much oozing. Blood clot could so readily become infected. He preferred drainage by tube to gauze; the latter was so painful when removed.

Dr. CAMPBELL, in reply, maintained that, from the surgeon's point of view, a pelvic inflammation was the same whatever its source might be. He always left behind as much ovarian tissue as was possible. He had not tried inflating the tubes with air. He was not at all convinced that his analogy between the tube and the appendix was wrong; both might burst and leak, thus endangering the patient's life. The treatment of the acute chronic case differed from that of the primary acute case, as the adhesions one knew must be present in the chronic case encouraged one to wait.

VAGINAL INVOLVEMENT IN CANCER OF THE CERVIX.

[Abstract.]

Dr. ARCHIBALD LEITCH (London) called attention to the liability of cancer of the cervix uteri to extend down the vaginal wall. *Post-mortem* examination of several hundreds of cases showed that in 97.5 per cent. the vagina was more or less extensively involved; in fact it was the commonest of all the findings at autopsy. Involvement of the parametrium, of the interiliac lymph glands, and the occurrence of hydro-nephrosis were indeed less common. His argument was that these naked-eye appearances found *post mortem* were an indication of the microscopic spread that would be taking place during life. But in addition to such evidence, he had frequently found lymphatic involvement in operation specimens where a vaginal cuff had been removed, and he held that Wertheim, in advocating the removal of a portion of the vagina in order to enclose the septic cervix, had thus unconsciously done a greater service to radical treatment. Such vaginal removal, however, was not sufficiently thorough. Dr. Leitch in pursuing these investigations had on some occasions encountered irregular proliferations of the vaginal mucosa penetrating the underlying tissues, early epitheliomata in fact, which were quite distinct from lymphatic spread, and he suggested that these were due to the same cause, possibly an endogenous irritant, which had produced the original malignant tumour of the cervix. They were later in manifesting themselves, probably because the vaginal epithelium was more resistant to the causal agent.

THE ETIOLOGY AND TREATMENT OF NON- PYOGENIC NEPHRITIS (BRIGHT'S DISEASE).

BY

W. M. CROFTON, M.D.,

LECTURER IN SPECIAL PATHOLOGY, UNIVERSITY COLLEGE, DUBLIN,
AND PATHOLOGIST TO DR. STEEVENS'S HOSPITAL.

THERE is, with the possible exceptions of the cancer problem and the cause of certain acute infections such as measles, no more obscure region of pathology than that of non-pyogenic nephritis, or Bright's disease. It is with the hope of stimulating further observations, more extensive and more completely controlled, that I describe the following small series of cases.

The first cases that came my way to observe and treat were just before the war and during my war service in Malta (cases already referred to elsewhere), but from the war cases one could not draw very definite conclusions, since when convalescent these patients were shifted home and lost sight of; all of them improved very considerably under therapeutic immunization.

Before describing cases it may be well to consider briefly the present state of opinion on the subject of nephritis. It is recognized, of course, that acute nephritis is associated with acute infections undoubtedly caused by microbes, and it seems to be accepted that the cause of the nephritis is the same as that of the original lesions—for example, tonsillitis. It is recognized, too, that the chronic disease may follow the acute, and one presumes that it is recognized that the same microbial cause may persist, and that in this class of case the chronic nephritis is due to microbes. In the largest class of cases, however, no microbial cause appears to be recognized, and treatment is purely dietetic and directed to the treatment of symptoms.

H. Maclean in his recent excellent monograph on the diagnosis and treatment of renal disease assumes the position, if I do not misinterpret him, that protein and casts may be present in the urine but renal disease is not present so long as (a) there is no retention of urea, uric acid, creatinin, and the purin bases, (b) there is no retention of chlorides with consequent oedema, or (c) both. This doctrine appears to me very dangerous from every point of view, for if we adopt it it will tend to prevent our using specific methods of diagnosis and treatment in a large group of cases until the disease is advanced. He himself quotes the fact that experimentally three-quarters of the total kidney tissue may be removed before any accumulation of urea occurs in the blood. Surely this must hold good for destruction brought about by disease, and it is not until approximately a similar amount of essential kidney tissue is interfered with that symptoms of non-protein nitrogen retention (azotaemic type) or of dropsy (hydraemic type) occur.

It appears to be logical, then, to take up the attitude that no kidney can be considered undamaged which is letting through blood proteins, especially if casts are present as well, for such kidneys, if the lesion does not progress, may remain physiologically functional during a normal lifetime. Of course, the original lesion may retrogress owing to the removal of the cause and the recovery of the damaged tubules, the destruction of the cause preventing the damage of further tubules, so that sufficient functional tissue is left to prevent the appearance of symptoms. On the other hand, the primary illness with acute symptoms may entirely clear up and if the cause is only partly overcome and persists in a less virulent form a slow sclerosis may develop gradually, cutting off the blood supply of the tubules and lead to the strangulation of the whole tubular system.

This sclerosis, as is generally recognized, may follow on an acute attack or begin in an insidious manner and slowly progress. What, then, is the cause of albuminuria without symptoms and albuminuria with symptoms? One may rule out such minor causes as acute or chronic poisoning by inorganic or organic poisons such as lead or turpentine, and one must admit in the trench nephritis occurring in France the urine on culture was constantly sterile, but in the cases coming from Gallipoli that I saw, acute or subacute, and in the ordinary cases in civil practice there is no difficulty in isolating micro-organisms from the urine and identifying them, for reasons to be stated below, as the cause of the disease.

The functions of the kidneys are usually stated to be:

1. Excretion of water.
2. Removal from the body of certain waste products of nitrogenous metabolism.
3. Removal of acid products from the body.
4. Maintenance of the optimum concentration of salts in the fluids and tissues.
5. Excretion of toxic materials artificially introduced.

This list leaves out one of the most important functions of the kidney—namely, the excretion of micro-organisms, or, in strictly localized infections, such as diphtheria, the excretion of their toxins.

The resistance of the kidney to virulent micro-organisms is very remarkable; in only a minority of cases of acute septicæmias from whose blood the kidneys abstract and excrete the causative organism do the kidneys become acutely inflamed and damaged. It is not yet generally recognized that many infections thought to be strictly localized are in reality focal manifestations of a subacute or chronic septicaemia. In my experience in cases of boils, carbuncles, and such like infections the staphylococci can always be recovered from the urine. So, too, in the few cases of scarlet fever I have had to treat streptococci were recovered from it. In a proportion of cases of "rheumatic conditions" staphylococci or streptococci, or both, or *B. coli*, are found in the urine; sometimes other microbes, such as diphtheroids—in all these without, as a rule, any signs or symptoms of nephritis. It is not surprising, then, that in some patients whose kidneys are excreting microbes the kidneys should fall a victim to the microbe and become diseased. The lowering of the resistance of the kidney cells may be brought about by any of the general causes of lowering of general or focal resistance—grief, chilling of the surface, alcohol, or the excretion of abnormal waste products from a distant focus of microbial action—for example, of the intestinal tract, of the bones, and so on.

In all the cases treated by me I have isolated a microbe from the urine; in the majority of cases staphylococci, in a few streptococci as well. I shall be asked at once how I know

these microbes are the cause of the disease. Do they fulfil Koch's postulates? Did they produce the disease in animals? Were they isolated from the animals? Of course not. In how many cases of human disease certainly associated with a given cause can Koch's postulates be fulfilled? In 10 per cent.? If this is so it must be the extreme limit.

If Koch's postulates are not fulfilled what criteria of infectivity are we to accept? The finding of specific antibodies—adapters (a generic name for amboceptor, immune body, substance sensibilisatrice, coferment), agglutinins, and so forth? Perhaps so, but always in the animal body will these antibodies be found for such common microbes as staphylococci, streptococci, diphtheroids, and the tubercle bacillus. Fluctuations of the opsonic index may help, but in my experience the following criteria are by far the most reliable—namely, the production of (1) focal reactions, (2) general reactions, (3) cure or improvement, with an antigen made from a microbe or microbes isolated from the patient himself, or alternatively the production of local, general, and focal reactions with an antigen used for diagnostic purposes, such as tuberculin.

Let me take this case first as it is most familiar to most people. It may be said that the tubercle bacillus fulfils Koch's postulates, but it is at least arguable whether the human lung disease is reproducible in animals, for lung tuberculosis is practically never an unmixed infection, while animal tuberculosis nearly always is. Local reactions are of little or no use either for the diagnosis of tuberculosis or any other disease, since the presence of antibodies in the circulation enables an intradermal reaction to occur. Any antigen given under the skin may produce a redness or swelling.

General reactions are more important. My experience is that in the case of tuberculosis, if the tuberculin is given in the prescribed doses, a general reaction is at least 90 per cent. diagnostic, for when a lesion is present it is accompanied by a focal reaction. Indeed the site of the lesion may be made manifest by this focal reaction such as the occurrence of crepitations in an area of a lung where they were previously absent, the increase or decrease of the physical signs or symptoms in a kidney or joint or bone, the increase of discharge from a mucous membrane or sinus, the decrease or increase of albumin in the urine. The late Professor White in a case of discharging wounds or sinuses used to work out the curves of focal reaction by periodical counting of the microbes in the discharge. In nephritis, as I shall show below, the curves of reaction can be precisely worked out by the daily estimation of the protein in the urine. When the lesion is closed to the surface the reaction is very definitely shown by a sudden increase or decrease of symptoms and physical signs—in a knee-joint, for instance, or in the central nervous system in epidemic meningitis or encephalitis. The sensitiveness to small doses of the infecting antigen is very remarkable. For instance, in tuberculosis I have quite often produced a slight but definite general reaction after a dose of 0.0000001 mg. H.T.S., while in a patient without active lesion 0.1 mg. has no effect. In mucous colitis focal reactions after 1 million (about 0.0003 mg.) *B. coli* antigen are quite common. One might multiply instances indefinitely; on the other hand one could give one hundred times the dose of a non-specific microbial antigen subcutaneously without reaction. Finally, if having given a course of microbial antigen to a patient the lesion retrogresses or completely heals up, it is in my experience 99 per cent. at least probable that the antigen or antigens used are specific.

I have argued many times before the question of the use of non-specific antigens. I shall only ask again, If they are so successful as some would have us believe, why were they such a tragic failure in wound infections in the late war?

Now, if the criteria I have laid down are correct, the identity of the infecting micro-organisms is completely proved, for in the majority of cases to be described there were general and focal reactions and marked retrogression or cure in almost every case. I have only lost one patient so far, and he was so far advanced that no hope of recovery could be entertained; I have not therefore described his case.

Albuminuria without Obvious Oedema.

CASE I.

A patient of Dr. Cooke, a man aged 28, seen first in 1914. Had been rejected three times for life insurance on account of albuminuria. The amount was 1 gram per litre. Staphylococcus isolated. The doses given were 10, 25, 50, 75, 100, 150, 200 million. The albumin disappeared after the 100 million dose. The patient then disappeared for three months, but was still free from albumin when he turned up again, and has remained free since.

CASE II.

D. B., aged 17. Seen in 1919. Laboratory assistant. Had been cured of tuberculous glands in neck with tuberculin (H.T.S.). Was pale and easily tired. He found distinct cloud of albumin in his urine on several occasions. Cultures of special specimen gave culture of *Staphylococcus albus*. He was given doses of 10, 25, 50, 75, 100, 150, 200, 300, 400 million. The albumin rapidly disappeared, and has remained absent since (September, 1922).

CASE III.

Medical student, aged 26. Seen first February 25th, 1920. For three years or more noticed frequency of micturition during the day, especially during cold weather. Examination of mixed twenty-four hours' collection gave 0.75 gram per 1,000 albumin. *S. albus* isolated. Doses 10, 25, 50, 75, 100, 150, 200, 400, 600, 800, 1,000, 1,500, 2,000, 3,000, 4,000 million given at suitable intervals according to reactions. After the 200 million dose the albumin which had reduced to a trace increased to 0.5 gram per litre and then gradually disappeared, three weeks' interval being left. He remains now (1922) completely free from albumin.

CASE IV.

Boy, aged 6. Seen first on November 10th, 1921. Sent to me by Dr. Strangman for chronic bronchitis, asthma, and constipation. The boy looked pasty, and on examination of a sample of a twenty-four hours' collection

Case IV. Focal reactions.

it was found to contain about 0.6 gram per litre of albumin. From his sputum were isolated *S. albus*, *M. catarrhalis*, and streptococci. *S. albus* was isolated from his urine and *B. coli* from his faeces. A mixed antigen was made. I omitted the *S. albus* from his urine as I was anxious to see whether the *S. albus* from his sputum would produce focal reactions in his kidneys and thus confirm my opinion as to its probable mode of entrance into his circulation. These focal reactions occurred early in his treatment, and very prettily demonstrated the occurrence of focal reactions in the kidneys.

The series of doses was—

<i>S. albus</i> .	<i>M. catarrhalis</i> .	Streptococci.	<i>B. coli</i> .
10	+	1½	+
25	+	2½	+
50	+	5	+
50	+	5	+
75	+	7½	+
100	+	10	+

and so on to

2,000 + 200 + 200 + 200
Some of the doses had to be repeated owing to focal reactions in his lungs. After the second dose of 175 + 17½ + 17½ albumin completely disappeared. His treatment was concluded on February 2nd, 1922, and he has remained well since.

These cases will suffice to illustrate the functional albuminuria type of case. I have not so far met a case in which I did not isolate a microbe from the urine and cure it by immunization. But my experience is still small.

Cases with Obvious Oedema.

CASE I.

Constable X, aged 30. Admitted to Dr. Steevens's Hospital under Dr. Kirkpatrick, October, 1916, with general oedema and a heavy cloud of albumin. When I saw him he had lost the oedema under ordinary treatment, but still had 1 to 2 grams per litre of albumin. I isolated *S. albus* from his urine. Doses of 10, 25, 50, 75, 100, and 200 million were given at suitable intervals. At the end of three weeks albumin had completely disappeared from his urine, and he was sent home apparently cured at the end of four weeks.

CASE II.

J. B., aged 14. Came under my care in February, 1918, with generalized oedema, severe headache, and amblyopia. She was passing 50 oz. of urine containing 1 gram per litre of albumin, and giving a profuse growth of *S. albus*. Temperature normal. After the first dose, 25 million of antigen, there was a general and focal reaction, her temperature going to 99.4° for two nights, her oedema and headache increasing and her urine to 3½ pints, containing still 1 gram per litre. The doses were increased at suitable intervals to 4,000 million, when the urine contained a bare trace of albumin and the patient had no symptoms. On re-examination five months after a catheter specimen still contained a trace of albumin and staphylococci were again isolated, so she was given a second course of antigen beginning with a dose of 100 million and increased to 20,000 million. Her urine had then been free of albumin and microbes for some time, and remains so still (September, 1922).

CASE III.

J. C., aged 18, admitted to Dr. Steevens's Hospital in an unconscious state, under Dr. Kirkpatrick, November 29th, 1919, having had a fit on a railway station platform on his way home.

He gave a history of three weeks' illness. He had general oedema, evening temperature 101° F., pulse 124. He was bled, given an enema and hot pack, with only water to drink. He recovered consciousness under this treatment. I saw him a fortnight after. He was then generally oedematous, passing 20 oz. of urine, which contained a large quantity of albumin and a few pus cells. *S. albus* and streptococci were isolated. He was given 25 million staphylococcus antigen + 2½ streptococcus antigen on December 18th, 1919, and the doses were increased to 1,000 + 100. The series was 25 + 2½, 50 + 5, 75 + 7½, 100 + 10, 150 + 15, 200 + 20, 300 + 30, 400 + 40, 800 + 75, 1,000 + 100. He had distinct focal and general reactions after the first few doses. After the first his temperature went to 101.8° F., and his urine increased from 20 to 40 oz. in twenty-four hours. He was discharged apparently cured on February 11th, 1920.

CASE IV.

J. K., aged 39, labourer, was admitted into Dr. Steevens's Hospital on December 23rd, 1919, with severe headache and general oedema. He was passing 15 oz. of urine loaded with albumin. He gave a history of several similar attacks. When I saw him at the end of January, 1920, he was still oedematous and had severe headaches. His urine contained 4 grams per litre of albumin, and he was passing about 70 oz. in the twenty-four hours. *S. albus* was isolated from his urine and 5 million antigen was given on February 2nd, 1920. The series of doses was 5, 10, 15, 20, 30, 40, 50, 60, 75, 100, 150, 200, 300, 400, 600, 800, 1,000, 1,250, 1,500, 1,750, 2,000. He steadily improved, losing his headache and oedema, and was discharged May 9th, 1920, his urine containing 0.75 to 1 gram per litre. He returned to work June 20th, 1920, and has remained in full work ever since. His urine now (September, 1922) contains 0.5 gram per litre, so that the improvement in his kidneys has continued.

CASE V.

P. C., aged 14, admitted Dr. Steevens's Hospital under Dr. Kirkpatrick with general oedema. Temperature 101° F., pulse 104. Urine contained blood. *S. albus* and streptococci were isolated from his urine, and on March 2nd he was given 10 million staphylococcus antigen + 1½ million streptococcus antigen; the series of doses was: 10 + 1½, 25 + 2½, 50 + 5, 75 + 7½, 100 + 10, 150 + 15, 200 + 20, 400 + 40, 600 + 50, 800 + 75, 1,000 + 100, 1,500 + 150, 2,000 + 200. The focal reactions in this case were very pronounced after the third dose; for instance, the albumin, which was 1.5 grams before the dose, increased to 4 grams on the next day, and then fell to 1 gram on the fifth day after. The boy left hospital on June 7th, 1920, with a bare trace of albumin. He has remained well since and is now (September, 1922) quite free from albumin.

CASE VI.

Girl aged 17, under the care of Dr. Pepper, gave a history of chronic nephritis with acute exacerbations for many years. When she came under treatment she was suffering from violent headache, general oedema, and her urine contained 2 grams per litre albumin. Staphylococci and streptococci were isolated from her urine. She was given 5 million staphylococcus + 1 million streptococcus antigen, which was steadily increased until a dose of 4,000 + 500 million was attained. The patient had then greatly improved. Her headaches had greatly diminished and her oedema had disappeared. The albumin had reduced to 0.75 gram per litre. She is now (September, 1922) in good health; no oedema of her legs, her only symptoms being occasional slight headaches. Her urine still contains 0.7 gram per litre albumin.

CASE VII.

V. F., a boy aged 5, admitted to Dr. Steevens's Hospital under Dr. Winter, October 19th, 1921, with general oedema and headache, passing 10 oz. urine containing over 12 grams per litre of albumin. The albumin fluctuated in an extraordinary way, being sometimes as low as 0.5 gram and as high as the U mark on the Esbach tube. When I saw him in December, 1921, his oedema and general condition had greatly improved, but he had still an enormous quantity of albumin. Staphylococci and streptococci were isolated. He was given 5 + 1, and had a very distinct increase of oedema after this and several other doses. As the albumin did not show any improvement after the 50 + 10 dose I reinvestigated the bacteriology of his urine, and found as well as the other microbes a coliform bacillus. The addition of an antigen of this did not, however, make any difference, and he left hospital May 31st, 1922, in very good general condition, but still passing as much albumin as ever. Evidently his kidneys were irretrievably damaged. The initial dose was 5 million staphylococcus + 1 million streptococcus antigen, and the series was: 5 + 1, 7½ + 1½, 10 + 2, 15 + 3, 20 + 4, 30 + 6, 40 + 8, 50 + 10, 60 + 10 + 2½ (coliform antigen), 75 + 15 + 5, 100 + 12½ + 7½, 150 + 20 + 10, 200 + 25 + 12½, 300 + 30 + 15, 400 + 40 + 20, 500 + 50 + 30. This boy now (September, 1922) is playing about like a normal child with no sign of illness, but has still 3 grams per litre of albumin. His after-history will be interesting.

I could add other cases, but I hope these will sufficiently illustrate the possibilities of the treatment. Even if complete cure is not possible one can often, as in Cases iv and vi, restore them to good health and full working capacity. If the cases are taken in time, complete cure ought to be possible in the large majority of them. I am as ever deeply indebted to my colleagues at Dr. Steevens's Hospital for placing their cases at my disposal.

RESTORATION OF THE SUNKEN NOSE.

BY

HAROLD BURROWS, C.B.E., F.R.C.S.,
ASSISTANT SURGEON, ROYAL PORTSMOUTH HOSPITAL.

THE practice of making good a defect of the contour of the nose by inserting a graft of cartilage beneath the skin is one the soundness of which is sufficiently well established. Nevertheless, I suppose that most surgeons have sometimes had cause to lament that the practical result has fallen short of the ideal. This being so, any little idea that may help toward the achievement of better results will be acceptable. I would like, therefore, to describe the operation which I have employed, in order to introduce a mechanical detail which has been of considerable assistance.

FIG. 1.—Cast of nose before operation. (In addition to the sunken bridge there is considerable deformity of the anterior nares, from old ulceration.)

FIG. 2.—Cast of same nose after operation.

Preliminary Measures.—The first step is to obtain a plaster cast of the patient's nose and neighbouring features. Having acquired this, the nasal defect which is shown in the cast is filled with plasticine, which is moulded with care so as to produce on the plaster model the shape of nose which it is hoped to reproduce on the patient. This plasticine model of the nasal defect is then removed from the plaster cast and well powdered with boric acid. This dries the plasticine, which, when dry, is less likely to become altered in shape under subsequent handling. With a small metal

FIG. 3.—Plasticine models. The two small pieces represent grafts used to stiffen the alae nasi, which were sunken and lacking in cartilaginous support.

calliper the length of the plasticine model is measured.

Operation.—With the patient under general anaesthesia the right fourth rib cartilage is removed. The separated fragment is replaced in its bed and the skin wound temporarily closed with towel clips. This having been done, a transverse incision is made across the nose at the level where the bridge of a pair of spectacles would naturally rest. Through this incision the skin of the nose is separated from the underlying structures over the whole area of the nasal defect. The towel clips are now taken from the chest wound and the cartilage is removed for modelling. First of all it is cut to the correct length as shown exactly by the calliper. Then, with the plasticine model held in front of him by a nurse who can manipulate it as required, the surgeon carves the piece of cartilage in the likeness of the clay model, and having completed this fashioning the graft is slipped into its bed in the nose, the skin incision being closed by two or three horsehair sutures. The chest wound is then sewn up and a dressing applied. But no dressing other than a dusting with boric powder is used for the nose.

FIG. 4.—Metal calliper for measuring the grafts.

After-Course.—The horsehair stitches are removed on the fifth day. The cartilage graft having been properly modelled lies comfortably in its bed without any tendency to slip out of place.