consideration; and the more thought you give it, and the more experience you have of it, the more, I feel confident, will you cling to it as a decided advance in surgery.

ON ADDISON'S DISEASE.

By BEDFORD FENWICK, M.D., M.R.C.P.,

Assistant-Physician to the City of London Chest Hospital, Victoria Park; and to the Hospital for Women, Soho Square, etc.

FOR nearly a quarter of a century, Addison's disease has been recognised by the medical profession in England. More have believed in its specific existence, more have worked at its pathology in this country, than in any other. And yet to-day our knowledge on the matter is but little greater than when its first historian died. And this is the more to be deplored, because we have not here a mere medical curiosity, of rare occurrence, of definite duration, of certain cure, but a disease which has killed its hundreds, whose course is not accurately known, whose pathology and etiology are involved in obscurity, and which is still an *opprobrium medici*; for hitherto, I believe, no case of permanent recovery has been put on record. Our present knowledge may be very briefly summed up. The patient suffers from intense weakness, which gradually but steadily increases, despite all treatment. He is languid, and utterly indisposed for any exertion of body or mind. He generally suffers from breathlessness on exertion, from anæmia, from pain in the epigastrium and across the loins. There are usually no physical signs of disease found to account for the symptoms, and these are at first diagnosed as due to atonic dyspepsia, and the patient is treated accordingly. But the asthenia and the intense feebleness of the heart increase; the anæmia does not diminish, and, if the patient live, a new feature presents itself, or, in some cases, is evident before the onset of the constitutional symptoms. The skin becomes abnormally dark, and this pigmentation increasing, and extending, may cover the whole surface, and give the patient the aspect of a mulatto. Then, with still advancing feebleness, comes death, either very suddenly or in gradually deepening coma; and, on *post mortem* examination, we find caseous degeneration of one or, more commonly, both suprarenal capsules, with chronic inflammatory changes in their immediate vicinity. Now, some argue that these bodies play no essential part in the disease. But, inasmuch as in some hundreds of cases showing the above symptoms during life, a caseous degeneration of the adrenals was the only or chief lesion found after death, it is only logical and scientific to conclude that there may be, and probably is, a very close connection between them. And inasmuch as in nearly every case where the capsules are, *post mortem*, found in an advanced state of caseation, pronounced symptoms of Addison's disease have been noticed during life, it is hard not to believe that the relation between the facts is simply one of cause and effect. Now, the constitutional symptoms have for many years past been generally supposed to be due to nerve-changes. These, for example, would cause the relaxation of the abdominal vessels, and so the intense blood-stasis evidenced by the condition of the spleen and mucous membranes, and the consequent external and cerebral anæmia. In like manner, the characteristic cardiac, gastric, and pulmonary symptoms, are explicable as due to reflected nervous irritation. So far we know or we theorise at present; but now three great practical questions suggest themselves. 1. What is the cause of the bronzing? 2. What is the seat of the cause of the constitutional symptoms? 3. Will increased pathological knowledge suggest a method of cure? It is the object of this communication, first, to detail a well marked case of the disease, and then to offer some original and, it is hoped, some practical views on the above questions.

William McC., a labourer, aged 33, was admitted into the London Hospital on September 22nd, 1881, under the care of Dr. Samuel Fenwick. The following is an abstract of his case. He had always been addicted to beer, generally consuming from five to six pints a day. He had suffered from gonorrhœa and a soft chancre fifteen, and from typhus fever twelve, years ago. Otherwise, except for an annual attack of psoriasis, his health had always been very good. Four months before admission, he suffered from a "cold," attributed to exposure, and never felt well thereafter. A month later, his urine became scanty, scalding, and high coloured. He began to suffer from vomiting, headache, giddiness, and great lassitude, and ceased to work. These symptoms steadily increased in severity. On admission, he was noted to be a well made, fairly well nourished man, anæmic, deaf, and very dull both in mind and manner. He slept badly, ate

little, and rarely spoke. He lay in bed utterly "limp," and profoundly quiet. There was tenderness on pressure over the epigastrium, the left hypochondrium, and the spines of the first and second lumbar vertebrae. The skin was in no part abnormally dark; the tongue generally appeared red at the tip and edges, with fur down the centre and at the base. The teeth were regular and good. There was no discoloration of the gums or inside the cheeks. He occasionally vomited, and complained only and entirely of weakness and lassitude. There were no marked physical signs of disease in the chest or abdomen, but the heart-sounds were dull and feeble, and the first sound, both at the base and apex, was prolonged. The pulse varied from 72 to 80, always weak and compressible; the respirations generally about 18, easy; the temperature between 97.6° Fahr. and 99.2° Fahr. The urine was straw-coloured, faintly alkaline, with a specific gravity of 1012 to 1015, with albumen always present, from a mere trace up to about one-half on the morning of his death; the urea was generally 1.3 per cent., and there was usually a deposit of phosphates and epithelial casts.

On September 27th, Dr. Samuel Fenwick saw him, diagnosed Addison's disease from the constitutional symptoms, and prognosed death, probably by syncope, at an early date.

On September 28th, the patient endeavoured to get out of bed against orders, and fainted. He rallied, but died suddenly a few hours later.

The necropsy was made twenty-nine hours after death. Much adipose tissue was found beneath the skin and around the various organs; the skin seemed generally dark compared with that of a very fair-complexioned body next to it, but not abnormally so, and no patches of pigmentation could be found. The liver was fatty, and weighed seventy-two ounces; the spleen was enlarged and congested. The kidneys, lungs, and heart were perfectly healthy. The brain and spinal cord, the nerves in the vicinity of the capsules, the blood-vessels, and the spinal column were all closely examined, and presented no naked-eye changes. There was no ulceration or evidence of tubercle in the intestines or peritoneum, but the mucous membrane of the stomach and duodenum was of a dark slaty colour, and covered with a thick ropy mucus. Microscopically, the gastric tubules seemed fewer than normal, but no abnormal pigmentation was found. Both suprarenal capsules were enlarged, hard, and nodulated. On section, it was found that the normal gland-tissue had been transformed into a translucent softish grey matter, mixed with a yellow opaque substance, which in parts was quite calcareous and gritty. It was very observable that the former translucent appearance seemed almost confined to the cortical portion, while the central or medullary part seemed to be mapped out in white, and also that this caseous material was much more abundant at one end of each capsule, gradually diminishing in extent thence to the opposite extremity of each organ. Microscopically, except in parts here and there of the cortex, no normal structure could be found. It all appeared to be transformed into a mass of oïd globules, scattered fibrils, and a few small indifferent cells.

The chief point of interest in this otherwise typical case, was the absence of all bronzing of the skin. It suggests afresh the old question, "Why should bronzing occur in most cases, and yet not in some few others, of undoubted Addison's disease?" In the hope of obtaining some faint light on this matter, I collected and tabulated all the cases of the disease recorded in the last sixteen volumes of the *Transactions of the Pathological Society*, and this in order to be sure that each case had been critically tested and typical. I now desire briefly to lay before the profession the facts the above obtained table exhibits, and the theory as to the course of the disease which these facts seem to support.

1. *Age*.—The average age at death in males was 30.1 years; the extremes were 5 and 55. The average age in females was 35 years, the extremes being 19 and 55.

2. *Sex*.—Of the thirty cases in the table, 23 were men, and only 7 women, or rather more than three of the former to one of the latter. In Dr. Wilks's classical monograph on the subject, he gives (p. 18) the proportion of his cases as 19 men to 6 women, or almost exactly the same ratio. Dr. Headham Greenhow, however, in the Croonian lectures for 1875 (p. 94), deduces from his collection a much lower proportion; namely, 119 men to 64 women, or not quite two to one.

3. *Duration of Illness*.—This varied very much, and very remarkably. (a) For bronzed cases the average duration of life from the onset of the symptoms was 23.6 months; the extremes being (?) three months and five years; but (b) in non-bronzed cases the average was only 4.8 months, the limits being six weeks and twelve months.

The fact seems remarkable at first sight, but the more it is considered the more remarkable does it become. Dr. Addison thought that in some cases bronzing did not occur, because the patients did

not live long enough for the slowly occurring skin-change to take place; but though I have searched through many monographs on the subject, I cannot find that any one has tried to discover *why* they died so early. And I venture to believe that the explanation is not only a perfectly simple one, but that it opens up a marvellously wide field for future investigation. For if patients, without bronzing of the skin, die in almost exactly one-fifth of the time lived by those in which pigmentation occurs, it is perfectly plain that bronzing of the skin, *per se*, does not conduce to death, and therefore that the cause of the greater fatality, in the first class, must be looked for in an unusual gravity of the constitutional symptoms, which, together with the skin-change, make up the whole outward expression of the internal capsular disease. That these are unusually grave, is self-evident, seeing that the heart fails so rapidly. It may, therefore, plainly be inferred that the mischief which produces these, must be more intense in non-bronzed than in bronzed cases. Now, inasmuch as the skin-change occurs sometimes long after, and sometimes before, the onset of the constitutional symptoms, and sometimes not at all, it follows that these two constituent features of the disease cannot be of absolutely identical origin. In other words, either two distinct causes must be at work, or the same cause must act upon two separate parts, attacking first one and then the other, in order to produce these two non-contemporaneous results. I think that the idea of two distinct causes may be dismissed, because, after twenty years of patient and accurate investigation of this subject, by the most able pathologists and clinicians of this and other countries, no evidence in favour of such a theory has been shown to exist. It is probable, therefore, that we have to deal with one settled cause, acting upon two separate organs, or upon two separate parts of one and the same organ. Now, let us turn to the pathology of the disease, and what do we find? First, we find that the constitutional symptoms, the anæmia, the asthenia, the breathlessness, the evidences of cardiac and of gastric irritation, have all been, and I think well, explained by the theory of nerve-implication. But this has hitherto been looked for, and supposed to occur, *outside* the suprarenal bodies. And the one weak point in the theory has hitherto been, that nearly every observer has found different or modified changes in these nerves from that recorded by nearly every other investigator. Turning, however, to the minute anatomy of the capsules themselves, we find that Leydig (*Lehrbuch der Histologie*, Frankfurt, 1857, p. 189), as the result of his laborious investigations, comes to the conclusion that the medullary portion of the organ is essentially a "ganglionic nerve-centre," and also that numerous observers have traced branches from the sympathetic, from the pneumogastric, and from the phrenic nerves, into the substance of the medulla. I would ask, then, what need have we to hunt through neighbouring structures, when it seems that we have, in the very capsules themselves, both nerves to be affected, and a degeneration which must affect them?

And now I would suggest, what our argument has led us to believe to be at least possible, that the constitutional symptoms of Addison's disease are due to degeneration of the *medullary portion* of the suprarenal capsules, and that the reason, therefore, why bronzing does not occur in some cases, may be because, in such, the intensity of the mischief is greatest in that part, and causes death before the slowly developed skin-change is perceptible.

But, secondly, as to the bronzing of the skin. We find, histologically, that it is due to the deposit of pigment in the deeper layers of the rete mucosum. Clinically, we find that it is predominant where pigmentation is normally present; and, so far as I can discover, that is all we know about it. Our argument above led us to the belief that we have to deal with one common cause, a caseous degeneration, acting on two separate parts, perchance of one and the same organ. Now, it is noteworthy that we have, apparently, in the suprarenal body, an organ which is, it seems, in a superlative degree, composed of two totally distinct parts. For, turning again to the minute anatomy of the capsule, we find that Kölliker (*Manual of Human Histology*, Sydenham Society's Translation, vol. ii, p. 219), while agreeing with Leydig, above quoted, in referring the medullary portion to the nervous system, regards the cortical part as made up of "blood-vascular glands." If this be correct, I would suggest, as an almost logical sequence, that bronzing of the skin may be due to degeneration of the *cortical layer* of the suprarenal bodies, perhaps in consequence of some physical or chemical change in the constitution of the blood, taking place through the affection of the "blood-vascular glands."

I have noted, in my description of the case above given, that parts of the cortex were healthy, and that generally, in that portion, the disease appeared to be in its initial stage; whereas the medullary portion had undergone much caseous, or farther advanced, degeneration;

and in several museum-specimens, I have found the same naked-eye appearances where bronzing was absent. Argument then, and the still more forcible logic of hard facts, seem to point to the above conclusions. The truth, or the error of the theory, must be decided by accurate and extended observation as to the distribution of the disease, macroscopically and microscopically, in future cases. If it be true, I need hardly point out what a wonderful field for investigation it will open up, not only into the functions of the ductless glands, not only into the chemical phases of degenerative changes, but also into the great practical question of cure. For, seeing that the disease is inevitably fatal, if it be proved to be confined simply to the suprarenal capsules, why should not the organs be extirpated? Physiologists have shown that their presence is not essential to life. I venture then to think that the question I would leave future observations to finally settle, is not only important theoretically, but, in its aim, intensely practical also.

I would briefly summarise, therefore, that (1) the average age at death in Addison's disease is between 30 and 35; (2) males are much more subject to the disease than females; (3) cases with bronzing of the skin usually die within three years, and cases without bronzing, within five months from the appearance of symptoms from progressive asthenia; (4) the *constitutional symptoms* are probably due to degeneration of the *medullary portion* of the suprarenal capsules; (5) *bronzing of the skin* may be due to degeneration of the *cortical layer*; (6) if death be chiefly due to the capsular changes, then the successful extirpation of these bodies might cure the patient.

EVISCERATION OF THE EYE, AND ITS RELATION TO THE BACTERIAL THEORY OF THE ORIGIN OF SYMPATHETIC DISEASE.

By P. H. MULES, M.D.,

Surgeon to the Eye Hospital, Manchester.

IN the last paragraph of my paper on "Evisceration of the Globe," *BRITISH MEDICAL JOURNAL*, Dec. 19th, 1885, I assume that "freedom from sympathetic inflammation, after evisceration, will prove conclusively the bacterial origin of sympathetic disease." I will shortly give my reasons for this statement.

For sympathetic disease to arise in a sound eye, it is necessary that the infecting eye shall have, first, a nidus, or point of infection or irritation; secondly, a track by which such shall be forwarded to the second eye.

In removing the contents of the globe, we certainly remove all soil for the growth of bacteria; but we leave the "tracks," be they blood-vessels, lymph-spaces, or nerves; and although such forcible removal may eventually obliterate the blood and lymph-channels, this can hardly be said of the nerves themselves, at least, for a very long time. Now, if the tracks are there ready to conduct whatever may be required of them, be it sympathy, blood-poison, nerve-inflammation, or bacteria, and we irritate them to the utmost by forcible tearing, medicated application, a permanent foreign body, and other hitherto supposed incentives to secondary sympathetic disease; yet under this treatment, the injured globe quiets down, the sympathetic irritation (reflex neurosis) of the sound eye passes away, and sympathetic inflammation does not occur, obviously the tracks in that portion where they are ruptured, cannot originate sympathetic disease, but must be the conductors only of what is produced, irrespective of themselves. Can the removal of the end organs account for this absence of initiative? Such a view has never been held, nor has it anything to recommend it. Experiment, then, having so far proved that from eviscerated globes sympathetic inflammation does not extend; that the nerves, blood and lymph spaces, under excessive provocation, cannot originate of themselves a disease capable of progression to the sound eye; we arrive, by a process of exclusion, at the fact that it can only be a new formation, an independent cell-growth, introduced probably from without. This point, once allowed (and it appears to me incontrovertible), we have left only the views of Berlin, Leber and Snellen, and Mr. Hutchinson.

Berlin, Leber, and Snellen agree as to the nature of the infective material being bacterial, but differ as to its track, whether vascular or lymphatic; so that, for the purpose of this paper, we may assume them to be one. There remains Mr. Hutchinson's view; "that sympathetic ophthalmitis is of a simple inflammatory character, depending on parallelism of structure for its secondary deposits." To emphasise this Mr. Hutchinson (*Ophthalmological Transactions*, vol. v, p. 74) refers to puerperia. Now this is a disease in which infecting micro-organisms must bear a large share in the production, and is strong evidence in favour of the "bacterial theory of sympathetic