of senile insanity, excluding 101 others which were cases of epilepsy, mania or dementia of long standing, or climacteric insanity. He says that heredity as a cause was uncommon. The age was from 60 to 90 years, and of these 203 persons, 72 were discharged "recovered"—that is, in all of them their worst mental symptoms disappeared, they passing into normal senility. In many cases they became quite well in an absolute sense." This is in the proportion of 30 per cent.—a large number when the time of life is considered. So that our prognosis is not utterly without hope, though it may be doubtful or even unfavourable. It is to be remembered that all Dr. Clouston's patients and my own which I have mentioned recovered in asylums. I do not think the same results would be attained by any home treatment.

SOME RESEARCHES INTO THE CHEMISTRY OF TYPHOID FEVER.¹

BY

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IN a paper which we read at the Annual Meeting of the Association in 1893 we gave an account of some researches which we had carried out respecting the pathological effects of certain chemical substances extracted from the spleen after death from scarlatina. An opportunity having lately arisen of obtaining the spleens from five cases which had succumbed during the third week of enteric fever, it occurred to us that perhaps the same method of investigation might in this case also yield interesting results. In the following paper many of the minuter details of the work have been purposely omitted, since the method adopted was identical with that advocated by Sidney Martin in his various valuable papers on animal toxins, and followed by us in our former work.

MODE OF EXTRACTION, ETC.

The spleens were removed from the body as soon after death as possible, and, having been freely incised, were placed in bottles containing strong spirit. On their receipt at the laboratories the organs were thoroughly minced and the pulp mixed with an excess of absolute alcohol and put aside for some weeks, in order to ensure the coagulation of all the albuminous matter which might be present.

The next procedure was to separate the precipitate by filtration through linen, and, after washing the precipitate with absolute alcohol, to add the resultant fluids to the original spirituous solution. This mixture contained (a) any

albumoses or peptones which were present in the spleen, (b) alkaloids, (c) extractive matters and fat, (d) salts.

The solid residue was next extracted with distilled water, the process being aided by the employment of an automatic shaker. After a second filtration, which was generally a matter of some difficulty, a clear yellowish fluid was obtained, which contained nearly all the proteid material which had not been rendered insoluble by the action of alcohol. This watery extract was then added to the spirituous solution just mentioned, and the mixture concentrated *in vacuo* at a temperature not exceeding 40° C. By means of an apparatus devised by one of us, and now in frequent use at the laboratories, we were enabled to evaporate as many as six flasks at a time, the distillates being collected and preserved in separate vessels. The great saving of time secured in this way was an important point, since, owing to the low temperature at which the process of concentration had to be carried on, the operation was necessarily very tedious.

As soon as the contents of the flasks had attained a syrupy consistence, they were poured into a bottle containing a large quantity of absolute alcohol, the result of which was to produce a copious precipitate consisting of those proteid substances which had been dissolved in the water or weak spirit. As soon as the precipitate had settled, the supernatant fluid was poured off, evaporated as before, and the residue again treated with absolute alcohol, the manoeuvre being repeated until further precipitation failed to occur. The various precipitates were then collected, thoroughly washed with fresh alcohol, dried *in vacuo* over sulphuric acid, and preserved in a dry and well-stoppered bottle.

The alcoholic filtrate was next evaporated several times to dryness, the residue being extracted on each occasion with absolute alcohol, and then finally collected and preserved. Both these extracts were found to contain a certain quantity of fatty material, which imparted an acid reaction to their solutions. To eliminate this recourse was had to extraction with anhydrous ether and chloroform, after the plan devised by Sidney Martin. By these various processes we were enabled to obtain amongst others, the following chemical substances:

1. A material which was insoluble in absolute alcohol but freely soluble in water, and which afforded all the chemical reactions of an albumose. The maximum quantity of this substance, or more probably mixture of albumoses, which was extracted from a spleen, was 3.93 g., and the minimum 2.1 g.

2. A substance which was extremely soluble both in water and in absolute alcohol, and possessed most of the characteristic features of an alkaloid. The maximum amount obtained from any case was 0.8 g.

3. A dark-coloured, semi-solid material consisting of a mixture of fat and fatty acids (1.2 to 0.9 g.).

MODE OF ADMINISTRATION.

The animals which we employed in order to determine the pathological effects of the various chemical substances consisted of rabbits, guinea-pigs, and rats. In each instance the animal had remained for some time under observation prior to the commencement of the experiment, and a daily record was kept of its temperature and body weight. Each dose of the albuminous or alkaloidal substance was dissolved in 3 c.cm. of distilled water when required for use, but the fatty extract was reduced to a fluid state by the action of heat. In the case of the guinea-pigs and rats the injections were invariably made beneath the skin of the abdomen, but the rabbits were also submitted to the intravenous method of inoculation. The strictest antiseptic precautions were observed, and in no instance did we notice any signs of inflammation at the site of puncture. After an injection the animal was placed in a separate cage and its temperature recorded on a chart every hour or two. The condition of the appetite, the body weight, and the character of the dejecta were also noted day by day.

The animals were killed at intervals of time varying from a few hours to three weeks after the injection, and the principal organs of the body put aside for microscopical examination. The tissues were embedded in paraffin, cut with a rocking microtome, and the sections stained with hæmatoxylin and eosin.

¹ Report to the Scientific Grants Committee of the British Medical Association. This research was carried out in the laboratories of the Conjoint Board of the Royal Colleges of Physicians (London) and Surgeons (England), and we owe our best thanks to the Council of that body for the liberal accommodation provided, and to the Director, Dr. G. Sims Woodhead, for much valuable interest and criticism during the progress of our work.

1. *The Albumose*.—This substance gave rise to no immediate results when injected in the proportion of less than 0.02 g. per kilo. of the body weight, but larger doses were usually followed by symptoms of local irritation, the animals violently scratching or biting the site of puncture for some considerable time.

In rats and guinea-pigs the injection was sometimes followed by evidence of a general constitutional disturbance, characterised by a slow and laboured respiration, bristling of the hair, and frequent efforts at micturition and defecation. These symptoms, however, rapidly subsided, and the animal usually regained its normal condition within an hour.

The subcutaneous administration of the albuminous extract in doses exceeding 0.02 g. per kilo. of the body weight was invariably followed by fever. In each variety of animal the first effect of the injection was to cause a slight fall in the temperature of the body, but this seldom exceeded 1.5° F., and did not persist for more than an hour. When this phase of shock had passed off the thermometer in the rectum failed to show any evidence of fever until after the lapse of from four to five hours, when the mercury commenced to rise, and continued to do so until it attained a maximum of 105° to 106.5° F. After remaining at this elevated point for a variable period of time, the temperature gradually but steadily declined, and finally regained its normal point from 18 to 32 hours after the commencement of the experiment.