THE CROONIAN LECTURES ON DISEASE OF THE SUPRARENAL CAPSULES.

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LECTURE I.

MR. PRESIDENT AND GENTLEMEN,—Upon my appointment to the honourable position of Croonian lecturer of the present year, I selected for my subject Addison's disease. The first, and perhaps the chief, reason which induced me to make this selection was, that the study of this disease has always been to me a matter of special interest, and has engaged my attention at every available opportunity ever since the announcement of its discovery. But another reason which also weighed with me in making a choice of my subject was, that the discovery, which must be accounted among the great medical discoveries of the present century, and which may with propriety rank side by side with Dr. Bright's discovery of the relation between dropsy and disease of the kidneys, has never to this time been made the subject of any of the lectures delivered before this College, of which the discoverer was an eminent Fellow. And now, sir, before I address myself to my proper subject of Addison's disease, permit me to say a few words respecting Dr. Addison himself. For it seems to me that to show—though of necessity but briefly—from what and how Thomas Addison rose to become one of the most eminent physicians and ablest clinical teachers of the day, is on the present occasion only a fitting tribute to his memory.

Dr. Addison belonged to that class of men, numerous in this country, who, by their abilities and energy, have raised themselves from the lower ranks of society to the most exalted position in their respective callings. He was born in the year 1795 at Long Benton, a small village in Northumberland, three miles and a half from Newcastle-upon-Tyne. His father was a grocer and flour-dealer. Though of humble station, he must have been a man of enlarged views, for he not only gave his son the best elementary education within his reach, but he aspired to start him in life on a higher social level than his own. Dr. Addison himself told me that his father designed him for the law; but personal predilections induced him to embrace the profession of medicine. He was first sent with his brother to a school kept at a roadside cottage by one John Rutter, a parish clerk, from whom, some years later, Robert, the son of George Stephenson, received elementary education in the same house, whilst his father was engaged as an engine-worker at the neighbouring Keworth collieries. He was subsequently removed to a school of the higher class, and thence he went to Edinburgh, and became a medical student. Fortunately, his father had both the means and the desire to afford his son every possible advantage for acquiring a knowledge of his profession. The opening out of collieries in the parish had largely increased his custom among the good folks in the neighbourhood, and he had become rich for his station. Addison, therefore, after passing through the necessary curriculum of medical study, took the degree of M.D., and was enabled to come to London, where he first became House-Surgeon to the Lock Hospital, and subsequently Physician to the Carey Street Dispensary, and also, I think, to the Royal Infirmary for Women and Children in the Waterloo Road. Soon after his arrival in London, he entered as a pupil at Guy's Hospital, and, in a comparatively short time, he was raised to be a member of the medical staff. In this position, he speedily made for himself a great reputation as a practical physician and clinical teacher. A wide experience acquired in such various fields of study, together with his own great natural powers of insight, sufficiently explain the apparently intuitive knowledge of disease, and the almost unrivalled powers of diagnosis, which formed the basis of his great and real success in professional life. For his success was real; it was not small, if estimated in the lower sense by pecuniary results; but, if estimated in the far higher sense by his achievements and reputation, his success was great indeed, and such as only a favoured few can hope to equal. In some subjects, he was far in advance of his day. Pathological truths which

he enunciated thirty years ago, with respect to diseases of the lungs, have only recently won their way to general acceptance. The discovery with which his name will ever be associated was published to the medical world nearly twenty years ago, and has not yet been generally accepted, nor even generally understood. Dr. Addison died at Brighton in June 1860, and was interred in Cumberland, from which county his family had sprung, and where his maternal grandfather had been a respectable yeoman. I trust that this slight sketch of one of the most eminent members of this body will not be deemed an unsuitable prelude to lectures devoted to the elucidation of his most famous work.

Dr. Addison had been nearly thirty years on the medical staff of Guy's Hospital when he discovered the disease to which you, sir, if I mistake not, were the first to apply the name of Addison's disease. To quote his own words, he had for a long period observed a form of general anæmia occurring without discoverable cause in cases in which there had been no previous loss of blood, no exhausting diarrhoea, no chlorosis, no purpura, no renal glandular tumours or malignant disease, and which he, therefore, designated idiopathic anæmia; a disease which presented in every instance the same general character, pursued a similar course, and, with scarcely a single exception, was followed at a variable period by the same fatal result. He further stated that the leading characteristic features of the state to which he directed attention were anæmia, general languor and debility, remarkable feebleness of the heart's action, irritability of stomach, and a peculiar change of colour in the skin, occurring in connection with a diseased condition of the suprarenal capsules. The characteristic discoloration, he said, pervade the whole surface of the body, but commonly most strongly manifested on the face, neck, superior extremities, penis, scrotum, flexures of the axilla, and round the navel. It presented a dingy smoky appearance of various shades, deep amber or chestnut-brown; and in one instance the skin was so universally and deeply darkened, that the features of the patient might be taken for those of a mulatto. This discoloration was never attended by any harsh dry condition of the surface. To complete the picture, he added that there were occasional actual vomitings, palpitation and breathlessness on exertion, indications of a disturbed cerebral circulation, a strongly marked tendency to the formation of fat, in striking contrast to the failure and exhaustion observable in every other respect. He had, therefore, before his eye a distinct definite morbid state, the nature and cause of which he sought to discover; and his discovery, when made at length, was no chance hit, but the result of long and careful investigation. Accurate clinical observation had first led him to discriminate in the living patient a remarkable train of obscure and apparently causeless symptoms, always of fatal augury; and, while searching out the hidden pathological cause, it was only after the careful exclusion of all other morbid conditions that he referred them to a disease which he found seated in the suprarenal capsules.

It is necessary to dwell upon this point, because at a subsequent period, when he came to publish his monograph, Dr. Addison deviated from his own accurate conception, and subjoined to his own cases several others which he had not seen during life, which, so far as could be known, had presented no constitutional symptoms that could not be accounted for by malignant or other obvious disease, and in which there was only very partial discoloration of skin, or discoloration not at all corresponding with the graphic description I have quoted from his pages. These mistakes of Dr. Addison's were the more remarkable, because, in the first place, as we have seen, he himself states that the chief motive of his investigation had been to determine the cause of symptoms which could not be accounted for by any discoverable disease; and, in the second place, his great knowledge of skin-affections must have made him familiar with the fact that various organic and cutaneous diseases are attended by more or less pigmentation of the skin, though none of them by a pigmentation presenting all the peculiar characters of the discoloration which he had described. These mistakes were doubtless due to the enthusiasm of mind attendant on his discovery, which led him to endeavour to include as much as possible within its scope; but, unfortunately, their effect has been to confuse his own true clinical and pathological description, and to give rise to misconceptions which are still far from being eradicated. We have Dr. Wilks's authority for the fact that, at a later period, Dr. Addison's views were more in accordance with present knowledge; but unfortunately he died, and did not revise his monograph.

As with respect to most other discoveries, several previous observers had stumbled upon the facts which Dr. Addison had discovered. His eminent colleague Dr. Bright had observed, and recorded in reports of medical cases, a case of Addison's disease. It was in all respects a well marked example, and Dr. Addison included it in his monograph, where it stands as Case 5. Mr. Sibley also in 1854 recorded in the

Medical Register of Middlesex Hospital a case of Dr. Seth Thompson's which presented all the main features of Addison's disease, including the discoloration of the skin. Dr. Kirkes likewise reported a case in St. Bartholomew's Hospital several years before the publication of Dr. Addison's discovery, in which the asthenia, nausea, and vomiting had been observed in life, and in which, after death, the only lesion was the lesion of the suprarenal capsules which I shall hereafter describe. At a more remote period than any of these, a case in the Hull Hospital was recorded, almost typical as regards its clinical history, and also its pathological appearances, and closely resembling the case of a girl who died under my own care in 1865. It is true that in neither of these early cases was any discoloration of the skin noted; but we need not infer that it was necessarily absent, seeing that in my own case the discoloration, though characteristic, was so slight that it might have been easily overlooked, more especially at a time when its importance as an indication of the nature of the disease was totally unknown. In such circumstances, we may be quite sure that the discoloration of the skin in Dr. Bright's and Dr. Thompson's cases must have been well marked, or it would not have held the prominent place it does in the description of the symptoms. I refer to these two last cases with special pleasure, because more striking illustrations can scarcely be used of a truth which I have always felt, and which was so well expressed by Dr. West, the last Harveian orator: that the mere details of which, when we have ascertained them, we cannot see the purport or the uses, will sooner or later surely find their place.

I cannot close these introductory remarks without some reference to two distinguished living members of the profession, but for whose labours Dr. Addison's discovery might possibly have attracted at the time but little attention. Soon after the publication of the monograph, Mr. Jonathan Hutchinson gave a wide-spread impulse to the discussion of the subject, by collecting and publishing all the cases he could obtain, bearing upon the question of the reality of the disease and its relation to a morbid process in the suprarenal capsules. To Dr. Wilks, we are even more deeply indebted for much of the advance towards our present knowledge of the disease. In a succession of papers published in the *Guy's Hospital Reports*, he described all the chief symptoms of the disease, and more especially the pathological appearances in the suprarenal capsules, in a large number of cases which had either occurred in the practice of the hospital, or had been submitted to him by other medical men for examination; and he further brought forward the truth obscured by the admission of spurious cases in Dr. Addison's monograph, that all genuine cases of the disease are due to one and the same characteristic lesion of the suprarenal capsules.

Notwithstanding the misconceptions which have prevented the general recognition of Dr. Addison's discovery, we have made, as I have said, much advance in the knowledge of the disease since Dr. Addison's time. More than three hundred cases have now been recorded, some in almost every country in which medical science is cultivated. Of these, many are so imperfectly reported that no conclusions can be fairly drawn from them as to the existence of the disease, and others again, which present neither the clinical nor the pathological conditions described by Dr. Addison, are obviously not cases of Addison's disease at all, although published as such. But, on the other hand, by far the larger number are true cases of the disease, having presented, in a more or less developed form, its characteristic clinical phenomena, together with the particular lesion in the suprarenal capsules; while a considerable number are what I may term typical cases, *i.e.* cases in which no pathological lesion of any importance was found, except the one particular lesion in the suprarenal capsules. Eight of these typical cases have come under my own care or observation, several of them in the Middlesex Hospital; and I pass now to the delineation of the living picture of Addison's disease, as it has repeatedly presented itself to me in these and other cases, unmitigable at first sight to one who held the key of the mystery supplied to Dr. Addison's discovery. There are progressive asthenia, having often originated without any apparent cause, seldom dating from any definite period; an indescribable aspect of listlessness or depression; great languor and indisposition for exertion; almost invariably a remarkable weakness of the heart's action; a small, feeble, compressible pulse; loss of appetite; irritability of the stomach; nausea and retching. There are usually more or less severe and frequent pains in the loins and epigastrium, and not uncommonly tenderness on pressure in one or both hypochondria; a rigidity of the abdominal muscles, as if instinctively contracted to protect deep-seated parts from pressure. In advanced cases, vomiting is seldom absent, and it is sometimes spontaneous and irrepressible. There are usually breathlessness, palpitation on making any muscular effort, frequent sighing or yawning, and sometimes a persistent hiccup; generally, faintness or giddiness on rising, or even on being raised up in bed. Notwithstanding, however, the great feeble-

ness, which is one of the invariable symptoms of the disease, there is, in uncomplicated cases, comparatively little or no real emaciation; but, on the contrary, together with some appearance of partial wasting, there is always a fair amount, and often a considerable excess, of subcutaneous fat, and the skin remains soft and smooth. The temperature, as a rule, is below the normal. The skin and extremities are cool, if not cold, to the touch. The urine is often small in quantity, and generally of low specific gravity, and deficient in solid constituents. The bowels are mostly confined, the tongue usually ruddy and moist until the advent of typhoid symptoms during the last days of life. The mind is often clear to the last; but so great is the prostration in the later stage of the disease, that the patient lies in a drowsy and semicomatose state, from which he can only be roused by questions addressed to him, and he then gives pertinent, though slow and monosyllabic, answers. In this stage of the disease, the temperature falls considerably below the normal, and death takes place by asthenia, and sometimes at the last almost suddenly, apparently in syncope. There is, on the other hand, in many cases towards the close of life, incoherence or delirium, sometimes low muttering, sometimes more loud and active, and in these cases death often takes place in coma. In one of my own most typical cases, the patient had a convulsive fit, and lay for hours before death with firmly closed jaws and great rigidity of the muscles of the abdomen and extremities. He was seemingly unconscious, but whenever he was touched convulsive twitchings took place, either of the face or of the whole body. Various other symptoms equally referable to the disturbance of the nervous system, such as vertigo, numbness or anaesthesia of the face and arms, and more rarely of the lower extremities, dimness of sight, flashes of light before the eyes, noise in the ears, deafness, tremors, rigors, and even epileptiform and other seizures, have been recorded in many cases as occurring in the course of the disease, and in a few as having been the principal symptoms observed during life, except the invariable languor and general debility.

To this sketch of the characteristic constitutional symptoms of Addison's disease, I must add the description of the peculiar change of colour in the skin as it has struck my own eye in every advanced case. This consists, as is generally known, in a gradual darkening of the skin on various parts of the body, or even the whole body. The aspect of this discoloration, when fully developed, is very remarkable, and gives the patient the appearance of belonging to one of the dark races of mankind. Most frequently it has a dusky, smoky, or yellowish brown hue; sometimes it is of a green brown colour, and when deepest approaches in parts the tint of negro skin. The discoloration is never uniform over all parts of the body. It commences paler, and becomes deeper on all or some of the exposed parts, the face, neck, dorsum of the hands and fingers, and all those parts which are naturally the seat of pigment on the general surface. Sometimes there is universal discoloration, but more frequently it is only distinctly obvious on certain parts of the body. Even in the latter case, however, it probably affects in some degree the whole cutaneous surface; for, on a microscopical examination of parts of the skin, which, by contrast with the darker parts, appeared normal, I have found in them small quantities of the pigment which imparts an abnormal colour to the skin. The transitions from the dark to the paler shades of discoloration on different parts of the body are never abrupt. The darker parts are never in defined patches, but merge into the other and lighter parts of the surface. There is, however, one marked exception to this. When the skin has suffered any superficial abrasion or injury, or when the patient has been blistered at a recent period, the injured parts not only become much darker than the surrounding portions of the surface, but present defined margins, coinciding with the extent of the cutaneous injury. In the case of two patients of my own, I found abrupt dark defined patches on the epigastrium, and I ascertained that they were the seats of blisters which had been applied a short time before. In the case of the second patient, who survived nearly two years, the dark patch gradually faded away, and before death ceased to be visible. In the other patient, the deep cicatrices caused by cupping more than twenty years before remained perfectly white. Each little scar was surrounded by a distinct border of dusky discoloration. It does not require, however, actual abrasion of the skin to excite a greater deposit of pigment in certain parts. Slight local irritation of the surface appears in a few cases to have produced the same effect. I have seen dark streaks on the skin corresponding with the lines of pressure exerted on particular parts by petticoat strings and garters, and the same circumstance has been noticed by others. In a case recorded by Dr. Nicholson in 1873, it is stated that the patient, a baker's lad, presented on his shoulders dark stripes corresponding to the bands by which the basket he carried was slung at his back. I was anxious to show some drawings illustrative of this remarkable discoloration of the skin, but it is most difficult to procure good drawings of it. The fact is, that the discoloration is so like the colour of a dark

person, that it is almost impossible to get a thoroughly good illustration. I have had, therefore, to fall back upon the two lithographs before you, one of a patient of Dr. Hughes of Dublin, and the other of a patient in Guy's Hospital. The dark picture represents a colour much darker than any that I have seen, but I was assured that it is not darker than the patient really was during life.

The discoloration of Addison's disease is not entirely restricted to the skin; it is also frequently observed upon the mucous membranes of the cheeks and gums, also upon the tongue, and on the lips, where it takes the form of an irregular bluish-black streak, running longways near the junction of the mucous membrane with the outer skin. It is seen on the gums and buccal mucous membrane in the form of irregular stains and patches, mostly brownish, with an ill-defined border. In two of my own cases, the stains on the buccal mucous membrane have corresponded with seats of irritation produced by the pressure of protruding teeth; but, in other cases, I have been unable to verify any such cause. These stains on the gums and buccal mucous membrane form another point of analogy between the discoloration in Addison's disease and the pigmentation natural to the dark races of men; for several Lascars who have come under my own care in hospital have presented on the same parts stains similar to those that I have described. The discoloration of the tongue appears usually in the form of sharply defined stains of a purplish blue, or somewhat inky hue. In my own cases, these stains have always been situated near the free margin of the organ. The conjunctivæ always remain normal, and the contrast between their pearly whiteness and the dusky hue of the discoloured skin is striking, and involuntarily recalls the similar contrast in the mulatto or negro countenance.

We see, therefore, that the discoloration of the skin in Addison's disease usually begins and eventually becomes deepest on those parts which are naturally most liable to become pigmented, either by exposure to the sun and air, or by the excitement of certain physiological processes. To these may be added such parts as may accidentally be subjected to the excitement of local irritation. In other words, this peculiar change of colour is, like many other pathological processes, merely an exaggerated, and therefore a morbid, development of a natural physiological process. On a microscopical examination of sections of discoloured skin, the discoloration has seemed to be due to a deposit of yellowish brown pigment in the deeper layers of the epidermis, more especially in the layer in immediate contact with the papillæ, while the more superficial layers of the outer skin mostly remain free from pigment. Here is a drawing, highly magnified, of a portion of the skin, showing the hair and some deposit in the papillæ; and there is also another drawing of the skin of a negro, which will show that the discoloration in Addison's disease is in the same part as the discoloration seen in the negro and Lascar. The deposit is generally seated in the layer immediately in contact with the papillæ; nevertheless, I have found in several cases traces of pigment in some of the more superficial scales of the epidermis, and also pigment-granules deposited here and there in the cutis. There is a specimen here under the microscope which shows very well the ordinary arrangement of the discoloration over the papillæ, and also shows some of these pigment-granules in the true skin: they are not usually found in that situation, but fortunately I have one specimen which shows that they are sometimes found more deeply seated than is usual. Dr. Sidney Coupland also microscopically observed pigment-granules, both isolated and in groups, in the connective tissue of the cutis at some distance below the epidermic layer. The principal part of the pigment, however, is in every case deposited in the cells of the rete Malpighii; it is accumulated round nuclei, but some of it is generally free and irregularly distributed; this latter portion of pigment has also been originally contained in cells, which have disintegrated and allowed the colouring matter to escape. A physician at Halle, in the case of two patients, on a sectional examination, found many pigmented connective tissue-cells in the papillary portions of the cutis; and Mr. Schäfer observed in the same portion of skin a number of irregularly shaped corpuscles containing a considerable amount of pigment. The colouring matter in the patches on the tongue is deposited in a corresponding situation with the stain on the skin, being seated in the lower cells immediately overlying the papillæ; the superficial layer of epithelium remaining quite free from pigment.

To those who have carefully examined the skin of negroes and Lascars, or persons belonging to other dark races of men, it would be obvious, from this description, that the differences between their normal colour and the abnormal pigmentation of Addison's disease are merely differences of degree; although in the former physiological conditions, and in the latter pathological causes, have operated to produce them.

(To be continued.)

CASE OF ACUTE OTITIS MEDIA: SUPPURATIVE INFLAMMATION OF THE MASTOID REGION: DEATH.

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THE following case presents some features of especial interest to aural surgeons, though not partaking of a very uncommon character. I regret that I had not the opportunity of making more detailed observations of this case; it was seen by me once only, and the rapid termination did not allow a second examination.

C. M. L., aged 16, mechanic, was admitted to the Hulme Dispensary on January 16th, 1875, under my colleague Dr. Railton, one of the surgeons to the charity. He had always enjoyed good health, and seemed a well made youth. He never had any fall or blow upon the head. One month before admission, he noticed slight deafness and pain in the right ear. About a fortnight later, the mastoid process became swollen and tender. A week before admission, after severe pain in the ear and about the temple, a purulent discharge came from the right auditory meatus. On admission, Dr. Railton, knowing my interest in aural diseases, requested me to see the patient with him. I found the boy complaining of severe pain in the depth of the ear, about the mastoid, and down the neck. There was a profuse purulent discharge from the right ear; the mastoid region was greatly swollen, red, and soft, and causing great projection of the auricle. The hearing distance for a watch was 48 c. No tuning-fork was at hand to test by that means. There was no paralysis or affection of any of the cranial nerves. A lotion of sulphate of zinc, with carbolic acid, was ordered to be instilled warm into the ear every two or three hours, and the entire part bathed with it. An incision was made into the mastoid swelling half an inch from, and parallel to, the auricle, without liberating any pus, and followed by linseed poultices, etc. When seen by Dr. Railton on the 19th, the patient had slept very little, owing to severe pain at the back of the head, which had been temporarily relieved by the incision, from which there was now considerable discharge of pus. There was no vomiting nor delirium, or any hæmorrhage from the external meatus. On the 21st, the discharge from the mastoid region was very offensive and profuse, that from the auditory meatus much diminished. The patient was very restless, frequently tumbled down, and kept his head clasped between his hands, which he said "relieved the pain at the back of his head and neck". Convulsive movements of his left arm and leg were now very noticeable. The left arm and leg were constantly being jerked about in an involuntary manner. His appetite and vision remained good to the last.

On the 22nd, the symptoms grew worse, though he still ate well, and was quite conscious, answering questions put to him. The convulsive twitching of the left extremities continued, and he sat with his head upon a pillow placed over the back of a high chair. About 8.30 p.m., his face changed colour very frequently; the left ear and side of the head suddenly became of a dark purple hue, his head dropped forward, and, after a few groans, he died. On carefully questioning his mother, she was certain that there was no squinting or facial paralysis; that "she was sure there was nothing the matter with his face at any time during his illness". No signs of cerebral irritation were present when he attended at the dispensary. Unfortunately, permission to make a *post mortem* examination could not be obtained.

REMARKS.—The above account gives all the facts of the case; but, in the absence of any pathological examination, some caution is necessary in accounting for the exact mode in which death ensued in this patient. This fatal attack of mastoiditis was unlike most cases, in being the result of an acute aural catarrh, and not of a chronic otorrhœa. Toynbee speaks of having seen but one case of abscess of the brain due to acute ear-disease. There was no history of any throat-affection, but it is probable that such existed to a slight extent at first. Want of opportunity did not enable me in this case to discriminate between mastoid periostitis and caries at the outset: a distinction often difficult to determine. The discharge from the right meatus did not suddenly cease, as it usually does, on the development of cerebral complications. If death arose from ulceration into the lateral sinus or carotid canal, there would probably have been hæmorrhage from the nose, mouth, and ear. Abscess of the cerebrum is scarcely probable in the absence of coma, vomiting, and delirium. May we not conclude that examination after death in this patient would have disclosed partial meningitis, with abscess in the right cerebellar lobe and purulent effusion about the medulla oblongata?