TREATMENT IN GENERAL PRACTICE

This article is one of a series on the management of some of the renal diseases met with in general practice. The first group of articles on Treatment in General Practice, thirty-five in number, was republished in book form last March by H. K. Lewis & Co., and a second volume will appear in the autumn.

TREATMENT OF PYELITIS

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The term "pyelitis" is used in a general way to include not only suppurative inflammation of the renal pelvis but also the accompanying inflammation of the ureter and bladder. Pyelitis may be acute, subacute, or chronic, and may develop rapidly or insidiously. The infection may occur in a previously healthy urinary tract, or may arise as a complication of some other abnormality such as calculus or tumour. Acute pyelitis is common in pregnancy on account of the tendency to dilatation of the ureter and achalasia of the ureteric sphincters, which predispose to stagnation of the urinary flow and favour the growth of organisms.

Pyuria and bacilluria are the signs pathognomonic of infection of the urinary tract. The pus may be so abundant as to be visible to the naked eye, or so scanty that it can be detected only with the microscope. A highly purulent urine will give the "rope test" with liquor potassiae, but if this test is negative there is no justification for the conclusion that the urine is free from pus. The microscope is the only reliable means of ascertaining that pus and organisms have disappeared from the urine; the amount of pus may vary from day to day, and an apparent clearing of the urine may mean nothing more than a temporary retention of pus in the upper part of the tract.

In acute pyelitis there is always some degree of general disturbance from toxic absorption. In severe cases there is high fever with rigors, and lumbar pain is often distressing. In all cases, whether mild or severe, the patient should be kept at rest in bed until the acute phase has passed. When the temperature has settled and the coxaemia has lessened he should get up for short periods each day, as this helps to promote drainage of the ureter, but he must be careful to avoid chill or over-exertion.

Diet and Bowel Regulation

Diet during the early stages should be restricted to fruit, light farinaceous foods, bread-and-butter, and toast or plain biscuits. How much solid food of this kind may be allowed depends on the severity of the toxæmia. If there is much fever glucose and fruit drinks only are to be given. Milk is not desirable in large quantities, but may be used in the preparation of puddings, or in tea, up to about one pint in the day. When the fluid intake is not restricted buttermilk may be given, and patients often appreciate a little plain ice-cream. When the febrile stage is passing off egg and fish dishes and vegetable purée may be added to the diet, but excepting an increase in the size of the meals no further liberty should be allowed until convalescence is definitely established.

Regulation of the bowels may be difficult. As a preliminary there is nothing better than castor oil (4 to 8 drachms) if it can be given without undue disturbance to the patient. A soap-and-water enema (1 oz. of green soft

soap in a pint of warm water) is sometimes necessary to clear the colon. It may have to be repeated for several days, and in obstinate cases an olive oil enema may be required (10 oz. of warmed olive oil run in, under gravity, through a rubber catheter). After the bowel is cleared regular evacuations should be secured by giving the following mixture, three times a day, after food:

R	Ext. casc. sagrad. liq.	...	...	...	m x
	Tinct. bellad.	...	...	...	m v
	Tinct. hyoscy.	...	...	...	m v
	Syr. zingib.	...	...	...	3 j
	Aq.	...	...	...	ad 3 iv
	Ft. mist. sig. 3 iv, t.i.d., p.c.				

An additional dose of 1 to 2 drachms of liquid extract of cascara sagrada may be required each evening for the first few days.

Pyrexia, Pain, and Fluid Intake

Pyrexia is best controlled by sponging with tepid water. Pain can usually be relieved by a simple analgesic, such as:

R	Aspirin	...	...	...	gr. v
	Phenacetin	...	...	...	gr. iij
	Codein. phosph.	...	...	...	gr. 1/12
	Ft. pil. vel. pulv.				

Occasionally, it may be necessary to give hypodermically morphine sulphate, 1/6 grain, and atropine sulphate, 1/100 grain. Irritability of the bladder and dysuria may be lessened by giving 10 minims of tincture of hyoscyamus, in half an ounce of water, thrice daily.

It depends on the treatment selected whether fluids are restricted or given freely. With the alkaline diuretic method large quantities of water must be given, but with all other methods of treatment the fluid intake is cut down to approximately two pints a day.

Alkaline Diuretic Treatment

Until recently the best treatment for acute pyelitis was alkalization of the urine and the production of free diuresis by giving large quantities of water. Properly carried out this simple and inexpensive treatment is of the highest value in the early stages, but after the acute phase of the illness mandelic acid is preferable in most cases. The alkaline diuretic treatment gives satisfactory results only if careful attention is paid to the following details. The patient must be kept at rest and treated on the general lines indicated above. Fluid must be given in large volume so that there is a minimum daily intake of five pints. The output of urine must not be allowed to fall below ninety to a hundred ounces, and if it fails to reach this level the fluid intake must be further increased.

Enough sodium citrate is given to render the urine alkaline to litmus. There is no fixed dosage, but during the first day or two it is usually necessary to give from 30 to 60 grains of sodium citrate every two hours, up to a total of 300 to 400 grains in twenty-four hours. When there is difficulty in getting the patient to take so much citrate smaller doses may be supplemented with equal quantities of sodium bicarbonate. The insipid taste of sodium citrate may be concealed by making a mixture

containing 60 grains of sodium citrate and 6 minims of concentrated compound infusion of gentian to each ounce of water. This can be used in doses of 4 to 8 drachms (equivalent to 30 to 60 grains of citrate). The only reliable guide to dosage is the reaction of the urine. Test each specimen as it is passed; when it becomes alkaline to litmus the citrate may be reduced to 30 grains, four times a day. There is very little risk of alkalosis if the dosage is reduced in this way as soon as the urine becomes alkaline. To prevent hypochloraemia from the free diuresis 1 to 2 drachms of sodium chloride should be included in each daily diet.

Failure to obtain marked improvement is rare if the treatment is carried out exactly as described. Pyuria may be expected to clear up or to be reduced to a trace, but resistant cases occur in which a sterile urine cannot be obtained even after many weeks of treatment. In such cases alternation between the alkaline diuretic and one of the other methods involving acidification of the urine is usually effective.

Mandelic Acid Treatment

About 1931 the treatment of pyelitis with ketogenic diets was introduced, but the general experience has been that this method is unreliable and difficult to control. The principle employed is the production of ketosis by restricting carbohydrate and increasing fat in the diet. The production of a ketonuria should be confirmed by testing the urine for acetone bodies with sodium nitroprusside and ammonia—Rothera's method. Observations made in connexion with these ketogenic diets showed that β -hydroxybutyric acid has a powerful action in preventing the growth of organisms provided the urine has an acid reaction (pH 5.3). Hydroxybutyric acid cannot be given orally, because it is broken up in the upper part of the alimentary tract, but mandelic acid has been found to be an effective substitute for it. Sodium or ammonium mandelate is now used instead of the more irritating mandelic acid.

In giving mandelic acid or one of its salts the urine must be strongly acid and the pH must not rise above 5.3. With a moderate restriction of fluid this degree of acidity may develop, but if it does not, ammonium chloride must be used to correct it. To begin with, 15 grains of ammonium chloride is given four times a day; if the urine does not become sufficiently acid the dose may be increased to six or eight multiples of 15 grains, but it is not desirable to continue this high dosage for more than two or three days. The urine should be examined for casts and blood cells, the appearance of which indicates renal irritation. Nausea and vomiting may make it necessary to stop using ammonium chloride. In such cases the attempt to treat the patient with mandelic acid must be abandoned unless the pH of the urine comes within the necessary range.

The normal dose of mandelic acid is 45 grains (3 grams) four times a day, and the equivalent of this in the form of sodium mandelate is 50 grains (actually 3.43 grams). Sodium mandelate is sometimes dispensed in tablets, each containing 3.43 grams, but is more conveniently given in solution. I have found the following mixtures effective:

No. 1.—Ammonium Chloride Mixture

Ammon. chlor.	...	...	...	...	3 j
Ext. glycyrrhiza liq.	...	...	...	...	5 iv
Aq.	...	...	...	...	ad 3 viij

One tablespoonful in water, four times a day, before food.

No. 2.—Sodium Mandelate Mixture

Sodium mandelate	...	...	...	...	3 jss
Syr. aurant.	...	...	...	...	3 jss
Aq.	...	...	...	...	ad 3 viij

One tablespoonful in water, four times a day, after food.

The reaction of the urine is tested regularly during the treatment by adding five drops of a buffered methyl-red solution to 5 c.cm. of urine in a test tube. The colour is bright pink at pH 5.3, but is orange or yellow if the reaction is too alkaline. The indicator solution can be purchased from any reliable chemical supply house.

The use of ammonium mandelate obviates the separate administration of ammonium chloride. It is now supplied in palatable mixtures by several makers—for example, "mandelix" by British Drug Houses Limited, and "ammoket" by Boots Pure Drug Company Limited. The dose of the former is 2 drachms, four times a day, in water, and of the latter 4 drachms. If the urine is not sufficiently acid 10 grains of ammonium chloride may be given three or four times a day until the reaction is corrected. If the mandelic acid treatment is carried out carefully as described the urine should become sterile within seven to ten days, unless there is some anatomical abnormality. There are exceptionally resistant cases, but on the whole, the results are excellent.

Like all other methods of treatment that involve restriction of fluid and acidification of the urine the mandelic acid treatment is unsuitable if there is active renal disease. Careful watch must be kept for signs of renal irritation, and if they appear the drug must be stopped. Mandelic acid is sometimes tried in acute pyelitis from the start, but in my opinion it should be used only in mild cases. When the patient is febrile and toxic the alkaline diuretic method is preferable, and until the acute phase is passing off mandelic acid should not be introduced.

Hexamine

Hexamine (hexamina, *British Pharmacopoeia*, 1932 hexamethylene-tetramine) is marketed under various names, of which the best known is urotropine. The dose is 5 to 15 grains for a single dose, but it may be necessary to give 40 to 60 grains in the day. Hexamine is broken down in acid media, liberating formaldehyde, upon which its bactericidal action depends. To ensure acidity of the urine sodium acid phosphate is given (20 to 30 grains) thrice daily; sodium benzoate (5 to 30 grains) or ammonium chloride (5 to 20 grains) is sometimes preferred for this purpose. The dosage should be adjusted so that the urine is acid to litmus. On account of the tendency of hexamine to irritate the kidney it is usual to prescribe plenty of fluid (3 to 5 pints daily). The resulting diuresis has the disadvantage that the formaldehyde in the urine will be present in relatively low concentration. Doses of the order of 10 grains produce so little formaldehyde that the concentration cannot reach the zone at which bactericidal action occurs. Higher doses are irritating, and so hexamine is limited in its usefulness. It would appear nevertheless, that the continued presence of quite low concentrations of formaldehyde in the urine has some effect in inhibiting the growth of organisms in cases of chronic infection. If hexamine is used the total dosage should be divided evenly throughout the twenty-four hours.

There are several proprietary preparations containing hexamine. In obstinate cases it is worth while trying them, but the temptation to change from one remedy to another should be resisted. It is important to make sure that the patient is having the maximum dose that he can tolerate, and that the reaction of the urine is being properly controlled.

Pyridine and Hexyl-resorcinol

Several dyes of the pyridine series have been widely advertised as urinary antiseptics. They can be given orally in sufficient amount to produce a high concentration of the dye in the urine, particularly if the fluid intake is

restricted. Favourable results are reported from many sources, but in my experience this form of treatment is uncertain in its action. The relatively high cost of these preparations and the risk of damage to the patient's underwear are additional disadvantages. Two of the best known are phenyl-azo-alpha-alpha-diamino-pyridine hydrochloride (trade mark "pyridium") and butyloxy-diamino-azopyridine (trade mark "neotropin"). Both are dispensed in coated dragées containing $1\frac{1}{2}$ grains (0.1 gram) of the dye, and the dose is 2 to 3 dragées three times a day.

Hexyl-resorcinol (1:3 dihydroxy-4-hexylbenzol) is obtainable under the trade mark "caprokol." It is a powerful germicide, acting in either acid or alkali. When given orally it is secreted by the kidney, and in therapeutic doses exerts an antiseptic action without intoxication or irritation. It appears to be more potent in coccal than in coliform bacillary infections. It acts by lowering surface tension, and for its optimum effect the fluid intake must be low. Sodium bicarbonate should not be given along with it. Hexyl-resorcinol is dispensed either in gelatin capsules, containing 0.15 gram of the drug in olive oil, or as a 2½ per cent. solution in olive oil. The dose is 2 to 4 capsules, thrice daily immediately after food, or 3 to 6 drachms of the solution. The latter is convenient for the smaller doses required for children; each drachm contains 0.1 gram of the drug. Opinions vary as to the clinical value of hexyl-resorcinol. In my experience it is inferior to alkaline diuresis or mandelic acid, but is useful as an alternative treatment in subacute cases, particularly where the bladder is irritable. Its cost is a disadvantage.

Vaccines, Bacteriophage, and Wash-outs

In very chronic cases of pyelitis vaccines are sometimes used, but it is doubtful if they can be relied on to clear up the infection. Vaccines have no place in the treatment of acute or subacute attacks. Attempts have been made to treat pyelitis with bacteriophage, but there is as yet insufficient evidence to allow of a fair judgement of its efficacy.

Cystitis may persist in a troublesome form after the infection of the upper part of the urinary tract has become quiescent. In such cases local treatment by lavage and the instillation of antiseptics into the bladder may be beneficial. Bladder lavage may be carried out daily for several days, then every other day for 10 to 14 days, and after that once or twice a week. The fluid used must be non-irritant, such as silver nitrate 1 in 5,000 or acriflavine 1 in 5,000. In elderly patients with basal cystitis it is often helpful to wash out with boric acid lotion, empty the bladder, and instil 10 c.cm. of 10 per cent. argyrol, which is retained.

Drainage and Lavage of the Renal Pelvis

In some cases, particularly in the more severe forms of pyelitis of pregnancy, there is difficulty in establishing satisfactory drainage of the renal pelvis. Achalasia of the ureter may be treated by giving atropine (5 to 7 minims of tincture of belladonna, in water, three times a day), but it is not easy to deal with the tendency to stagnation of urine and accumulation of pus in the dilated ureter and renal pelvis. If this is not overcome by diuresis, it may be necessary to catheterize the ureter and wash out the renal pelvis with silver nitrate (1 in 5,000) or acriflavine (1 in 5,000). This requires special technique and experience, and should not be attempted in the ordinary conditions of practice. In severe cases with recurrent blocking of the ureter and hyperpyrexia I have seen striking improvement after such lavage, followed by continuous drainage with ureteric catheters kept in position for twenty-four hours at a time.

Conclusion

For the initial stages of acute pyelitis the most satisfactory treatment is a combination of rest, warmth, copious fluid intake, and alkalization of the urine.

After the toxic febrile stage has passed off mandelic acid with restricted fluid intake and acidification of the urine may be substituted. Mandelic acid may be used from the beginning in mild acute cases, and in the subacute exacerbations of chronic infection of the urinary tract. It should not be used if there is active renal disease, and must be stopped if it causes renal irritation.

Opinions vary as to the value of other methods of treatment. In my experience pyridine and other dye-stuffs, hexyl-resorcinol, and hexamine are inferior to the two methods referred to above, but many practitioners appear to be satisfied that these drugs are effective.

Disappointing responses to treatment can often be traced to insufficient dosage, careless technique, or lack of co-operation of the part of the patient.

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The Heart in Exercise

In his presidential address to the Section of Physiology, on September 11th, Professor R. J. S. McDOWALL discussed the various mechanisms which worked together to provide an adequate blood supply to any part of the body, whatever its activity, and whatever the posture of the body. He confined his survey to the effects of physical exercise, since most of the mechanisms were thus brought into action. Increased blood supply to any tissue resulted from the same blood being pumped more rapidly round the body, by increased activity of the heart, or from redistribution of the blood following variations in the calibre of the blood vessels. The force of the contraction of the heart was increased by stretching the cardiac musculature. Change in the rate of contraction depended on the balance between the sympathetic and the vagal groups of reflexes. When exercise was taken the sympathetic accelerator impulses increased and the vagal impulses were reduced. The range of acceleration was determined by the degree of activity of the cardio-inhibitory reflexes. In athletes during mild exercise the cardiac output was increased with a trivial acceleration of the rate, the increase being effected by a greater output during each beat. Certain procedures, such as sensory stimulation or asphyxia, increased the heart rate partly by reducing vagus activity, but subsequently this reduction was followed by an increase in the activity of the vagus.

Variations in Vessel Calibre

The local dilatation of vessels to accommodate the greater volume of blood was accomplished by chemical and nervous means; the substances concerned in the first case were the products of carbohydrate metabolism—namely, carbon dioxide and lactic acid—vessels being sensitive to the most minute changes in the hydrogen-ion concentration of the blood, and histamine. The nervous vaso-dilatation was probably of sympathetic origin, sympathetic nerves having been proved to contain vaso-dilator fibres. Once exercise had begun it seemed likely that local vaso-dilator reflexes were set up by afferent impulses arising within the muscles, possibly as a result of mechanical and chemical changes there. Hitherto closed capillaries in active muscles were also opened up, the blood to fill them being drawn from all other parts of the body, except possibly the voluntary muscles, the heart muscle, and the brain. Just as in the heart the reduction of the vagus restraint increased the range of cardiac activity and created a cardiac reserve, so there probably existed an exactly parallel mechanism which increased the range of vascular activity and similarly enhanced the reserve.