Dr. Jokichi Takamine for the separation of what appears to be the active principle of the suprarenal bodies. To this alkaloid he has given the name adrenalin. The alkaloid itself is not to be had, as it is impossible to make a solution of it by ordinary methods. It is therefore supplied as adrenalin chloride solution. In this form the drug has been used for some time with satisfactory results in the United States, both in the treatment of throat and eye affections. Papers on the action of the preparation were read last year at the Chicago Laryngological Association, by Casselberry and Wilson, who with many others spoke of its use in very favourable terms.

I am indebted to Messrs. Parke, Davis, for a supply of this preparation. Adrenalin chloride is supplied diluted in normal salt solution (1 in 1,000). It is colourless, odourless, sterile, and stable if protected from light, heat, and oxidation, particularly the latter.

I find that when instilled into the healthy eye adrenalin chloride solution (1 in 1,000) causes first a slight smarting, and, within a few moments, a blanching of the conjunctiva, which is best marked at the caruncle. This blanching reaches its maximum within five minutes. The action very gradually passes off, and the eye resumes its usual colour in about the same time or a little longer. The solution is non-irritating, and does not cause any dilatation of the pupil (Königstein found dilatation of the pupil with a 10 per cent. solution of the extract), neither does it render the conjunctiva or cornea insensitive to any extent. The solution has also no effect on the accommodation. Under its influence the eye feels slightly dry.

Applied to the inflamed conjunctival sac it gives relief in a few moments, evidently by checking the congestion; indeed, in some cases, especially those of foreign bodies in the cornea or under the lid, the relief obtained is not unlike that given by a weak solution of cocaine. In severe acute conjunctival hyperaemia several instillations may be required before complete blanching takes place. The hyperaemia of acute inflammation does not appear to yield so readily as chronic hyperaemia. The inflamed eye resumes its injected appearance within fifteen minutes after the instillation of the solution; but repeated instillations gradually overcome the hyperaemia provided, of course, the original cause of the irritation be removed. The solution is rapidly absorbed into the anterior chamber, and its action is seen on the congested iris, especially if the instillations be frequently repeated (once every fifteen minutes). This fact renders the drug particularly valuable in iritis. It relieves photophobia, and by its control over congestion assists atropine in dilating the pupil. The solution seems, too, to hasten absorption of serous exudation. It certainly assists the absorption of subcorneal deposits and thus improves vision; it also reduces tension, especially when above normal. This fact was also noticed by Zimmermann in using a preparation of the extract. Landolt's experience of the extract, however, is that it does not affect the tension of the globe. But Darier, at the Congress of the Société Française d'Ophtalmologie, recommended surrenaline (another preparation of the extract?) as useful in reducing intraocular tension.

In operations on the eye adrenalin chloride solution will be also found of use. In tenotomy and advancement of the rectus, the previous instillation of the solution helps to control the haemorrhage. It is necessary often to reinsert a drop or two during the operation. A minim or two previously injected beneath the conjunctiva has, however, a more lasting effect. In this way most operations on the superficial tissues are rendered practically bloodless. The solution is also of use in stricture of the lachrymal duct from swelling of the mucous membrane. Its use facilitates the passage of a probe. No secondary haemorrhage has been observed, but when we consider that the drug only temporarily influences the blood vessels, such a sequence is, when larger vessels are divided, quite possible. In rhinology, Hopkins states that secondary haemorrhage does occur after the use of a solution of the extract (due evidently to delayed relaxation). Peters, too, has had similar experience with the extract, and found secondary haemorrhage occurring two hours after. Landolt also experienced troublesome haemorrhage. The experiences, however, of Mullen and Macleod Yearsley are contrary to these observers. In inflamed conditions of the eye, especially chronic, it will be noticed that there is a tendency for a reaction to set in after

the influence of the drug passes off and the hyperaemia is temporarily increased.

So far, I have observed no toxic effect. In eye work it is not likely that such evil effects will readily occur, the solution being used in such small quantities. It must not be forgotten, however, that suprarenal extract can produce marked toxic effects (Corona). Landolt likewise reminds us of the fact. How long and to what extent adrenalin chloride solution influences the deeper tissues of the eye it is not as yet possible for me to state definitely. So far, my observations tend to point that the influence is much the same as on the superficial tissues. The action of the drug varies with the intensity and chronicity of the inflammation. It is not easy to arrive at precise conclusions from instillations into the eye. The size of the drop, its dilution owing to varied lachrymation, etc., all render precision in such observation almost impossible.

My experience of adrenalin chloride solution is that it will prove a valuable addition to the small pharmacopoeia of the ophthalmologist. Indeed, since the introduction of cocaine no drug of greater interest and use in eye work has come before us. But it is essential to bear in mind that the preparation in its action is only indirectly of use, that is (like the extract) it contracts the muscular coats of the blood vessels (Schäfer, Olliver), and thus by controlling congestion promotes healing and absorption.

According to Grünbaum, suprarenal extract does not cause clotting. In eye operation I have noticed that coagulation takes place more readily when the solution of adrenalin is used; this, however, may be due to the haemorrhage being scanty. The solution may be combined with atropine or cocaine, but it is better to use it by itself. First, because to be of much use it requires frequent instillations; and next, because the solution, if exposed, tends to oxidize and lose its original potency. The action of cocaine on inflamed tissue (which, as is well known, is not satisfactory) is greatly promoted by the previous use of the solution. Finally, I must not omit to state that in cases where the nutrition of the tissues is at fault the solution of adrenalin chloride is contraindicated. In certain forms of corneal ulceration, for instance, the use of the solution appeared harmful. It will be thus seen that the drug must not be used indiscriminately.

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CASE OF TOTAL SUPPRESSION OF URINE DUE TO THE OBSTRUCTION OF BOTH URETERS BY RENAL CALCULI.

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CASES of obstructive suppression of urine are of peculiar interest: first, from their rarity; secondly, from the "latency" of the symptoms produced; thirdly, from the good results which may be anticipated from operative interference; and, fourthly, from the light which they throw upon the pathology of uraemia and on the functions of the kidney. These cases are, therefore, of interest not only to the physician but to the surgeon, the pathologist, and the physiologist.

For an account of the symptoms observed in the following case, and for obtaining permission to perform a necropsy, I am indebted to my friend, Dr. Fred Evans.

History.—The patient, a publican, aged 58, a stout, flabby man, 5 ft. 7 in. in height, and weighing 15 st., first consulted Dr. Evans in December, 1898, complaining of loss of flesh, thirst, and the passing of excessive quantities of urine. Sugar in considerable quantity was found in the urine, and under treatment for this condition by July, 1900, he had regained his former weight, and the sugar had entirely disappeared.

State on Examination.—On January 3rd, 1901, having enjoyed good health in the meantime, he again came under observation complaining of shooting pains in the right loin with blood in the urine. The urine was now found to be normal in quantity, but it contained much blood and also a trace of sugar. These symptoms continued without any alteration until April 5th, 1901, when without any warning complete suppression of urine suddenly set in, and this continued until his death on April 12th, that is, on the eighth day of suppression. From the 5th to the 12th not a drop of urine was passed, nor could any be obtained by the introduction of a catheter into the bladder. The only symptoms observed during the seven days of suppression of urine were pain and tenderness in the right loin, a gradual and progressive loss of muscular strength, gradual enfeeblement of the pulse and respiration, slightly-contracted pupils, and obstinate constipation. The temperature was normal. The tongue was clean, though somewhat dry towards the end. There was no nausea or vomiting, no tremors or twitchings. The mental condition remained clear to the last, and the immediate cause of death was probably respiratory failure.

Necropsy.—The abdomen only was opened. The abdominal walls contained a large quantity of subcutaneous fat. There was an entire absence of any ammoniacal odour. The liver showed well-marked cirrhotic changes. The right kidney was large, weighing 12½ oz. The upper half of this organ was represented by a bulging, tough swelling, which on examination was found to be composed of hard fibrous tissue arranged in a coarse spongy manner, the interstices of which contained blood clot for the most part completely decolorized. The capsule stripped off fairly easily. The kidney substance was pale and tough, and the pyramids had almost disappeared. The pelvis was much dilated and contained a small quantity of grumous fluid together with much decolorized blood clot. Projecting into the entrance of the ureter was a stone weighing 100 gr.; it was wedge-shaped, with the apex fitting tightly into the orifice of the ureter. The ureter itself below the obstruction was normal. The left kidney weighed 8½ oz. This organ, on section, was of a dark-red congested appearance, but otherwise it looked healthy. The pelvis was not dilated, but contained a few drachms of pale-coloured urine but no blood clot. A small stone weighing under 3 gr. and mixed with mucus and blood clot was found fixed in the entrance of the left ureter, producing a complete obstruction. The ureter itself was normal. The bladder was quite empty.

I. Clinical History.

Under this heading there are several interesting points in the above case:

(a) *The History of Glycosuria.*—The association of glycosuria with renal calculi, whether a coincidence or not, is worthy of notice.

(b) *The Short History of Symptoms Pointing to Renal Calculus.*—Previous to three months before the patient's death there was no history of symptoms indicating any lesions in connexion with the kidneys. From the *post-mortem* conditions found in the right kidney one cannot doubt that a stone had been present in that kidney for a long period, but nevertheless the patient had apparently suffered from no symptoms. Within three months from the first appearance of symptoms of pain and haematuria the patient died from total suppression of urine.

(c) *The Onset of Total Suppression of Urine without Symptoms of Renal Colic.*—The onset of the suppression was quite sudden and without any warning, which shows that sudden obstruction of a ureter may occur without any special symptoms.

(d) *The Suppression of Urine was "Absolute."*—Not a drop of urine was passed from April 5th until his death on April 12th, and none was found in the bladder either during life or after death. In most cases of "obstructive suppression" of urine which are on record small quantities of pale urine have been passed, a condition of the urine which, as pointed out by the late Sir William Roberts, is characteristic of that secreted in cases of "obstructive suppression."

(e) *The Absence of Symptoms of Uraemia.*—In the above case no uræa was excreted for seven days and yet there was not a single symptom pointing to uræmia.

(f) *The Duration of Life.*—In the above case the duration of life from the onset of the suppression was seven days. Sir William Roberts states that the duration of life in these cases is, as a rule, from nine to eleven days. It is quite possible that had this patient lived for a day or two longer slight symptoms of uræmia would have been observed such as muscular twitchings, drowsiness, or delirium. However, in all recorded cases marked symptoms of uræmia have been absent, and thus these cases present a strong contrast to those of "non-obstructive suppression," in which there is no mechanical interference to the flow of urine.

II. Pathological Conditions found at the Necropsy.

The dilatation of the pelvis of the right kidney with atrophy of the pyramids shows that this organ had for some time ceased to perform its functions on account of the blocking of its ureter. The pelvis of this kidney contained no urine. The fibrous mass situated in the upper part of the kidney was no doubt produced by calculus irritation, and was probably the part of the organ in which the calculus was originally formed. At first sight this mass looked very like a growth, but microscopical examination demonstrated the fact that it consisted only of fibrous tissue and blood clot.

The left kidney had undergone compensatory enlargement, and up to the time of the blocking of its ureter it no doubt performed efficiently the excretory functions of both organs. The stone which blocked the ureter of this kidney was very small but yet larger than one recorded by Sir W. Roberts, which weighed only 1½ gr. It is indeed remarkable that such a small pathological object should be the cause of death. The pelvis on this side was not dilated, showing that a certain amount of time is necessary to produce a dilatation of the pelvis of the kidney after obstruction of its ureter. It contained a small quantity of pale-coloured urine, a fact which shows what a comparatively small pressure is capable of stopping the secretion of urine. The congested condition of the left kidney was very noticeable in this case, and contrasted with the pale colour of the right kidney.

III. Treatment.

The treatment which should be adopted in these cases would, of course, depend upon the diagnosis. It is obvious that an obstruction which produces sudden suppression of urine must occur simultaneously in connexion with both kidneys, or if it occur on one side only the other kidney must have been rendered useless by antecedent disease. Now it is most unlikely to get simultaneous blocking on both sides, therefore we must assume that one kidney had suffered previously either from stone or other disease, and that the immediate cause of the suppression was the obstruction of the ureter on the other side. In this case there was no history of renal pain until three months before the death of the patient (though the stone was probably present before that date) or of any other symptom referable to kidney disease. This pain was on the right side, and was associated with tenderness on palpation. At no time were there any symptoms referable to the left side.

When the sudden suppression of urine occurred the question would arise, In connexion with which kidney has this sudden obstruction occurred? I think that when we take into consideration the above facts we might assume that it occurred in connexion with the left kidney, which we have no reason to believe had suffered from previous disease, and here I may again remark that a sudden blocking of the ureter does not necessarily produce pain. As in 90 per cent. of the cases of total suppression the cause is stone, we may, I think, fairly arrive at the conclusion that we have to deal with obstruction of the left ureter from a stone.

Having established a diagnosis the treatment would be obvious—namely, to remove the obstruction. It is possible that the obstruction may in some cases be removed by manipulation of the abdomen in the course of the ureter. There is, of course, the possibility of spontaneous recovery, and a remarkable example of this is recorded by Professor J. Reczey, of Buda-Pesth, in a man who had suppression from renal calculi for ten days, when he was seized with a sudden desire to micturate, and passed several calculi, which was followed in a little time by his passing 12 pints of urine. The patient made a good recovery.

I think, however, that in most cases the sooner an operation is performed the better, and the relieving of the obstruction would probably at once be followed by a copious secretion of urine. To wait for some days until muscular twitchings and other symptoms arose would be to throw away valuable time, and would be allowing the patient to get into a very weak state, and in these cases loss of muscular strength is one of the most marked symptoms.

IV. Remarks on the Pathology of Uraemia.

Cases of obstructive suppression of urine throw a good deal of light on the pathology of this condition. The absence of

marked symptoms of uraemia is very striking in these cases; indeed, cases are on record in which, though there was total suppression for several days (for example, a case recorded by Professor Reczey) not a single bad symptom was observed. In non-obstructive suppression, although a certain quantity of urine may still be passed, the cases end fatally in a few hours or in a day or two, and symptoms of uraemia are prominent. It is obvious, therefore, that uraemia does not simply depend upon an accumulation in the blood and tissues of the body of excretory products such as urea which are normally excreted in the urine.

A comparison of the state of the kidneys in the two kinds of suppression of urine gives us a clue to an explanation of the striking difference observable in the symptoms. In "non-obstructive" cases the suppression is due to acute pathological changes in the kidneys themselves. In "obstructive" cases the suppression is due to a mechanical cause outside the kidney, this organ itself being healthy and quite capable of resuming its functions of secretion directly the obstruction is removed. Now, if the function of the kidneys were purely "excretory," and nothing else, there would not be such marked differences in the symptoms observable in the two kinds of suppression of urine, and it is therefore probable that these organs have some other important function. In cases of obstructive suppression the excretory function only is in abeyance, whereas in non-obstructive suppression some other function beside that of excretion is seriously affected, and it is quite apparent that in such cases every function of the kidney would be practically in abeyance when we consider the severe inflammatory processes present. Of course the abolition of the excretory function alone will cause a fatal result, but this, as we have seen, is generally delayed for some days (in one case even as long as twenty-two days), and the symptoms of uraemia are late in appearing, and, indeed, may be quite absent even for as long as ten days, and when they supervene they are ill-marked, convulsions and coma rarely set in, and the mind generally remains clear to the end. The explanation of this probably is that the kidney is practically healthy and is carrying on its other functions.

These other functions of the kidney are possibly due to some "internal secretion" which has some influence on certain metabolic processes as yet unknown. Dr. Bradford, in his experiments, has shown that excision of large portions of the kidneys in animals actually causes an increase in the quantity of urine secreted, and also in the amount of urea. He believes that the kidneys, beside excreting toxic products normally found in the blood, have also a further function of inhibiting their abnormal formation. In obstructive suppression of urine one can conceive that there is an accumulation in the blood only of those substances normally excreted by the kidney, and that this organ being still healthy is capable of fulfilling its other functions, but that in non-obstructive suppression there is an accumulation in the blood not only of these substances but of others normally formed as the result of perverted tissue metabolism, the kidney being unable to perform any of its functions either as a "secretory" organ or as an organ "influencing metabolism," and on examining the condition of the kidneys in such cases it is not surprising that there should be a state of complete, or almost complete, paralysis of function. The pathology of so-called uraemia is a very complex question, but I venture to think that clinical observations, taken in conjunction with experimental researches, will tend to throw much light on the matter.

MEMORANDA:

MEDICAL, SURGICAL, OBSTETRICAL, THERAPEUTICAL, PATHOLOGICAL, Etc.

CARCINOMA AND MALARIA.

In a letter published in the *BRITISH MEDICAL JOURNAL* of January 11th, Dr. J. S. Davidson gives some interesting remarks under the above heading, in the course of which he implies that the negro in Africa is practically free from the former disease, and that where malaria is prevalent cancer

is rare. The truth can only be obtained by the collation of a large number of reports from different places.

As regards this matter, my experience during the last five years in Uganda, Central Africa, is diametrically opposite to this. In the Church Missionary Society's Hospital at Mengo, the capital of Uganda, we had over 1,000 in-patients and about 16,000 out-patients under treatment last year. These were all Baganda, or the nearly allied tribes Banyoro, Batoro, or Basoga. Among this number were some 1,300 cases of malaria; while cases of malignant disease, though much less common than among Europeans, were by no means rare.

My brother, J. H. Cook, M.B., M.S., F.R.C.S., who is associated with me in the charge of the hospital, has had the same experience. We have had cases of carcinoma of the lip, oesophagus, intestine, breast, uterus, penis, etc., sarcoma of the parotid, lower and upper jaw, and melanotic sarcoma. Malaria is certainly no bar to the occurrence of carcinoma, and I would enter an earnest protest against "inoculating cases (of carcinoma) with the protozoan of tertian fever" as a preventive of carcinoma.

Were we able to overcome the prejudices of the natives and make more frequent necropsies, we should doubtless find cases of carcinoma to be more frequent than we suspect.

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A DANGER OF LACHRYMAL STYLES.

A LADY came under my care suffering from an old-standing obstruction to the lachrymal duct.

On December 13th, 1901, I slit open the canaliculus and passed a full-sized probe down the canal. The obstruction, however, tended to recur owing to cicatricial contraction, and to obviate the necessity of passing the probe every day I introduced a style (Bickerton's). The flange of the style was not, however, sufficiently large to prevent it slipping down into the nasal duct, and two days later, when the patient returned, it had disappeared into the bony canal. From this it was extracted with great difficulty by Dr. Hill Griffith, after opening the sac.

Such an accident might be obviated by making the flange larger, but this might introduce the still more serious danger of the globe being injured by the flange in the movements of the eye, and the possible introduction of septic pus from the sac. Dr. Hill Griffith tells me that this accident has actually occurred.

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E. VIPONT BROWN, M.D.Lond.

PINCE-NEZ IN OPHTHALMIC PRACTICE.

WITHIN the last eighteen months a considerable number of persons wearing pince-nez have come under my notice, complaining of epiphora or flowing of tears. In some cases two pairs of glasses were in use—pince-nez and ordinary spectacles; and only when the former were used were the tears troublesome.

At first I supposed this to be due to the fact that, at least in some cases, the pince-nez frame did not sit quite straight on the face, thereby causing the wearer to see obliquely through the glasses. This would cause the lenses to act as cylinders which might produce a condition of irritation in the eyes—an asthenopia from wrong glasses in fact—associated with increased lachrymation.

However on further investigation of the matter, I found that the trouble was caused by another condition altogether. This was that the compressing force of the pince-nez dragged on the tissues at each side of the nose to such an extent that the lower lid was actually pulled away out of position and no longer lay up in close contact with bulbar conjunctiva. The displacement of the lid, with of course the inferior punctum, was small in amount, only about 0.2 or 0.3 mm., and this easily escapes detection, all the more so, as it has to be looked for while the glasses are on the patient's face. But even this small amount of eversion—this ectropion—is amply sufficient to cause the epiphoria.

This is a very important matter, as such an eversion of the lid, present at first only when the pince-nez is actually on the face, will become permanent in time, and set going all the troubles associated with ectropion.

The surgeon, for the patient's sake, as well as for his own protection, should guard against this, by closely examining