milk passed into the trachea and bronchi. This was quickly followed by a fatal result; and on the *post mortem* table the milk was found in the respiratory passages. In this case, the afferent branches of the pneumogastric failed to excite the sensory centre and to induce the expulsive efforts of violent cough. The afferent fibres of the fifth were also weakened. We have in this latter disease the opposite condition to that observed in hydrophobia; hyperæsthesia in the one, anæsthesia in the other.

The same connection of the fifth nerve with the pneumogastric is found in the effect of severe chill or shock from cold; this reflex action is shown in ordinary sneezing, but it is more decided when the power of the pneumogastric is weakened and severe bronchitis or pneumonia is induced. The shock on the nerve-power of the respiratory organs may be so great that the patient is in a few hours in a state of the greatest prostration, with dry and brown tongue, resulting in advanced fever, but without cough or ordinary external signs of inflammation of the chest. The pneumogastric is almost paralysed; but the first effect was upon the fifth nerve, and a mistake is made in the treatment of these diseases if this connection of the fifth nerve be overlooked. The face should be kept warm, and no draughts of cold air allowed to play upon it. It is quite true that in the perspiration and craving for air in severe pneumonia fanning the face is a temporary relief to the patient, but this is an expression of the exhaustion and of the desire for pure air which the system needs.

We might adduce other instances of the manner in which the pneumogastric nerve is affected by reflex action, but would only here advert to the effect produced upon the centres of the nerve by disturbance on the cerebral aspect of the ganglia. It is powerfully influenced by the emotions and by the passions. The special senses directly influence it; an offensive object, and, still more, a disgusting smell, induce violent retching: sudden alarm at the sight of danger, or the sound that terrifies, at once affects the heart and the respiration, as well as the action of the abdominal viscera supplied by the nerve. The nerve is placed as the custodian of essential vital functions, but it is, as it were, the willing handmaid of the mind and will. We have spoken of its extensive distribution, and each branch of the nerve has, we believe, a definite purpose; and by its means the throat, the larynx, the lungs and the heart, the stomach, the liver, and other abdominal viscera are brought into the closest union. During health, the hidden connections are united in harmonious working; but in disease the jarring of disturbed action spreads its sympathy to all the parts thus linked together. The following laws of action are often observed in the study of clinical medicine.

I. Disease at the origin of the nerve may induce symptoms in any of the peripheral branches; and this reflex state may be one of irritation and hyperæsthesia, or one of diminished power and anæsthesia; the one is spasmodic in character, the other paralytic.

II. Irritation in any set of peripheral branches may produce disturbance in any other part to which the nerve is distributed, or in the centre itself.

III. Alternation of irritation may be induced, at first one set of nerves, then another, becoming implicated. This alternating character of functional diseases is of great clinical interest. We see an irregularity of type and rapidity of recovery which contrast remarkably with the severity of the disease. Spasmodic asthma of the most distressing kind suddenly gives place to disturbance of stomach, this to cerebral symptoms, and these to severe neuralgia. Violent vomiting and marked gastric irritation are followed by loud cough and by loss of voice, indicating that an affection of one set of nerves has given place to change in another set of branches. In general weakness, there is loss of power in all the parts supplied by the nerve, and the fact is often of great importance in the close of disease. In exhaustion, the voice fails; many patients who are suffering from chronic disease are said to die from the supervention of bronchitis or of pneumonia, when the pulmonary condition is really the expression of exhaustion of the pneumogastric nerve; so, also, when there is great weakness, there is greater liability to affections described as bronchitis and inflammation of the lungs, the power of the respiratory centres being lessened, disturbance of nutrition more readily takes place. Still further, when patients are reduced by chronic disease of the stomach, or of the kidney, similar pulmonary changes may be due to exhaustion; this statement is not opposed by the fact of cedema of the lung and broncho-pneumonia coming on from uræmic poisoning.

A further evidence of exhaustion of the pneumogastric nerve is the loss of appetite, and the diminished power in the stomach to digest food placed in it.

[To be continued.]

THE CROONIAN LECTURES ON THE PATHOLOGY AND RELATIONS OF ALBUMINURIA.

Delivered at the Royal College of Physicians.

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LECTURE I.

MR. PRESIDENT AND GENTLEMEN,—I propose to bring under your consideration some of the larger facts connected with the several forms of renal disease which are ordinarily characterised by an albuminous state of the urine, marking their pathological distinctions, tracing their points of mutual relationship, and touching upon their associations with changes external to the kidney, or more or less widely distributed through the economy. The types of Bright's disease may fitly engage the attention of the College of Physicians of England. Whether we have regard to the early researches of Wells upon albuminous urine, to the paramount observations of the great physician whose name is inseparably connected with the disorders to which he gave structural place and organic habitation, or to the still progressing inquiries of others, of whom we hope that it may be long before they will take the place which they have earned among the worthies of the past, we are entitled to say, and with no extravagant boastfulness, that the members of our ancient and learned body have taken a part in the development of this branch of knowledge, which more than equals that of all other nations and of all other guilds. And it is appropriate, too, that the successors and inheritors of Harvey should concur, whether as looking from the same point of view, or as co-operating to secure a true figure by regarding the object from different quarters, to add to Harvey's discovery a pathological supplement; and, in working out the changes which disease produces in the circulation, to append to Harvey's propositions a set of corollaries which are among the most important of the results which have sprung from it.

The organic conditions of persistent albuminuria may be broadly divided into three.

1. *Nephritis, Tubal or Diffuse*, the product of simple inflammation of the secreting structure, and of causes directed especially upon the renal function. This, though essentially tubal, may, if intense or long continued, involve the interstitial tissue in the inflammatory process, and supply the granular kidney with one mode of origin. At first localised as strictly as any other organic inflammation, it ultimately tells upon the whole body, and produces in a lesser measure the arterial and cardiac changes which are more largely developed with chronic disease.

2. *The Granular Kidney, or the Kidney of Chronic Interstitial Hypertrophy*.—In this, the fibroid overgrowth has begun as a solitary change, or has been left behind as the more persistent and at last the more prominent portion of a mixed inflammatory process. The general association of this organic state with a morbid condition of the entire arterial system is one of the leading characteristics of the disease, and involves questions which will need a somewhat cautious examination.

3. *The Lardaceous Kidney*, a condition in which this gland participates only in an infiltration which pervades many organs and structures, and is immediately due to a condition of blood in virtue of which it deposits in many arterial districts a material which is different from any of the normal constituents of the body.

The first begins with changes local to the kidney, but often ends in results general to the arterial system; the second is so constantly associated with arterial changes, that it is in dispute whether the renal and the arterial changes are cause and effect, or are simultaneous results of circumstances antecedent to both; the third begins, without question, systematically, producing renal disease only as one of a series of secondary organic changes.

Each of these conditions is broadly separate from the others, but yet has its points of contact with them. Nephritis at first tubal may end interstitially, and thus the large smooth kidney may, however rarely, yet in a recognisable minority of cases, become small and granular. The granular kidney, or the interstitial fibrosis which is its essential, though usually of independent origin, may take its rise in either of the

other forms of change. And the lardaceous state, to complete the complicated relationship, may become associated with inflammatory processes, whether interstitial or by way of tubal catarrh.

I will trace in brief and general terms the origin, nature, and connections of each disorder, touching somewhat more heedfully upon points which are of current pathological interest, or bear practically upon the art of healing.

1. *Tubal or Diffuse Nephritis*—for tubal nephritis so often begins diffusely or becomes diffuse, that no more definite line of separation can be drawn between them than between slight and severe—is a catarrhal exasperation of the secreting function, due to some excessive or unsuited stimulus. Mere tubal catarrh, with attendant obstruction and congestion, is happily, in a large majority of cases, the only organic change. But, when the process is intense or persistent, it is apt to cause in the interstitial tissue a delicate supernucleation, which, in its early stages, may easily escape notice, but may lead in the end to obvious fibroid thickening. The results of this process, as presented to the naked eye, are swelling of the kidney white or red, as blood or epithelium predominates, smooth so long as the tubes only are affected, the smoothness to be succeeded by dimpling, or even by granular inequality of surface, should the interstitial tissues become involved, and time be given for consequent and gradual changes. For it may be laid down as an axiom in renal pathology that granulation invariably implies fibrosis. No mere tubal condition, whether of distension or collapse, breaks the superficial level. Thus, according to date and intensity, the following outlines may be drawn of the phases of renal inflammation.

a. *The Congested Kidney*.—The blood-dripping chocolate kidney of acute congestive nephritis.

b. *The Large White Kidney*.—Swollen and pale, either absolutely smooth, or with a surface but sparsely dimpled, dependent upon nephritis mainly and from the first tubal, but which may have come to involve the intertubal tissue. Superficial depressions, if they exist, are a sign that it has become thus complicated.

c. *The Contracting Kidney of Nephritis*.—Granulating and fibrotic, like the granular kidney, of latent origin, not often thus ensuing upon acute inflammation, but to be recognised as a rare and late result.

The intimate mechanism of these several conditions may be briefly reverted to. The first noticeable changes are an excessive production of epithelium with an excessive influx of blood. The epithelial cells are swollen, but not necessarily changed in other respects. These accumulate and distend the tubes; and, cemented into cohesion by the solidifying fibrine which is discharged from the Malpighian bodies and exudes through the tube-walls, form more or less impassable obstructions. In some cases, blood also is extruded. The congestive type is well marked and often rapidly fatal. The kidney becomes gorged with blood and much swollen, usually as the result of some recent exposure to severe cold. The patient is an adult, usually a man. The gland becomes injected to a chocolate or to a plum colour; when cut, it drips with blood at every pore, and may—at least I have seen it so in one instance—actually burst its capsule, so great and so sudden may be the swelling. In the case to which I refer, the patient had suffered much from cold in driving across a bleak moor in Yorkshire. As an immediate result, he had, along with shivering, bloody, and nearly suppressed urine, and other symptoms of acute renal inflammation which I need not detail, lancinating pain in the loins, which gave rise to a suspicion that his disorder was complicated with renal stone. The pain proved to have been due to the capsules of both kidneys having burst nearly symmetrically; a gaping rent in each, which involved also the superficial renal substance, had given exit to a quantity of blood which was found as a massive coagulum in the circumrenal cellular tissue. In this instance, beside the usual distension of the tubes by epithelium, blood, and fibrine, there was a somewhat profuse formation of corpuscles or large nuclei in the interstitial tissue: not regularly, but at scattered spots throughout the organ, both in cones and cortex. This participation of the extratubal structures in the inflammatory process is to be found more often when the disorder is more chronic. In the slower forms of the disease, which are characterised by white enlargement, epithelial accumulation is the most obvious change. This may early become fatty under the process, as in many other instances fatty degeneration succeeds closely upon inflammatory action. When it occurs from scarlatina, the fatty change is less marked than when the disease has originated in cold. With the epithelial overgrowth, a fibrinous exudation is poured out both from the Malpighian bodies and by the walls of the tubes. When very abundant, it seals up the tubes with an impenetrable barrier, almost abolishes the secretion of urine, and gives to the complaint a destructiveness almost as rapid as is that of the most severe congestive form.

So much for the tubal interiors and the disturbance to which the inflammatory process is in most cases limited. But the inroads of disease are apt to overrun scholastic lines of demarcation. Morbid change, to be simple, must always be recent. When the disorder has been protracted, and even sometimes when of recent origin, the nuclei of the interstitial tissue multiply in a manner to which I have already incidentally alluded, sometimes to such an extent, that closely packed corpuscles are conspicuous almost to the exclusion of everything else. These are arranged concentrically around the Malpighian bodies, and are abundantly, but less regularly, sprinkled in each of the once pellucid bars by which the secreting elements are separated. This helps to give the extravagant bulk which belongs to the white kidney of old disease, and to render return to health impossible. The nucleation may outlast the catarrh, and be at last the only prominent structural change. Usually the two persist together, and, with tubal distention and intertubal nucleation, much increase of bulk, and a smooth surface, the large white kidney finds its close.

More rarely, time is given for the nuclei to develop into fibre and the fibre to contract, causing the surface to become marked by depressions, which at first are few and far between, but afterwards become more numerous and closer, until, should the patient survive for as many years as the ordinary course of the disorder comprises months, a general superficial granulation may bring the organ into a condition which is difficult to distinguish from that of granular degeneration which has come on after its accustomed manner, not with an inflammatory outbreak, but with the slow and creeping advances which make it difficult to note when health ceased or disease began.

With regard to the question how long it takes the once smooth kidney of nephritis to become granular, I may refer to a boy who died at the age of 11, whose kidneys had become granular and contracted, as the result apparently of scarlatina three years before. In a girl who died of the same disorder at the age of 21, it was traced with equal probability to scarlatina eleven years before. And, to adduce a case which has not yet reached its conclusion, a girl aged 16 is the subject of chronic albuminuria, undoubtedly associated with the granular kidney, the renal disturbance having distinctly succeeded upon the same exanthem no less than thirteen years previously.

We may pass now from the kidney itself to touch briefly upon those consequent changes in other organs and tissues which supply the disease with its chief mortality. Inflammatory affections take the first place in frequency and fatality. Those of the respiratory organs in especial are the more deadly, the more acute the renal disease and the younger the patient, until, with the nephritis of childhood, they, to say the least, do as much mischief as all the other results of the disease taken together. Among forty children who died of the disease, death was mainly due to pneumonia, pleurisy, or bronchitis in twenty, pneumonia being so far the most frequent as to have occurred in fifteen of the number. Among adult patients, these affections sink into insignificance as compared with dropsy and its results, and the effects of uræmia upon the nervous system. Inflammatory oedema of the larynx occurs in a small proportion of cases, but is not characteristic of one form of renal disease rather than another. The pleurisy which originates in nephritis will sometimes be or become suppurative, as also may the peritonitis which more rarely occurs in similar circumstances. When thus arising, it often proceeds insidiously, and remains unsuspected until it has produced its fatal result. As to the effects of uræmia upon the nervous system, convulsions are frequent, but by no means necessarily fatal with the disease as it occurs in childhood; they take place in about a fifth of the cases, causing death about half as often. In later life—that is, after the age of 16—such affections, together with a non-convulsive coma, are the main cause of death in nearly half the instances which terminate fatally.

Affections of the inflammatory kind, together with the cerebral results of uræmia, convulsion and the like, are more declared in connection with the nephritic and comparatively rapid form of disease than are the changes in the heart and arteries which are so constantly found with the chronic and granular kidney. But, in connection with the origin of such vascular changes, it is of especial interest to inquire whether, in their lesser degrees, they ever ensue from disease like that in question, which begins locally to the kidney, and affects other organs, not by original participation, but by dependent disturbance.

I have examined somewhat carefully into the state of the arteries, together with that of the kidney, in as many well marked cases of inflammatory disease as recent opportunities have allowed. The results are displayed in the table. I have included only cases in which not only the organs, but the symptoms were typical; sudden and severe disturbance of health, with oedema, scanty and generally bloody urine, and the characteristic course of acute renal dropsy.

Heart and Arteries, with Inflammatory Affections of the Kidney, Tubal and Diffuse.

Name.	Age.	Cause of Disease.	Duration.	KIDNEY.		Heart.	Arteries (Pia Mater).
				Obvious Changes.	Microscopically.		
Harriet Luxford	10	Scarlatina (?)	3½ months	Weight 7½ oz.; smooth, mottled, yellowish white; capsules loose and thin	Epithelium accumulated, with loose oil-globules; tubes greatly and irregularly dilated; traces of intertubal nucleation	Weight 6 oz.; simple hypertrophy of left ventricle	Slightly changed; muscular coat somewhat thickened; traces of fatty degeneration.
Wm. Warren	7	Acute rheumatism (?)	10 weeks	Weight 8½ oz.; smooth, white; patched with vascularity; cortex greatly increased	Tubes enormously and irregularly distended with epithelium; general slight intertubal nucleation	Weight 6½ oz.; left ventricle greatly hypertrophied; right, slightly so	Granular degeneration of muscular coat, especially of nuclei; translucent uniform thickening of fibroid coat of arterioles
Annie Jones	13	Uncertain	16 weeks	Weight 12 oz.; smooth, yellowish, mottled; cortex greatly increased	Tubes generally distended with blood and epithelium; general interstitial nuclear growth	Weight 9 oz.; left ventricle increased in thickness, otherwise natural	Very marked thickening of both muscular and outer coats, especially in arteries of about 1-300th in. in diameter; nuclei wanting; thickening more marked than degeneration
Ethel Algar	6	Cold; repeated exposure, and consequent catarrh, bronchial, etc.	Last attack 5½ months; 3 attacks during last 2½ years	Weight 13 oz.; smooth; capsule thin; cortex increased; mottled, red, and white	Obstruction & distension of tubes, with epithelium and fatty concretions; uniform interstitial nucleation around Malpighian bodies and everywhere	Left ventricle hypertrophied slightly; weight 4½ oz.	Pia mater not examined, but arteries in kidney greatly thickened, especially in their muscular coats; walls of small arteries nearly equal to calibre in thickness
Catharine Burr	19	Uncertain; probably scarlatina	10 months	Weight 19 oz.; large, smooth, ivory white; blotched with vascularity; cortex greatly increased	Large thick plugs in tubes, which were greatly and irregularly distended; uniform interstitial nucleation, dense & abundant	Left ventricle slightly hypertrophied; wt. of heart 10 oz.	Great thickening both of muscular and outer fibroid coats; nuclei wanting; muscular coat granular, or rendered glassy and uniform

In the instances referred to, five in number, of which the duration of the disorder ranged from ten weeks to as many months, the arterioles were invariably thickened and the heart invariably hypertrophied. The arterial thickening was not always great, but was always beyond doubt, on comparison with the healthy condition. Reserving for the present any discussion as to the cause of the thickening, but speaking only of its nature, it appears to involve more or less both of the coats of the vessel, though neither to the extent noticeable with the granular kidney. The muscular coat is in general not greatly, but measurably thicker than in healthy vessels of the same calibre; while, at the same time, it becomes somewhat granular, or abnormally uniform or hyaline in texture, and its nuclei exhibit granular, apparently fatty contents. The change in the nuclei is sometimes, as in the case represented in the diagram, the most noticeable among the early changes. With these I have satisfied myself that, even at the early period of disease to which these cases belong, there is some degree of thickening of the outer or adventitious coat, which, since it is to be seen under different methods of preparation, cannot be attributed to the reagents used.

It has been urged, as a source of error in observations as to the thickness of arteries, that it is impossible to tell how much of apparent difference may be due to inequality of vascular contraction at death, or by way of rigor mortis, in any two cases where the arteries may be made the subjects of comparison; and we might suppose a single pair, or a few pairs, of observations to be thus vitiated; but, when in a large number the difference is found to be always on the same side, we may cease to torture our minds with doubts of this nature, but be content to attribute the difference to constant, not accidental, causes.

In the consideration of this part of the subject, it behoves us to use more than ordinary care, since it is difficult to exaggerate the importance of the conclusion—one as to which I myself entertain no doubt—that, under the influence of renal disease of inflammatory origin in a previously healthy subject, the arteries undergo changes similar in kind to those which accompany the granular kidney, however smaller in degree than those which belong to that more protracted complaint.

In the cases of which I have spoken, the hypertrophy of the heart was in some instances well marked, in others less so. There seemed to be no constant ratio in amount between the arterial and the cardiac thickening; where one was much sometimes the other was little, as if the two were the independent and variable results of a condition antecedent to both. That these changes ensue upon disease at first local to the kidney is certain. But it is not so easy to assert that they occur independently of renal fibrosis. With the improved means of examination now at our command, it can almost always be found that, in the fatal cases in which alone the arterial thickening can be ascertained, the tubal disturbance is complicated, originally or by acquirement, with interstitial nucleation; so that, if we could conscientiously regard the multiplication of connective nuclei which is present in these cases as part of a general fibrosis, we might find in the vessels but an extension

of the same constitutional change. But probably no one would thus explain these cases. The subject of each was a young and hitherto presumably healthy person; the attack in each began by way of glandular inflammation, and what ensued must necessarily be taken as its direct consequence rather than attributed to a general deterioration which the kidneys have shared, but have had no part in producing.

With the arterial thickening, as recognised by the microscope, an increase of tension is to be appreciated by the sphygmograph, and even detected by the educated finger. It is not my purpose to repeat in detail what was recently so conclusively demonstrated in this room by Dr. Sibson; but, to give completeness to my own cases, I may say that, among the tracings which Dr. Sibson adduced in proof of the increased tension proper to the inflammatory disease of the kidney were those taken from the patients Warren and Burr, the condition of whose structures, as ascertained after death, is given in the table.

Beside the changes in the structure and in the fulness of the arterial system are sometimes to be noted, when the acute dropsy has become chronically protracted, the retinal results of these conditions, the extravasations and white spots, which, though more frequent with the more chronic form of renal disease, are yet to be distinctly recognised in association with the inflammatory type which is at present under consideration. In the case of Burr, hæmorrhagic and white patches were conspicuous. A girl nine years of age, the subject of chronic albuminuria, consequent upon scarlatina, had the hæmorrhages and spots in a very marked form; and I could adduce, did time permit, other instances where the same retinal change has ensued upon scarlatinal nephritis.

Thus, to conclude a crucial part of a debated question, vascular tension, hypertrophy of the heart, arterial thickening, and retinal hæmorrhage, are all found with, and, considering the tender years and previous healthiness of the subjects, are presumably caused by disease, beginning locally to the kidney, as the result of glandular inflammation.

To this sketch of the pathology of tubal or diffuse inflammation, it is not my purpose to superadd any detailed account of the symptoms by which the disorder is declared; before this audience, any recapitulation of familiar experience would be intrusive. The sudden outbreak of acute dropsy, the abruptly diminished and bloody urine, the profusion of exudative and glandular products moulded into the shape of the tubes they have obstructed, the frequency and danger of the secondary inflammations which are set up as if by an irritating quality in the contaminated blood, the convulsions which so often endanger and the coma which so often destroys life,—all these are well known as marking the course of the disease of which the organic results have been before us; and scarcely less distinctive is its origin in the irritation of a morbid poison, or what perhaps cannot be better described than as a glandular strain, as, on the one hand, when the disease arises in scarlatina or the like, or, on the other, when it follows upon the external action of cold.

[To be continued.]