THE CROONIAN LECTURES ON ADDISON'S DISEASE.

Delivered at the Royal College of Physicians, London.

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LECTURE II.

I SAID in my last lecture that Addison's discovery has not yet been generally accepted, nor even generally understood. The connection of the constitutional symptoms and bronzing of skin with the disease in the suprarenal capsules, is still regarded by many rather as a matter *sub judice*, than as a certain and definite relation. This scepticism is no doubt partly due to the fact that the relation between the disease of the suprarenal capsules and the clinical symptoms associated with it, is much less susceptible of obvious explanation than the relation between the organic lesion and the clinical symptoms in many other diseases. To this part of the question I shall refer in my next lecture; but, in the meanwhile, it is evident that the obscurity of the relation can be no bar to the recognition of its reality, if this latter be substantiated by a sufficient number of well attested facts.

The general acceptance of Addison's discovery has, however, been mainly retarded by the prevalence of misconceptions which have prevented its being generally understood. I propose, therefore, to review in the first place the evidence proving the reality of the relation, and subsequently to deal with the misconceptions which have interfered with its general recognition.

If it were only that so obscure a disease, as one particular lesion of the suprarenal capsules, has been often correctly and publicly diagnosed from the symptoms supposed to be connected with it, it seems difficult to understand that the connection should not be universally allowed to have passed out of the region of theory into that of established truth. I have myself, on twelve occasions, diagnosed Addison's disease of the suprarenal capsules in the presence of medical students and friends, and in eight of these cases the correctness of the diagnosis has been verified at the necropsy. Two of the twelve patients died at a distance from London, and the remaining two are still living. There have now, indeed, been so large a number of cases similarly diagnosed, that it is impossible to enumerate them; and the evidence they afford of the reality of the connection between the clinical symptoms and the pathological condition, would alone seem to me to be unanswerable.

It is still argued, however, in some quarters, both at home and abroad, that, although a diseased condition of the suprarenal capsules may frequently coincide with certain clinical symptoms, it is by no means essential to their development, and consequently cannot be their cause. I shall therefore proceed to show that the whole weight of the evidence furnished by the large number of cases published since Addison's time, as bearing upon the subject of the disease he discovered, goes to prove that the coexistence of the clinical symptoms of Addison's disease with one particular lesion of the suprarenal capsules, is the almost invariable rule; the exceptions to which, if duly investigated, may be satisfactorily explained. I shall also be able to show that this particular lesion is essential to the development of those symptoms, in so far that medical records have as yet produced no single case exhibiting the really characteristic features of Addison's disease, in which this particular lesion of the suprarenal capsules was not also present.

For many years past I have from time to time collected all the cases I could find in the *Transactions* of medical societies, or in the British or foreign medical journals, published under the name of Addison's disease, Bronzed skin disease, disease of the suprarenal capsules with or without bronzing, and bronzing of skin with or without disease of the suprarenal capsules. I cannot suppose, however, that none have escaped me, for I have not had access to all the medical works in which cases may have been recorded, and latterly my leisure for such researches has been less than in former years. This collection now amounts to 332 cases, in all of which there is a more or less complete report of the morbid appearances found after death; for I have disregarded, as useless for my present purpose, all those cases which have not undergone the test of *post mortem* examination.

Of these 332 cases, a very considerable number fall into three classes, which must be set aside till the latter part of this lecture. One of these classes includes all the cases in which no disease at all of the suprarenal capsules was found; the second, all those

cases in which the disease found in the suprarenal capsules was altogether of a different nature from the particular lesion characteristic of Addison's disease; whilst in the third class are comprised all those cases in which the description of the condition of the suprarenal capsules leaves doubtful the nature of the lesion, and in some instances the existence of any lesion at all. After deducting the cases which fall under these three classes from the total number collected, there remain 228 cases, in all of which the suprarenal capsules are reported to have undergone the one particular morbid change which I described in my last lecture.

As regards the reality of the relation between this particular lesion of the suprarenal capsules and the clinical symptoms supposed to be associated with it, I take first, because most indisputable, the evidence furnished by 101 of these cases, which may be classed in one group as typical cases of Addison's disease—typical as corresponding in all their main facts with the outline of Addison's own description—more or less typical, according as the length of their course or as opportunities of observation have enabled their reporters to present more or less in detail the remarkable features which fill in that outline. In all these 101 cases, the train of constitutional symptoms and the peculiar change of colour in the skin were observed, during life, more or less fully developed. In all the 101 cases, the suprarenal capsules were found after death to be diseased, and the disease was in every case of the same nature, corresponding with one or other of the stages of the particular lesion which I have described. And, lastly, in none of the 101 cases was there any other organic lesion existing which could be of the slightest importance. There can surely be no reasonable doubt that, in every one of these cases, the disease of the suprarenal capsules was, either immediately, or mediately through its consequences, the sole cause of death.

But although, with the view of adducing first the most unanswerable argument to be derived from the facts collected, I have placed in a group these 101 cases which I have called typical by themselves, there is another large class which, in reality, affords scarcely less convincing proof of the connection between the clinical symptoms and the suprarenal disease. In 51 more cases, both the constitutional symptoms and the discoloration of the skin were observed during life in a more or less typical form, but either the other organs were not examined so as to place beyond question the absence of any coexisting disease; or else some complicating disease actually existed, giving rise to its own symptoms independently of those characteristic of the suprarenal lesion. A large proportion of these cases, however, are, in fact, as typical examples of the disease as any of those I have placed in the previous group. Again, in 31 other cases, some of the characteristic constitutional symptoms are reported, together with some discoloration of skin, but in some of these cases the descriptions are too meagre to justify my placing them in the first or second group; whilst in others there was coexisting disease serious enough to modify or obscure the symptoms of suprarenal disease.

We have thus, out of the 228 cases in which the one particular lesion of the suprarenal capsules has been found, no fewer than 183 cases in which the peculiar change of colour in the skin, and some at least of the characteristic constitutional symptoms, were observed during life.

In 16 of the remaining 45 cases, the clinical history and symptoms are either altogether wanting, or are too imperfectly recorded to warrant any conclusions being founded upon them. Amongst this number are included several cases which occurred before the announcement of Addison's discovery. These 16 cases being necessarily left out of the question, there remain only 29 of the 228 cases still to be accounted for; and in these 29 cases it is distinctly stated either that no bronzing of the skin existed, or that it was almost inappreciable.

In 18 of these 29 cases, the disease of the suprarenal capsules co-existed with advanced phthisis or vertebral disease, with tuberculosis, ascites, or Bright's disease. In two or three of them, the coexisting disease was acute tuberculosis, which always runs a very rapid course; and in most of the others the coexisting diseases were attended by a considerable and exhausting drain, such as profuse suppuration from abscesses in vertebral disease, or from the lungs in phthisis, and loss of albumen from the blood in Bright's disease. Three of these cases occurred in the Middlesex Hospital, and I was present at the *post mortem* examination of one of them, and verified the absence of all trace of discoloration of the skin; but the patient, a boy aged 13, had been rapidly worn down by profuse discharge of pus from an abscess connected with carious vertebrae. A few of these cases have presented, however, some of the peculiar constitutional symptoms due to the suprarenal lesion, in addition to those of the more obvious disease, though not of sufficiently marked form to give rise to any suspicion of their real cause until it was discovered at the necropsy. Thus, in the second of the three Middlesex Hospital cases to which I have referred, Dr. Thomp-

son recorded in the case-book that the patient, a man aged 40, who died after an illness of only six weeks, with extreme disorganisation of the lungs, had, before he took the cold which brought on his rapidly fatal illness, been suffering from languor, failure of appetite, and vomiting after food. The third case, one of vertebral disease and incipient phthisis, was under the care of Mr. Hulke, who stated that the patient suffered from a degree of feebleness quite out of proportion to the loss of flesh, a very irritable stomach and obstinate constipation. In this last case, it was obvious that the suprarenal lesion was in a comparatively early stage when the patient died, for the inflammatory exudation with which the right capsule was infiltrated had not undergone the process of caseous degeneration, and the left capsule appeared still healthy.

The inference which I draw from the absence of the bronzing of skin, and mostly, also, of the constitutional symptoms in these eighteen cases, is that, in most of them, the diseases coexisting with the disease of the suprarenal capsules proved fatal before this latter had produced its characteristic effects; whilst in others, the end was probably hastened by the debility and depression which are usually the first symptoms of the suprarenal lesion, but which, in such circumstances, would naturally pass unnoticed. As we have seen, Dr. Thompson's and Mr. Hulke's patients did both present such symptoms, distinct from those of the more acute diseases which caused death—a fact which seems to confirm the inference I have drawn with respect to these cases.

The explanation of the other eleven cases in which it was stated that there was no bronzing of the skin, is at first sight less obvious. In none of these cases was there any coexisting disease of importance, and some of them are amongst the most typical on record as regards the constitutional symptoms. Nearly all of them, however, have been cases in which the illness has been of comparatively short duration, only two having exceeded a course of four months; in several there must have been, notwithstanding the absence of any developed bronzing, some peculiarity in the colour of the skin sufficient to attract attention, as slight duskiness, unnatural darkening of skin, peculiar sallow hue, and so on, are noted, together with the absence of bronzing. In one case, however, fully reported by Hertz in *Virchow's Archiv* for 1870, there was no trace of discoloration of the skin even at death; but the illness appears to have been of short duration; for, although the patient reported himself to have been failing in health since an attack of cold and ague a few months previously, he only presented himself at the hospital a few days before his death. At that time, he had still some appetite, and the description of his condition is not that of an advanced stage of the disease; but he sank suddenly with severe nervous symptoms. In another case, under Dr. Owen Rees, reported by Dr. Wilks, which was most characteristic as regards the constitutional symptoms, and in which the patient was failing in health a year and ill nine weeks, there was no discoloration. The same may be said of two other cases recorded by Dr. Bristowe and Mr. Crossman, lasting four and eight months respectively. This last case of Mr. Crossman's is the longest on record, in which death has taken place with all the characteristic constitutional symptoms of Addison's disease without any bronzing of the skin. There is, however, one case included in the eleven, in which the illness is said by Mr. Bruce, who reported the case for Dr. Russell Reynolds, to have lasted eighteen months. But, as the patient had been always delicate and a hard drinker, and as the only symptoms observed were sickness, loss of flesh, and a sense of emptiness at the epigastrium, it may have been difficult to fix the commencement of the illness due to the disease of the suprarenal capsules. It is certain that this latter was not in an advanced stage at the time of the patient's sudden death, for a little of the proper tissue of the organs was still found remaining.

The simple and satisfactory explanation of all these cases lies, I believe, in the variable comparative date of the development of the constitutional symptoms and of bronzing of skin in different cases, to which I drew attention in my first lecture as one of the peculiar features in the course of this remarkable disease. It was at first thought that absence of bronzing of skin, in otherwise obviously characteristic cases of Addison's disease, might be accounted for on the supposition that a course of several months at least was requisite for the development of the bronzing. More extended clinical observation has now established the fact that, in a certain number of cases, the bronzing of skin is more or less developed for considerable periods of time before the patient feels any symptoms of illness; whilst, on the other hand, in a considerable number of cases, the constitutional symptoms have shown themselves for a longer or shorter period before the appearance of any discoloration of the skin. It is evident, however, that cases belonging to the former of these classes are far less liable to give rise to misunderstanding than cases of the latter class; for, whilst those patients who are affected first by the discoloration of skin will live on as usual

until the constitutional symptoms make their appearance, those patients in whom the constitutional symptoms are first developed may very possibly die, especially if exposed to any external depressing influence, before the appearance of the discoloration of skin. This is, in fact, precisely what I believe to have occurred in all the eleven cases I am now discussing. I believe them to have been all typical cases of Addison's disease, whose course was cut short by individual feebleness or by unfavourable circumstances before the development of the bronzing of skin, which would presently have taken place, as in the cases quoted in my previous lecture, if their course had been sufficiently prolonged.

Looking at all the difficulties which have stood in the way of our obtaining full and accurate reports of even the recognised cases of this rare and obscure disease, and to the certainty that many cases have remained unrecognised until after death, when it was too late to fill up deficiencies in the clinical records, I cannot but regard these statistics as furnishing conclusive evidence of the constant relation of a certain train of constitutional symptoms and a peculiar change of colour in the skin due to one particular diseased condition of the suprarenal capsules.

Such a weight of concurrent testimony to the truth of Addison's discovery would scarcely have remained so long without effect, had it not been for the extensive prevalence of those misconceptions to which I have alluded, as obscuring the true aspect of the question from the moment when it was first submitted to the profession. These misconceptions had reference chiefly to the characters of the discoloration of skin and of the lesions in the suprarenal capsules; and they originated, as we have seen, in a great degree in Addison's own mistakes. He subjoined to his own typical cases others presenting discoloration of the skin and disease of the suprarenal capsules of quite different characters, and unassociated with any of the apparently causeless constitutional symptoms which had attracted his attention. He also gave the disease the name of *Melasma suprarenale*, for which afterwards was substituted that of "Bronzed skin disease", thus identifying the disease itself with its most conspicuous, but least important, feature. Thus, the asthenia and the other peculiar constitutional symptoms, which at first revealed to Addison the existence of the disease, were in a great measure overlooked, both in reports of cases and in discussions based upon them. Numerous cases were brought forward, on the one hand, only to show that discoloration of the skin not unfrequently occurred without any disease being found in the suprarenal capsules; and, on the other hand, only to prove that discoloration of the skin did not always result from disease of the suprarenal capsules, even when sufficiently extensive to cause the entire destruction of those organs.

In both these classes of cases, the facts were undeniable, and the inferences drawn from them have constantly been alleged as the principal arguments against the truth of Addison's discovery—namely, that "discoloration of the skin not unfrequently exists without any disease of the suprarenal capsules", and that "disease of the suprarenal capsules not unfrequently exists without producing any discoloration of the skin." Both these allegations are undoubtedly true; but, as I shall proceed to explain, neither of them contravenes, in the slightest degree, the reality of the relation which subsists between the peculiar change of colour in the skin and the particular lesion of the suprarenal capsules which are found in Addison's disease.

First, then, discoloration of the skin does frequently exist without any disease of the suprarenal capsules, but it is discoloration which either presents altogether different characters from that associated with suprarenal disease, or which, if more or less resembling it, is easily referable to some other obvious pathological cause or to some known physiological condition. Neither Addison himself, nor any one who upheld his views, has ever maintained that disease of the suprarenal capsules was to be regarded as the only cause of discoloration of the skin. This would have been as absurd as to assert that disease of the kidneys was the only cause of dropsy. In both cases, the truth discovered was the relation between a hitherto undiagnosed local lesion and one particular form of an obvious affection.

There are various conditions, both physiological and pathological, which are frequently accompanied by general or partial darkening of the skin; but, as the former are universally known and attributed to their true physiological causes, I need not dwell upon them, and therefore pass on to the various discolorations of the skin produced by pathological causes which have more or less frequently been confounded with the peculiar discoloration of Addison's disease. Among these there is, perhaps, none more striking than the cutaneous discoloration often seen in elderly persons of very indigent circumstances and of uncleanly habits, especially when infested with vermin. I have the records of several such cases which have been under my own care in the Middlesex Hospital, either for obvious disease, or simply for the debility and sinking consequent on long continued hardships and exposure. In

the year 1864, I exhibited one of these cases at the Pathological Society, as a case of bronzed skin disease simulating the discoloration of Addison's disease. Such cases, however, though they undoubtedly present some appearances of Addison's disease, may be easily distinguished from it. In my patient, a woman, aged 65, the skin was extensively bronzed, especially over the abdomen, chest, and back; but the discoloration, when carefully examined, was totally different from the bronzing of Addison's disease. It was seated in the superficial instead of in the deeper layers of the epidermis. It was paler instead of deeper in the face, hands, and other parts, which are naturally the seats of most pigment. These small, isolated, dark spots were all on the pale instead of on the discolored parts of the skin. Moreover, the darkened cuticle was not soft and smooth, but in many parts raised and rough. Such constitutional symptoms as were present—debility, languor, and a sense of sinking at the epigastrium—were referable to apparent causes, and were soon removed by tonic treatment, and an ample supply of food. I should add that, by the use of alkaline warm baths and soap, the discoloration was greatly diminished, though the skin did not regain its normal hue.

Again, it is well known that pityriasis versicolor is attended by discolorations of the skin, and cases of this kind have been adduced to disprove the connection between bronzed skin and disease of the suprarenal capsules; but the nature and the distribution of these discolorations, as well as their modes of development and disappearance, are widely different from the two characters of the discoloration of skin in Addison's disease. The dark patches are more upon the trunk and limbs than upon the face. They have abrupt margins and convex borders, and are interspersed with spaces of normal coloured skin; they appear and disappear rapidly: and no asthenia or other constitutional symptoms are associated with them.

Syphilitic eruptions, also, notoriously cause more or less permanent stains on the skin; but, although their coppery hue and spotty character distinguish them clearly enough from the bronzing of Addison's disease, they are sometimes confounded with it, for two such cases have been sent to me in private practice, on the supposition that they were cases of Addison's disease.

There are, however, various kinds of discoloration of the skin which bear a somewhat more real resemblance to the bronzing of Addison's disease, in so far that the skin remains soft and smooth, and the pigment is deposited in the same layers of the epidermis, though not in the same quantity, nor usually to the same extent, nor in the same characteristic seats. Such discolorations are well known to be produced occasionally by diseases peculiar to women, by tropical and malarious fevers, by hepatic disease, and by very chronic phthisis. Of this last class of cases I have seen several remarkable examples since my attention has been directed to the subject. A woman, aged 26, who died under my care in the Middlesex Hospital of chronic phthisis in 1871, presented precisely the appearance of Addison's disease in an early stage, the face having the same peculiar duskiness, and the forehead, except where covered by the hair, being of a distinct brown colour; the skin was soft and smooth. Another phthisical patient, a man, aged 50, was sent to me in 1872 by my colleague Mr. Nixon, with abnormal pigmentation of the tongue, exactly resembling that seen in Addison's disease. My colleague Dr. Thompson asked me some time ago to examine a man, aged 55, who was suffering from bronchitis and emphysema, and, it was suspected, long-standing phthisis. He exhibited several brown patches, corresponding to the extent of superficial injuries received from a fall about a year before; and on the lower part of the sternum was a transverse irregular white cicatrix an inch and a half long and a quarter of an inch wide, encircled by a dark brown ring nearly half an inch in width, fading off into the normal hue. The skin of the groins was also slightly dusky. These partial discolorations strikingly resembled those found in similar situations in Addison's disease, but they neither deepened, nor spread over the general surface during the subsequent illness of the patients, nor did these latter show any symptoms but those of pulmonary disease. In all these cases, the suprarenal capsules proved to be perfectly healthy. The observation of these and similar cases has convinced me, that no partial discolorations of skin are to be relied on as diagnostic of Addison's disease, unless found in conjunction with the characteristic constitutional symptoms.

ROYAL COLLEGE OF SURGEONS.—Mr. John Hilton, F.R.S., who was elected a member of the Court of Examiners of the Royal College of Surgeons in 1865, has resigned his appointment which he has so long and so honourably filled. The Council, of which he was elected a member in 1854, will still retain the benefit of his experience. A special meeting of the Council will be held on Wednesday next, the 17th instant, for the election of a Fellow of the College, to fill his vacant chair.

THE GOULSTONIAN LECTURES ON PUERPERAL FEVER.

Delivered at the Royal College of Physicians, London.

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LECTURE III.

THE only point on which I now feel some hesitation is, whether this explanation of the origin of puerperal fever, and its contagious nature, is so generally admitted as to allow us to proceed in our inquiry without interruption by objections to it. Our students are generally told in the text-books that puerperal fever is "a continued fever communicable by contagion, occurring in connection with childbirth, and often associated with extensive local lesions, especially of the uterine system". (Aitken.)

There is no doubt that a considerable number of experienced practitioners believe in epidemic influences, and are quite ready to allow that there is strong evidence to make them conceive that in certain cases the fever has been communicated from one person to another. It is only a short time since that one of our leading journals, in remarking on a case of manslaughter which has excited attention very properly on the question of contagion, observed: "Is it certain that puerperal fever is contagious?" It seems to me a very important matter indeed that there should be no mistake on this question, at least as a practical one; for, whether we believe or disbelieve the theory of contagion, we must regulate our practice by the opinions of those of the greatest experience and knowledge.

Supposing even that we cannot demonstrate the perfect truth of the theory, and that we cannot explain certain apparent exceptions to it, it is necessary to remember that it is sufficient, if the proof can be carried so far as to obtain consent to the probability of the theory being true. In this case, "probability is the very guide of life"; and the rules laid down by an able writer, on the extent to which we ought to be satisfied with the evidence of such probability, are so much to the purpose, that I shall take advantage of them to express the opinion, which I think we shall agree in supporting, in respect of this matter.

"From these things, it follows", says that able logician Bishop Butler, "in questions of difficulty, or such as are thought so, where more satisfactory evidence cannot be had, or is not seen, if the result of examination be, that there appears, upon the whole, the lowest presumption on one side, though in the lowest degree greater, this determines the question even in matters of speculation, and, in matters of practice, will lay us under an absolute and formal obligation, in point of prudence and of interest, to act upon that presumption or low probability, though it be so low as to leave the mind in very great doubt which is the truth. For surely a man is as really bound in prudence to do what, upon the whole, appears according to the best of his judgment to be for his happiness as what he certainly knows to be so." (Butler, Introduction to *Anal. Relig.*) It is quite easy to perceive what a great difference must exist between the views entertained by one who believes thoroughly in the contagious theory and those of one who does not believe in or is doubtful of it. By the former, epidemics of the fever are not admitted; symptoms are all referred to the influence of a poison circulating in the system, which accumulates in tissues and produces general disturbance as well as local pathological changes. Variations in the pulse and temperature are explained by the same cause, and the remedies which appear most rational depend upon the principle of opposing the poisonous influence, while the fear of conveying septic matter from one case to another will always suggest precautions which would be disregarded by one who doubted such a possibility. In regard to the question of lying-in institutions, and in his views of the dangerous proximity of the *post mortem* room, he would hold only one opinion. In many other ways which need not be mentioned, his professional conduct would be regulated in regard to various cases which might occur in his practice of those diseases which are also the source of the infecting poison. If he engage in discussion on these practical questions, he carefully declines to argue on the meaning of the term contagion. If it be stated that puerperal fever, in a large number of instances, cannot be traced to any source of infection, he replies that his theory does not involve such a necessity; that the symptoms may arise from the decomposition of organic matter in the patient's