

and vomiting. A severe rigor set in, and the temperature had risen to 101°. The pulse was rapid and tumultuous. The patient became cyanosed. Respirations were rapid and stertorous. He became rapidly unconscious, with twitching of the hands and frothing at the mouth and nose. Profuse perspiration ushered in a violent convulsion. He had ten similar attacks following each other in rapid succession. These seizures were typical uræmic convulsions. Pilocarpine and venesection, baths, chloroform, &c., were all tried to alleviate his suffering and distress without success, and he died at 5.45 P.M. the same day.

*Remarks.*—The difficulty which surrounded the diagnosis of this most interesting case at a moment's notice will be evident at once, and several of my colleagues who were quite familiar with the early appearance of variola were startled at the eruption on the hands, wrists, and forearms, and admitted that it was an impossibility to distinguish the difference without minute examination and inspection of the fluid on puncture of the papule and a close analysis of the history of the case. There are several cases of a like nature recorded, after the internal administration of iodide of potassium, but I am unable to find any mention made of a typical, and what I should say in this case an aggravated, iodide rash, induced by the local application of the liniment to the skin of the back, which throughout remained in a healthy, unbroken condition. For a full description of the appearance and for the pathology and minute anatomy of the disease I beg to refer my readers to the account given at page 300 of Dr. Crocker's work on Skin Diseases, second edition.

Coldstream, N.B.

## ROUGH NOTES ON REMEDIES.<sup>1</sup>

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### No. IV.

#### MERCURY IN HEART DISEASE.

I HAVE been somewhat disappointed in the discussion at Edinburgh on cardiac stimulants, inasmuch as I see hardly any reference was made to the value of mercury in cases of heart disease. I fear that our views on this subject have not advanced of late, and the mind of the profession has not grasped the idea that mercury has a value in heart disease far beyond what may be termed its "alterative" action. The administration of this drug in cardiac dropsy and in all cases of passive congestion of the pulmonary and portal systems is as old as the hills, and we old-fashioned physicians know well enough that thirty or forty years ago no one thought of treating these conditions except by a mercurial pill followed by a saline or jalap purgative and a diuretic mixture containing digitalis. Then came the days when the diuretic mixture was changed for one of muriate or ammonio-citrate of iron with digitalis, and some of us will remember the remarkable papers of Dr. Handfield Jones on the value of this combination. Now we have come to the days of arsenic, strychnia, iodide of potassium, and a host of cardiac stimulants, together with rest and cardiac gymnastics. I expect that in all cases our remedies do but assist nature in bringing about healthy compensatory changes by preventing degeneration of the muscles and vessels of the heart and main bloodvessels. Repeated observation has convinced me that mercury possesses a value far beyond the supposed alterative nature of its action—not that it fails to relieve congested vessels by drainage or osmosis, for doubtless this lays the foundation of its further action on the heart itself, and it would fail to relieve the heart did it not eliminate biliary and other effete matter from the blood and tissues of the liver and portal system, for instance; but when due allowance has been made for these primary effects there remains strong evidence that it tells upon the heart itself. Its special benefits are exercised in cases of dilated and hypertrophied heart. By means of it the "thready," weak, rapid, and irregular pulse is made full, soft, regular,

and slow, with manifest relief of such symptoms as dyspnoea, pectoral weight and tightness, and sensations of faintness. The "angina sine dolore" is often marvellously relieved and removed by two or three grains of blue pill three times a day, and the severe forms of "angina pectoris" not unfrequently disappear under its influence. While the nitrites, nitroglycerine, &c., afford temporary relief, this remedy is much more permanent in its effects. Nor need I say that to give digitalis a fair chance it is absolutely necessary to pave its way by preliminary doses of mercury and to foster its action by repeated doses. Many of the cases where digitalis, &c., fail, or seem to fail by supposed accumulation depend on this, that we are giving the digitalis without the blue pill or calomel, and it often falls to the lot of the consultant to make a great hit by inserting the mercurial into the previous treatment. Much more true is this of iron and digitalis combined. We see a patient with engorged vessels and labouring heart taking iron and digitalis much to the detriment and not to the benefit of the case—each dose is but adding fuel to the fire—energising the heart in its futile attempts to drive the blood through the engorged vascular system, and thus exhausting the organ in its hopeless struggle. We change all this by frequently repeated doses of mercury; we drain the portal system, we exosmose the water from the general vascular system, we suck up dropsical accumulations, and by pushing the drug we get hold of the heart itself and produce the slow, soft, regular, and effectual pulse, giving the digitalis or strophanthus a fair chance to come in as cardiac tonics; and at last we complete the circle by arriving at the point whence we departed with the patient in a very different condition, and we can give the iron and digitalis now with impunity—nay, with immense benefit. Let the following case speak for itself, and its quotation is the more apt as the patient came from being under the care of an eminent Edinburgh physician in the very condition I have described—viz., a dilated and hypertrophied heart goaded to excess in a useless effort by iron and digitalis.

*A case of dilated and hypertrophied heart treated by 20,000 grains of blue pill; recovery from advanced cardiac dropsy followed by ten years of good health.*—The patient, a hard-working man, was a Scotchman, and had all the talent, physique, and energy peculiar to his race. He gradually developed symptoms of valvular disease and dilated heart when about forty-eight years of age. He went to Edinburgh and was under treatment there for several weeks. At last he was sent home with the assurance that nothing more could be done for him. My friend, Dr. Wilson of Wallsend, was summoned to see him, and he called me in consultation on the case. We found the patient in the following condition. He was propped up in bed. His countenance was anxious, his eyes seemed to protrude from their sockets, and his face was bathed in perspiration, with a livid colour of the lips and skin. His breathing was shallow, frequent, and difficult, accompanied by a constant hacking and ineffectual cough. His pulse was hardly perceptible, irregular, and thready. The heart's action was tumultuous and irregular, the cardiac sounds were almost inaudible, and a distant murmur could be heard with both sounds at both the right and the left apex. No cardiac impulses could be felt except a wavy movement at the epigastrium. The liver was enlarged, and the abdominal cavity was distended with fluid, as were also the lower extremities and the scrotum. The pleural cavities were also occupied to a considerable extent by fluid effusion. We determined to abandon the usual cardiac stimulants and gave him two or three grains of blue pill thrice a day, and at the end of two days we gave him a smart purge of jalap. Greatly encouraged by the result, we pushed the blue pill (two to three grains three times a day) for a week or more, and during that time a steady relief of all the symptoms ensued. The countenance became placid, the tongue (before dry and brown) became moist, and the pulse more regular, full, and soft; the dropsical accumulations gradually receded, and the breathing resumed a normal character. Now was the time for digitalis—always best given on a falling tide in dropsy—and doubtless the patient owed much of his rapid recovery to the temporary and occasional use of that drug; but the staple of the treatment was the steady use of blue pill, now gradually diminished to two pills a day, and finally to a five-grain pill at bed time. To sum up the results, the man felt himself to be quite free from all his troubles in six weeks, at which date I met him in the Newcastle railway station and had the pleasure of presenting

<sup>1</sup> Nos. I., II., and III. of this series were published in THE LANCET of Feb. 25th and Nov. 4th, 1893, and Sept. 21st, 1895, respectively.

my convalescent to an extra-mural teacher of eminence from Edinburgh. From this time the patient resumed his duties and became a useful and active member of society.

Now the point of interest in this case is this—and I want to emphasise it—that during the next ten years the patient stuck to his blue pill every night with few intermissions, and declared that whenever he did leave it off for a few nights his heart began to trouble him and his breathing became difficult. As will be seen from the post-mortem notes, this nightly dose was in some mysterious way enabling a heart, massive with disease, to discharge its duties in such a way as to make its owner feel quite well. During the ten or eleven years of his subsequent life, Dr. Wilson calculates, he took 20,000 grains of blue pill; it never salivated him, it neither purged nor nauseated him, and it never gave him breath a touch of fetor. At last, however, his old symptoms returned, the machinery was worn out, and he died chiefly from the pressure of abdominal fluid on his enormous heart. I regret that such a case should be so roughly handled, it deserves a more accurate and detailed description, and I trust Dr. Wilson will some day give his details of it. My son, Professor George Murray, and Dr. Wilson made a post-mortem examination, of which these are the notes:—“On opening the thorax the heart was seen to be enormously enlarged, and the space occupied by it measured eight inches across and eight inches from above downwards. The lungs were displaced backwards and compressed by the enlarged heart. Heart: The right auricle was very much dilated, almost to the size of a man's fist. The walls were thickened and the muscular tissue hypertrophied. The auriculo-ventricular orifice was very much increased in size and readily admitted eight fingers at once. The tricuspid valves were much thickened and opaque. The right ventricle was much dilated and the walls thin. The left auricle was much dilated, the walls thick, and the endocardium opaque. In one part of the wall of the auricle there were two bars of calcified muscular tissue united by a crossbar of the same substance. The auriculo-ventricular opening was much constricted and hardly admitted the tip of the index-finger. The mitral valves were adherent, so that there was only a small opening like a button-hole between them. The valves were thick and rigid, but not calcified. The left ventricle was dilated, but its capacity was only about one-half that of the right ventricle. The walls were not much increased in thickness. Abdomen: The peritoneal cavity contained a considerable amount of clear fluid. The spleen showed a dense white patch of scar tissue one-fourth of an inch deep in the centre—evidently the site of a very old infarction. The surface of the liver was nodular; on section it showed dense strands of connective tissue of advanced cirrhosis.”

*Remarks.*—I need not say that to rescue a man from the jaws of death and give him ten or eleven years of fairly good health confers on any drug a reputation. Its potency is established. We therefore ask, How does it act? Is it a cardiac tonic, stimulant, alterative, or what? Or does it act on the secondary apparatus of the circulation and the blood itself by reducing the resistance of the vessels, diminishing the volume of blood, and altering its fibrinity so as to make it circulate more freely? I think it does all these things, and at the same time it soothes the heart by purifying the blood of effete accumulations.

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## THE PREPARATION OF ANTIRABIC SERUM AND THE METHOD OF DETERMINING ITS STRENGTH.

By PROFESSOR GUY TIZZONI AND DR. EUGENE  
CENTANNI.

(Concluded from page 731.)

### IV.—THE ANTIRABIC SERUM AS A PROTECTIVE.

BEARING in mind the more exact methods established for the standardising of the dose of the serum and of the virus, we have proceeded to test the power of our serum by various methods of experiment. We began by seeking to determine what dose of serum injected under the skin prior to infection would be capable of preventing the action of the virus. These experiments

have no direct or important bearing upon practice, inasmuch as, rabies being a disease of rare occurrence, we cannot speak of its treatment in the healthy individual before there has been any contagion whatever. From the scientific side, however, these experiments are of very great importance, and constitute the starting-point of other researches and other tests of the efficacy of the serum; one knows, in fact, that the efficacy of the serum may vary according to the time which intervenes between its introduction and the moment of infection. We can inject the serum a long time before infection—weeks or months—with the aim of determining what is the duration of the immunity conferred by it—a question which has a certain importance, as we know that one of the points which we wish to establish between the immunity given by the serum and that given by means of vaccine is whether the first has a much shorter duration; we have, therefore, in the course of these experiments dwelt on the durations of the immunity, and shall deal with them in a separate paper. The serum can also be introduced a short time before infection; this is done very frequently and is adapted to solve certain important questions. We have carried out a more extended series of experiments of this kind in order to determine the following points. 1. The relation existing between the quantity of serum introduced prophylactically and that necessary to be introduced at various periods after the occurrence of infection. These doses are very different, and form an ascending series, starting from the moment at which the infection has taken place; in the various infections this rise in dose does not proceed with equal intensity, but the degree of this increase gives us an idea of the degree of infection, and hence of the greater or lesser difficulty of curing it, according to its intensity. As regards the curative use of the antirabic serum we shall see the importance of establishing the relation between the curative and the preventive doses. 2. The relation between the different methods of injection of the serum, with a view to hastening the absorption and lessening the loss of active material. One knows that serum may be introduced by way of the peritoneum as well as by way of the veins. We have adopted a new method, the immense advantage of which over the subcutaneous method will presently be seen. 3. A means of determining the dose necessary to counteract the infection made with the canine virus and one made with the fixed virus, and hence, indirectly, to return once more to the comparison of the two viruses. 4. A method of estimating the strength of the serum.

It has already been seen how by the method of subcutaneous injection we sought to determine the best type of vaccination. We have, however, abandoned this in our latest experiments in favour of more simple and exact methods. In the following table (Table XIII.) we have collected several groups of experiments made with serum upon sheep and after various kinds of vaccinations, the serum having the power of typical serum. This serum has been introduced twenty-four hours before infection, it being injected at one single time if a small quantity was being used, and at three or four times when the quantities were much larger. Only in the latter event did the animal suffer in any way from the injection, either from a little local oedema or from some diminution of the body weight. The infection was always made beneath the dura mater, the canine virus and the fixed virus being used. (See Table XIII.)

Passing in review the experiments made with the canine virus, we find that, in presence of an infecting unit introduced into the brain, our typical serum having the value of 1 to 25,000—that is, 0.04 c.cm. (corresponding to at least a drop or to three milligrammes dry product)—is sufficient to protect a rabbit of the weight of one kilogramme; against the fixed virus the dose must be raised considerably, this being safe up to 1 in 100, according to which a rabbit of the weight of one kilogramme demands at least 10 c.cm. This dose is to that with the canine virus as 250 to 1, whence one sees the great increase of activity which the virus has undergone by repeated introductions into the rabbit—an increase which appears the greater if the limit of dilution of each of these is not considered and they are taken at equal volumes. And since the fixed virus at an equal volume contains 200 more infecting units than the canine virus of mean strength (the relation between the dilution 4 in 1000 and 1 in 50), so it may be deduced that the fixed virus is 50,000 times stronger than the canine, or at least, that to protect against the infection practised with a given