

instillation of nitrate of silver (p. 139). In other forms of acute cystitis I have not found it remarkably efficient. In chronic cystitis of any kind it is one of the best of local applications (p. 393).

Protargol.—Of the newer synthetic silver salts protargol seems the most useful. I have employed citrate of silver, argonin, and argentamin, but with unsatisfactory results. Protargol is most useful in the urethra (p. 135); but it may be used in the bladder when nitrate of silver is too irritating. The dose by instillation is from 1% up to 20%, beginning at the low figure; by irrigation from 0.5% to 10%.

Potassium Permanganate.—This drug is to the urethra what the silver salts are to the bladder. In the latter organ potassium permanganate may be employed when nitrate of silver irritates. It is especially useful in acute cystitis when the silver instillation fails. It is employed only by irrigation. I have used it in strengths varying from 1:8,000 to 1:4,000.

Boric Acid.—Boric acid is very mildly aseptic; it has no very specific action upon the bladder, and yet it holds a place in bladder lavage from which it will not be easily dislodged. This is on account of its entire innocuousness. It may be placed in the hands of the patient with the assurance that it will do him a definite good and can do him no harm. As far as I know, it is the only wash that can be entrusted to the stupidest patient with entire safety. The reason of this is that even in saturated solution it is entirely unirritating. The saturated (4%) solution is always employed. About 10 grammes of the crystalline boric acid (pulverized boric acid dissolves less rapidly) is mixed with 200 c. c. of hot water. After stirring for a minute or so the residue is allowed to sink to the bottom and the solution is ready in sufficiently accurate strength for all practical purposes.

The ease with which the boric-acid solution is prepared makes it superior to salicylic-acid solution, Thiersch's solution, or physiological salt solution. I use it for all mechanical irrigating, for the purpose of cleansing the bladder and filling it for cystoscopy, stone-searching, etc. It is also most useful for the daily prophylactic irrigation of prostatics. It will not cure cystitis, but it helps to prevent it.

The numerous local remedies not mentioned above, of which thallin sulphate and mercuriol are the most important, are useful chiefly in inflammations of the urethra and of the prostate (p. 134). Corrosive sublimate is useful only in tubercular cystitis (p. 406). Carbolic acid is not suited to vesical irrigations.

3. General Urinary Antiseptics.—Thus far we have been concerned with remedies whose sphere of influence does not extend

above the bladder. The last two classes with which we shall deal relate chiefly to renal inflammations, though their influence may be marked in inflammation of the bladder as well.

Under the term general urinary antiseptics I mean to include those remedies which when administered by the mouth produce such change in the urine as to render it a germicidal fluid. The number of drugs that exercise this influence in some slight degree is doubtless very great. Several of the alkalies and most of the balsamics already enumerated give the urine some antiseptic properties; but the urinary antiseptics of these drugs is overshadowed by the stronger influence of certain remedies about to be described. The four chief ones are urotropin, salol, benzoic acid, and boric acid.

Urotropin.—Hexamethylenetetramin, the ammonium salt of formaldehyd, is the most valuable drug we possess for combating pyelonephritis and many other urinary diseases. Unfortunately it is sold only under such trade names as urotropin, cystogen, and aminoform. The drug was introduced to the profession by Nicolaier,¹ and it is to him that we owe most of our knowledge of its chemical, physical, and physiological properties. The most notable characteristics of urotropin are:

1. Its action is entirely confined to the urinary organs. (In a few cases I have known it to interfere somewhat with digestion.)
2. Its action upon the urinary organs is due in large part to its splitting up under the influence of the urinary acids, with the result that formaldehyd is liberated in the urine.
3. Its alleged effects are five: antiseptic, irritant, antiphosphatic, antiuric, and diuretic.

Antiseptic Effects.—Urotropin is the best urinary bactericide we possess. Yet it is not infallible. Sometimes it will even fail when other urinary antiseptics will succeed, and it will often fail unless used undestandingly, its merits appreciated, its deficiencies recognized, and its limitations defined.

Urotropin is employed in bacteriuria, in pyelonephritis, in cystitis, and in posterior urethritis. In the treatment of total *bacteriuria* urotropin is invaluable. It prevents and controls almost all cases of typhoid bacilluria (p. 366) and pyelitic coli bacilluria. It may be necessary to employ it to the limit of toleration, even in doses of 3 to 6 grammes a day, in order to control an existing catarrhal pyelonephritis; but once the bacilli have been driven from the urine they may be kept away by smaller doses, which, however, may

¹ Centralbl. f. d. med. Wiss., 1894, xxxii, 897. Zeitschr. f. klin. Med., 1899, xxxviii, 350.

have to be continued for many weeks in order to prevent recurrence. In vesical bacteriuria urotropin is a useful adjuvant to local treatment, but in such cases local remedies must be depended upon to effect the cure. In suppurative *pyelo-nephritis* the germicidal virtues of urotropin are again of the utmost value. Suppurative *pyelo-nephritis* is commonly encountered only after it has reached a chronic state, and hence little good may be expected to accrue from the high initial doses that prove so useful in overcoming catarrhal *pyelo-nephritis*. On the other hand, I recall at least 4 or 5 cases in which renal suppuration of long standing and some severity has been controlled by small doses of urotropin, 0.5 to 2 grammes a day, administered for several months.

The treatment of *cystitis* and *posterior urethritis* by urotropin does not at first sight seem entirely rational. The drug, though antiseptic, is distinctly irritating, and is therefore less likely to be beneficial than balsamics and anodynes. In straightforward cases of chronic posterior urethritis, and in cases of acute cystitis it has been my experience that urotropin does more harm than good. My happiest experiences with the drug in this connection have been (a) in preventing the occurrence of cystitis in old men reduced to catheter life and in the prevention of catheteral and operative infection in general, (b) in preventing the occurrence of urethral chill or suppression of urine after the passage of sounds as well as after urethrotomies, cystotomies, and other operations on the urinary organs, and (c) in conquering that irritable form of posterior urethritis that flies to chills and swelled testicles every time any attempt is made at local treatment. The singular freedom from post-operative chill and suppression enjoyed by my patients since I began employing urotropin as a prophylactic has led me to use it as a matter of routine. I administer two or three 0.5-gramme tablets the day before the passage of a sound in stricture cases (p. 218) and the same dose for two days before every operation upon the urinary organs. As urotropin is found in the urine for two or three days after its administration I do not feel called upon to resume its use until the second day after operation. I have related elsewhere¹ several striking examples of the action of urotropin in the conditions enumerated above.

Irritant Effects.—The dosage of urotropin is determined chiefly by its irritating properties, which vary with each individual, and with the same individual at different times. The irritation manifests itself under two forms: (1) Irritation of the neck of the bladder and (2) cauterization of wound surfaces. The *irritation of the neck of*

¹ Phila. Med. J., 1900, vi, 606.

the bladder is much the more important. This it is that marks the limits of tolerance to the drug. All observers are agreed that the more water drunk with urotropin—i. e., the greater the urinary dilution—the less likely it is to irritate. I have known 1.5 grammes a day to cause an intense strangury within twenty-four hours. Yet I have had a patient take 4 and 5 grammes of urotropin a day for weeks together without any ill effects, and Nicolaier states that certain individuals can take 6 to 10 grammes a day. The underlying cause of these peculiarities is not known, but they are a warning always to begin administering the drug in small quantities, not to increase the dose without at the same time increasing the amount of water imbibed, and to recognise that in some cases the limit of tolerance may be reached before the limit of efficiency is attained, in which case the drug must be given up. Yet such cases are quite exceptional.

Happily there is another not less interesting side of the question. A certain mild irritant effect produced by the drug upon the kidneys¹ and the neck of the bladder is probably the cause of its efficiency in certain cases. Thus a light renal stimulation may well be one element in the prevention of chill and acute suppression by this drug, and I have attributed the few cures of posterior urethritis that I have obtained by the use of urotropin to a similar stimulating effect upon the neck of the bladder.

An evidence of urotropin irritation that may not be overlooked is its effect upon the urine. If the urine is hazy with bacteria (e. g., in a case of light *pyelo-nephritis* or bacteriuria) and urotropin is employed in sufficient quantity to clear the urine of them, the irritation may be, and often is, sufficient to provoke an epithelial desquamation and flow of pus that clouds the fluid quite as much as before. To the casual eye there is no notable change in the urine. Yet the desired effect has been attained: the urine has been cleared of its bacteria, and is now clouded with the epithelial and purulent exudate due to mechanical irritation. If this fact is overlooked and the drug pushed vigorously, the irritation will increase and the bacteriuria apparently grow worse instead of better. The distinction, therefore, between pyuria and bacteriuria is a cardinal one, the neglect of which may lead the surgeon sadly astray. Of the several more or less accurate tests for establishing this distinction the test by centrifuge and microscope is easily the best. The supposedly bacterial urine is centrifuged for three minutes at about 250 revolu-

¹ Nicolaier has produced albuminuria and hematuria in rabbits and dogs by the administration of large doses of urotropin.

tions a minute. If the haze is bacterial the fluid remains hazy, while whatever pus is present will be found collected at the bottom of the tube. But if the urine has been cleared of bacteria the centrifuge renders the urine completely clean and sparkling, while what was before a haze is now a sediment. This sediment, if examined under the microscope, is found largely epithelial if due to the irritation of urotropin, largely purulent if due to inflammation. In the treatment of bacteriuria, therefore, it must be remembered that the effect of treatment often cannot be discerned without the aid of the centrifuge and microscope, and it is a safe rule in practice to gauge the progress of the case chiefly on this showing.

A very rare mishap, which has occurred once in my practice, is the *cauterization of a wound* in the bladder by the urine containing urotropin.¹ I have seen no similar case reported, and should hesitate to lay stress on this isolated fact were it not for the importance of the inference if correct (and its plausibility is manifest). This I need scarcely insist upon. If the surgeon at any time encounter a case whose operative wound instead of healing becomes covered with a leathery slough and seems daily less likely to heal, and if this result is due to urotropin, he must recognise the fact and eliminate the cause immediately. The theory that urotropin may be the cause of this sloughing seems plausible to me from my experience with similar sloughing that I have seen occur in wounds treated with formaldehyd.

Antiphosphatic and Antiuric Effects.—Although not germane to the subject of urinary antiseptics, the antiphosphatic and antiuric effects of urotropin merit a word here. Curiously enough urotropin was at first praised as a uric-acid solvent rather than as a disinfectant. German authorities have insisted that urotropinized urine is an excellent uric-acid solvent at the body temperature. It will even dissolve uric-acid calculi *in vitro*. Casper also insists upon its value in phosphaturia. According to this author, not only do the phosphates disappear from the urine while the urotropin is being administered, but the phosphaturic tendency is also permanently overcome if the administration of the drug is continued for a sufficient length of time. I have not been able to verify this claim.

Diuretic Effects.—Authorities do not agree on the subject of diuresis by urotropin. In most cases it is certainly not markedly diuretic, yet severe post-operative suppression is sometimes immediately relieved by it. In this connection a case in Dr. Chetwood's practice merits quotation.

¹ Cf. Phila. Med. J., *loc. cit.*

"Mr. A. B., about forty, submitted to an external urethrotomy for stricture. During the twenty-four hours following operation he passed but 2 or 3 ounces of urine. His temperature rose to 105° F., his pulse was tumultuous and irregular, and he was apparently about to die of acute suppression of urine. Urotropin was then administered (0.5 gramme *q. i. d.*) and within twenty-four hours the flood-gates were opened, the temperature and pulse came down, and for two or three days all went well. Then, to test its efficacy, the urotropin was withdrawn. Within a day the urinary excretion became much less and temperature and pulse ran high again. Again the urotropin was administered, kidneys, temperature, and pulse promptly reacted, and the convalescence thereafter was uneventful."

No more striking example of diuresis could be desired. I have seen similar effects in other cases, but only when the kidneys were acutely congested. This diuresis is due, I believe, to the mildly stimulating effect of the urotropin upon the kidneys. When these organs are normal or chronically congested (e. g., in chronic uremia) the diuresis produced by urotropin is insignificant. In acute congestion I have found it most notable.

Résumé.—I recognise that the above description of the qualities of urotropin is not in accord with the teachings of many of the best authorities. It is founded, however, on a large clinical experience extending over several years, and if I do not accept urotropin as an appropriate drug for the routine treatment of gonorrhoea, chronic urethritis, and cystitis, it is because I have been unable to convince myself of its constant efficiency in these maladies. The following facts I can vouch for from my own experience:

1. In total bacteriuria and in light pyelo-nephritis urotropin seems almost a specific.
2. To prove effective in these diseases it may have to be administered in high doses until the urine is practically clear of bacteria, after which smaller doses may suffice.
3. The progress of the cure can be judged only by constant recourse to the centrifuge and microscope.
4. The dose must not be sufficient to cause irritation of the neck of the bladder.
5. The possibility of such an irritation cannot be overlooked, even when very small doses are employed.
6. In diseases of the bladder and the prostate urotropin may often be depended upon to prevent inflammation, but is only of secondary importance in controlling it, and may even be positively harmful.

7. In the treatment and prophylaxis of the various forms of urinary septicemia and urethral chill urotropin is often most useful.

8. Its routine employment both before and after operations on the urinary passages is indicated.

9. The urine containing urotropin occasionally has an escharotic effect upon wounds, which may constitute a contra-indication to its employment.

10. Urotropin is an admirable diuretic in post-operative suppression.

Salol.—Salol is commonly placed second in the list of urinary antiseptics. This drug is disintegrated in the upper intestine into its component salicylic and carbolic acids. These antiseptics are absorbed into the system and excreted in the urine, where they exert their antiseptic action. But in order to obtain any very definite antiseptic effect on the urine as much as 3 or 4 grammes a day must usually be administered. This is a large dose for any stomach to bear, and as the patients for whom the drug is likely to be most serviceable are often urinary dyspeptics (p. 565), the stomach rebels before the drug does any good. When well borne, however, the effects of salol are excellent. It has not the immediate bactericidal effect of urotropin, but may be employed as a prophylactic against cystitis or in the treatment of any inflammation of the urinary organs when urotropin fails. It does not irritate the neck of the bladder, but when given in overdose produces the smoky urine of carbolic-acid poisoning.

Benzoic Acid.—Benzoic acid and the benzoates of sodium and ammonium are employed, as a rule, under the vague impression that they acidify the urine, and thereby antagonize ammoniacal cystitis. Happily the practice is sounder than the theory. As Dr. William Ashhurst¹ has shown in experiments with the sodium salt, its effects are:

“ I. An inconstant diuretic action, accompanied by a slight diminution of the acidity of the urine.

“ II. A retardation or absolute prevention of alkaline fermentation.

“ III. An action in nature germicidal or inhibitory to the growth of certain micro-organisms either within the bladder or when introduced into the urine after voiding, these susceptible organisms including especially those which tend to produce the alkaline fermentation, but which develop in the urine while it is still acid.”

Thus the administration of sodium benzoate diminishes instead

¹ Phila. Med. J., 1900, v, 457.

of increasing the acidity of normal urine, and maintains the urinary acidity only by opposing ammoniacal fermentation. Hence it is solely a urinary antiseptic. In strength it ranks a little below salol, but is rather more digestible than that salt. Dose: 3 to 6 grammes a day.

Boric Acid.—Boric acid and borax (sodium biborate) are both employed as urinary antiseptics, but their strength is less than that of the above-mentioned drugs. Two or 3 grammes a day may be administered.

4. Diluents.—Diluents are all-important in the treatment of every inflammation of the urinary tract. They diminish the density of the urine not by lessening the output of solids but by increasing the watery excretion of the kidneys. Thus their primary action is upon the kidneys. These organs are stimulated to a free physiological action, and any tendency to congestion or inflammation in them is minimized or entirely overcome. The urine itself is rendered more bland, its crystalline contents more fully dissolved, its acidity or alkalinity lessened. The flow of urine is increased, less time is given for bacterial proliferation in the pelvis of the kidney, and the bladder is scoured by more frequent acts of micturition. Thus the sum of the action of diluents is: (1) Diminution of any kidney congestion that may exist, (2) diminution of the irritating properties of the urine, and (3) increased irrigation of the inflamed cavities.

Dilution of the urine—diuresis—may be obtained either by administering drugs that increase the excretion of water through the kidneys or by increasing the amount of water drunk by the patient. It is convenient for our present purpose to divide diuretics into three classes:

1. Medical diuretics: drugs that are admirably diuretic in various diseases of the kidneys, but for one reason or another are not useful in inflammations of the urinary tract, except for their effect upon the kidneys. Such are digitalis, calomel, sodio-salicylate of theobromin (diuretin), broom, squill, pilocarpin, gin, etc.

2. Diuretic drugs that are useful in certain urinary inflammations—viz., the alkalies, especially potassium acetate, urotropin and the balsamics.

3. Water, the great diuretic.

Diluent Drugs.—All of the medical diuretics referred to above are of value for their effect upon the kidneys. They may be absolutely essential to the treatment of certain cases complicated by grave organic changes in the renal parenchyma; but for their simple diluent effect they are not employed, since the alkalies, the balsamics, urotropin, etc., have an equal diuretic effect combined with some

medicinal effect upon the inflamed surfaces of the urinary tract. But, after all, water is the diluent upon which we depend most.

Diluent Waters.—There are waters and waters. Some are diluent and some not, entirely apart from their chemical ingredients. The general test which may be applied to any given water consists in drinking it freely and noting whether it lies heavy on the stomach. The water that can be drunk in greatest quantity without overloading the stomach is in practice the best diluent. Thus rain water is more diluent than well water, as a rule; still water more than charged water; alkaline more than acid water. Yet, quite apart from these broad properties, some waters are more diluent than others, quite as gin is more diluent than brandy, and beer more diuretic to some persons than to others, and for reasons equally obscure. For ordinary dilution of the urine, such as is a part of the treatment of every one of the inflammations in question, rain water or re-aerated (not charged) distilled water suffices, if drunk freely up to 3 or 4 pints a day. For more marked dilution, such as is useful in the treatment of bacteriuria and pyelo-nephritis, Poland water, or any of the alkaline or lithia waters may be employed. In some cases, notably in acute or severe pyelo-nephritis, in obstinate bacteriuria, and in partial or total suppression of urine, post-operative or other, the greatest possible diuresis is required. Apart from drugs, such as potassium acetate, urotropin, etc., the best means I have found of overcoming these conditions is the use of Suwannee water. This water is more diluent than any other with which I am familiar. Like all mineral waters it is most efficient at its own spring, where as much as 5 gallons have been drunk in a day by one man. Stafford water is said to be equally good.

RADICAL TREATMENT

The radical treatment of any inflammation of the urinary organs is the removal of that predisposing retention, irritation, or congestion, which gives the bacteria their opportunity to attack the tissues. This implies special treatment for each special disorder. At the same time the palliative measures must be applied in order to help allay the inflammation. The cure of an inflammation by palliative measures alone, without recourse to radical treatment, is too often only temporizing with the main issue.

CHAPTER XXV

CYSTITIS

Classifications.—The inflammations of the bladder are reducible to a very small number of clinical types, though each of these types has many variations. Authorities differ so widely in their classifications of cystitis that an accepted classification can hardly be said to exist. The following simple scheme will suffice for our purposes:

Non-bacterial Cystitis	{	Traumatic.
		Chemical.
Bacterial Cystitis: Simple	{	Acute.
		Chronic { Acid.
		Alkaline.
Tubercular Cystitis		Interstitial.
		Pericystitis.

The non-bacterial cases will be dismissed briefly. Tubercular cystitis is considered in a subsequent chapter.

NON-BACTERIAL CYSTITIS

Non-bacterial cystitis is the natural reaction of the vesical mucous membrane to a mechanical or a chemical irritant.

Traumatic Cystitis.—A mild cystitis or irritability of the bladder, as it is often called, may be caused by the passage of concentrated urine containing phosphates, urates, or oxalates. There is more or less urinary frequency and distress, and besides the crystals the urine contains a certain amount of pus. The so-called gouty or rheumatic cystitis is of this nature.

A more severe inflammation without infection is commonly caused by stone in the bladder (p. 435) and by rough instrumentation. In such cases there may be much tenesmus and distress together with an abundance of blood and pus in the urine.

Treatment.—The irritation due to concentrated urine may be dispelled by diluting the urine and correcting the cause of the urinary