RESIDUAL SUBACUTE AND CHRONIC PROSTATITIS AFTER PENICILLIN AND SULPHONAMIDE THERAPY IN ACUTE GONORRHOEA

BY

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The condition I am about to describe has not, so far as I am aware, been given any prominence in the current literature. As a result of careful personal observation in Mauritius, East Africa, and Cyprus (and so presumably throughout the Tropics and sub-tropics), covering a period of 4½ years' continuous V.D. practice in the Army, I can affirm that subacute and chronic residual prostatitis after chemotherapy in acute gonorrhoea is of very widespread occurrence, and gives rise to physical signs as long as it remains untreated. Under chemotherapy I include treatment by the sulphonamides, as I consider that, from a purely therapeutic point of view, penicillin has only one advantage over the sulphonamides in gonorrhoea—that there is no evidence of penicillin resistance or "fastness" so far as the gonococcus is concerned. Hence, when the sulphonamides act favourably, they are therapeutically as effective as penicillin.

If the following are accepted as the criteria of cure in all cases of urethritis—(1) a persistently clear urine, (2) a persistently "dry" urethra, (3) a prostate which feels normal on palpation per rectum, and (4) a prostatic fluid which is macroscopically clear, and which, when fixed and stained, shows microscopically no pus cells, or at most only a few (not more than two or three in any field)—then I have found that after chemotherapy in every case of acute gonococcal urethritis return to normal is disappointingly infrequent. The departure from normality which occurs most often after treatment is the above-mentioned residual prostatitis, which fails to respond to further chemotherapy.

Clinical Features

The signs (there are no symptoms) of such a prostatitis may be the following:

1. Persistence of slight watery mucoid, or viscous opalescent or milky mucopurulent urethral discharge, which may be manifest only in the morning, or which may occur throughout the day. Microscopical examination of such a discharge will show mucus, either amorphous or inspissated; relatively few pus cells; small squamous epithelial cells from the urethra; and no organisms, or only scanty secondary organisms, such as Gram-positive cocci or bacilli. No gonococci can be detected after penicillin.

2. Persistence of mucus in varying quantities in the urine, with finely granular epithelial debris in suspension, or coarser sinking debris or small "comma" threads.

3. A palpably diseased prostate on rectal examination. It is difficult to describe the palpable features of a normal prostate: it is much easier to describe an abnormal one. The types of abnormality encountered are threefold: abnormality of size, shape, and consistence, depending on the severity and the duration of the prostatitis when first examined. Except in well-advanced cases, however, the physical signs appear to bear little relation to chronicity. In the early stages of prostatic involvement it may be difficult or impossible to assess the condition of the prostate by palpation alone, but by constant practice minor departures from the normal can be accurately assessed.

The physical signs of prostatitis are as follows:

- (a) The whole prostate may be symmetrically enlarged—that is, both lobes are prominent with a well-marked median raphe or furrow between them. It may be boggy in consistence or it may be tense or turgid. Such turgidity, how-

ever, will yield when the prostate is massaged—that is, the lobes are comparatively soft and yield to the palpating finger when pressure is exerted upon them.

- (b) The prostate may be symmetrically enlarged and smooth but of a rubbery consistence. This stage is reached surprisingly quickly in the course of prostatic infection. In this case greater pressure is required to produce any depression in the lobes by the examining finger.

- (c) There may be unilateral enlargement. One lobe (usually the left) is enlarged and turgid or rubbery.

- (d) One or both lobes may be not only enlarged but irregular in shape and consistence—that is, nodular. The nodules are portions of the prostatic lobe which are harder than the rest. There may be only one such nodule in either lobe.

- (e) Finally, the whole prostate may be somewhat shrunken, nodular, and hard, and no amount of pressure exerted upon it by the massaging finger will produce any impression. Such prostates are very difficult to drain. As it is virtually impossible to examine histological sections of such prostates, one can only suppose that the increasing hardness is due to fibrosis.

4. A pathological excess of pus cells (polymorphonuclear leucocytes) in smears of prostatic fluid expressed by massage. It is interesting to correlate the physical signs in the prostate, ascertained by rectal palpation, with the microscopical appearance of stained smears of prostatic fluid. If this is done, a palpably diseased prostate will almost invariably contain an excess of pus cells in the prostatic fluid. The smears show pus cells in either great or moderate numbers. In the former case the macroscopical appearance of the prostatic fluid is worthy of note: it is opaque and distinctly yellow in colour. Normal prostatic secretion is semi-translucent and faintly bluish. Patients should, of course, be made to urinate immediately before prostatic massage. In chronic cases—that is, where the prostate feels hard and rubbery—prostatic smears may show pus cells in either large or small, widely separated clumps. There may also be a great admixture of mononuclear cells, which are almost certainly epithelial cells from the prostatic ducts, although they superficially resemble large lymphocytes or plasma cells. These epithelial plugs admixed with leucocytes constitute the small flocculent debris which can be seen floating in the prostatic fluid in these cases.

In my experience it is rare to find organisms of any kind microscopically in such pathological prostatic smears. Out of hundreds of such smears that I have examined microscopically I have found gonococci in only three, and secondary bacilli in about the same number. I invariably stain my prostatic smears with Loeffler's methylene blue, as not only is it a quick and clean method, but the leucocytes stand out conspicuously. Any organisms present are also easily detected, and a full staining by Gram's method may be performed subsequently if doubtful cocci are encountered.

It occasionally happens that a palpably abnormal prostate usually one of tough, rubbery consistence—will yield negative smears in which pus cells are absent or only scanty. Conversely, where a prostate feels normal a large number of leucocytes may be present in the fluid expressed from it; but by far the most constant and reliable evidence of prostatitis is the microscopical appearance of pus.

Such, then, is the clinical and microscopical picture of this condition. As it might be objected that the prostatitis in question may be the direct result of the methods employed to combat the original urethritis, or may be due to a pre-existing prostatitis, I will quote a few illustrative cases. I can affirm that the condition is discovered in the course of primary acute gonococcal infections, after penicillin therapy alone, in patients who have never had local treatment directed to the prostate or any form of mechanical or adjuvant treatment.

I was fortunate to enlist the help of Dr. R. M. Dowdeswell, a bacteriologist at the Medical Research Laboratory, when I was working at No. 87 (Nairobi) British Military Hospital, between April and June, 1946. Dr. Dowdeswell had approached me for help to enable him to carry out some

independent research of his own on the blood concentration of penicillin over a period of hours after a single subcutaneous injection of the drug, under different atmospheric temperature conditions. The sodium penicillin used in Dr. Dowdeswell's cases was dissolved in sterile doubly distilled "pyrogen-free" water, and admixed with the patient's whole blood in the proportion of 3 : 1 (three parts of penicillin solution to one part of blood). The mixture was shaken in the barrel of the syringe and allowed to stand for six minutes before being injected subcutaneously into the abdominal wall.

It is important that the condition of the prostate be ascertained, so far as possible, before commencing treatment in acute gonorrhoea. The only available method is palpation of the gland per rectum. If this is done in all cases, it will be found that the prostate is palpably abnormal in a fair proportion of them.

Illustrative Cases

Case 1.—Sgt. A., admitted to 87 British Military Hospital on May 24, 1946. Exposure with European woman about twelve days before admission. Used condom, followed by prophylactic packet one hour after exposure. Appearance of urethral discharge about ten days after coitus. First infection. On examination, purulent urethral discharge. Urethral smear showed intracellular gonococci ++. Prostate felt normal per rectum. On the 27th 150,000 units penicillin injected subcutaneously. Dr. Dowdeswell, dissatisfied with the results of the blood penicillin maintenance in this case, reinjected 150,000 units on the 30th. On June 4 his urethra appeared dry. Early-morning two-glass test showed almost clear urine, no debris, in both glasses. Per rectum the left lobe of the prostate felt enlarged and slightly rubbery. On the 7th his prostate was massaged, a smear made, and prostatic fluid was collected and cultured by Dr. Dowdeswell. The prostatic smear showed pus cells ++ with clumps of mononuclear cells; the culture yielded two colonies of *Staph. albus* and two of diphtheroids.

Case 2.—Gnr. B. History of gonorrhoea treated in India with penicillin alone, 100,000 units, on April 16, 1946. Noticed slight urethral discharge two days before admission to 87 B.M.H. on May 14, 1946. On examination, scanty mucoid urethral discharge. An early-morning smear was sought for on the 15th, but none was found. Early-morning two-glass test showed clear urine with faint mucous cloud in suspension in both. Per rectum, lobes of prostate prominent and rather rubbery. Prostatic smear showed pus cells ++.

Case 3.—Cfn. C., admitted to 87 B.M.H. for penile sore on May 27, 1946. Exposure with half-caste woman ten days before admission. Used condom, followed by prophylactic packet three or four hours after coitus. Past history of syphilis in England ten years ago. He was absolutely certain that he had never had urethritis. On examination, small superficial non-indurated cribriform ulcer at muco-cutaneous junction of prepuce. No buboes. Blood Kahn negative. Dark-ground illumination negative for *Treponema pallidum* on three occasions. On the 29th he reported a purulent urethral discharge. Urethral smear showed intracellular gonococci ++. Per rectum the prostatic lobes felt prominent, smooth, and tense. Left lobe greater than right. On the 31st 150,000 units penicillin injected subcutaneously. On June 7 his urethra appeared dry. Two-glass test showed urine clear in both glasses. On the 12th his prostate was massaged, a smear made, and prostatic fluid was cultured. The prostatic smear showed pus cells +++ ; the culture yielded a few diphtheroids.

Case 4.—Cfn. D. Exposure on April 28, 1946, with African woman. First noticed urethral discharge on May 2. First infection. Admitted to 87 B.M.H. on May 4. On examination, viscous mucopurulent urethral discharge. Urethral smear showed gonococci ++. Per rectum the prostate felt normal. On the 5th 150,000 units penicillin injected subcutaneously. On the 9th two-glass test showed: 1st, slightly hazy with mucus and a few opaque threads in suspension; 2nd, slightly hazy with mucus. Per rectum the prostate felt normal. On the 10th he had a slight mucoid watery urethral discharge. Two-glass test

showed: 1st, very faintly hazy with mucus and a few small mucous shreds in suspension; 2nd, clear. On the 11th his early-morning two-glass test showed: 1st, clear with small mucous cloud, containing granular debris, in suspension; 2nd, clear, with small mucous cloud in suspension. He still showed a clear watery urethral discharge. On the 12th his urethra appeared dry. Urine was clear. On the 14th, reappearance of scanty mucoid urethral discharge. Two-glass test showed: 1st, almost clear, with small mucous shreds in suspension; 2nd, clear. Per rectum, slight cord-like thickening of left lobe of prostate. Prostate massaged. Prostatic smear showed pus cells ++. Prostatic fluid was cultured by Dr. Dowdeswell; culture yielded *Staph. albus*.

Case 5.—Cpl. E. Exposure with Seychelles girl thirteen days before admission to 87 B.M.H. on June 11, 1946. Used condom which broke. Prophylactic packet used half an hour later. Urethral discharge appeared eight days after coitus. History of gonorrhoea in Italy in August, 1945, treated with penicillin at No. 1 R.A.F. General Hospital. On examination, purulent urethral discharge. Urethral smear showed gonococci ++. Per rectum, prostate felt normal. On the 12th 150,000 units penicillin injected subcutaneously. On the 16th his urethra appeared dry. His urine was hazy with mucus and contained dense sinking threads +. Per rectum the prostate felt uniformly enlarged, smooth, and tense. On the 17th the prostate was massaged, and prostatic fluid was collected and cultured by Dr. Dowdeswell. Prostatic smear showed pus cells +++ ; the culture was sterile.

Case 6.—Sgt. F. Exposure with African woman sixteen days before admission to Military Hospital, E.A.A.M.C., Nairobi, on July 30, 1947. Used condom, but no prophylactic packet. Urethral discharge appeared on July 27. First infection. On examination, purulent urethral discharge. Urethral smear showed intracellular gonococci ++. Per rectum the prostate felt prominent and symmetrical, with well-marked interlobar cleft. Harder than normal. On the 30th penicillin started—three-hourly intramuscular injections of 50,000 Oxford units to a total of 250,000 units. On the 31st slight purulent urethral discharge. Urethral smear showed pus and small epithelial cells and mucus only. Very scanty secondary organisms. He was given pot. cit. 15 gr. (1 g.) three-hourly in water. On Aug 3 there was a viscous opalescent urethral discharge. Two-glass test showed: 1st, opalescent with mucus, with threads and debris ++; 2nd, faintly opalescent with mucus. He was kept on pot. cit. three-hourly. On the 7th he showed slight milky mucopurulent urethral discharge. Early-morning two-glass test: 1st, opalescent with mucus and coarse sinking debris ++; 2nd, opalescent with mucus. Early-morning specimen showed pus cells and mucus only. He was then put on daily posterior irrigations with 1 in 10,000 mercury oxycyanide solution at a temperature of 120° F. (49° C.) in the irrigation can. On the 11th there was a slight viscous mucopurulent urethral discharge. Early-morning two-glass test showed: 1st, opalescent with mucus and coarse sinking debris +; 2nd, opalescent with mucus. Per rectum, prostate prominent and turgid; no induration or nodularity. Prostate was massaged, and prostatic smear showed pus cells +++ . He was kept on daily irrigations. On the 17th his urethra was dry. Early-morning two-glass test showed: 1st, faintly opalescent with mucus and coarse sinking debris +; 2nd, faintly opalescent with mucus. Prostate was again massaged, and he was discharged from hospital with instructions to report weekly for prostatic massage.

Discussion

Such cases are so common in tropical V.D. practice that it is a wonder they have not been commented on before now. The clinical findings are above suspicion when taken in the aggregate. I have already mentioned the unreliability of digital examination alone in assessing the condition of the prostate in early cases. However, when physical signs are present in the prostate they are as definite and conclusive of disease as any time-honoured physical signs in medicine. However, the microscopical evidence of prostatitis associated with venereally contracted urethritis, past and present, is irrefutable. I have mentioned cases in which palpably pathological prostates yield negative prostatic

smears, although this is the exception rather than the rule. It is observed invariably in those cases in which the prostate is of tough, rubbery consistence. This effect may be connected with the incomplete emptying of the gland, caused by the rigidity of the prostatic stroma, for often in such cases great pressure must be exerted on the prostate before prostatic fluid appears at the meatus. It may also be due to inflammatory exudate in the stroma causing occlusion of part or parts of the prostatic tree.

The fact that the structural changes in the prostate are found, and pus is seen microscopically in the fluid expressed, at the very first massage precludes the possibility of the prostatitis being traumatic in origin. Much more ambiguous and inconclusive are the bacteriological findings, both microscopical and cultural, in this condition. I have already referred to the rarity with which organisms of any kind are detected microscopically in such pathological prostatic smears; and this seems to coincide, so far as can be judged from so small a number of investigations, with the results of culture. In the eight cases in which Dr. Dowdeswell cultured the prostatic fluid no gonococci were grown. The secondary organisms may have been contaminants.

As regards the duration of the condition, I can speak with some authority, as in Mauritius for two whole years (1943 and 1944) I had the opportunity of observing the clinical progress of these cases. Defaulting was rare, and the patients reported weekly with clockwork regularity for prostatic massage; they came with a full bladder and their urine was inspected. The prostate was then massaged with a view to draining it, and prostatic smears were examined week by week. The results of the urine test and prostatic smear were recorded in each case. I use an arbitrary scale of my own to record the number of pus cells (polymorphonuclear leucocytes) in each prostatic smear as a whole (that is, not in any one field alone), ranging from + to + + + +, so that I can record the progress from week to week.

All cases of moderate severity—those in which the prostate is not very hard, shrunken, and nodular—respond to treatment, albeit slowly. The average period required to restore such pathological prostates to normal is between two and four months. The diminution of pus cells in the prostatic fluid is extremely slow, and is not appreciable until after the seventh or eighth week, and occurs *pari passu* with the softening of the gland. The urine, however, becomes clear long before the prostatitis resolves, and all urethral discharge disappears. The condition may be regarded as cured after three consecutive negative prostatic smears.

Aetiology

I have no theory to advance in explanation of this condition. Certain facts, however, are known from which certain conclusions can be drawn. The cases that I have quoted demonstrate clearly that it occurs very early in the course of primary acute gonorrhoea. It is only recently that I have adopted the practice of examining the prostate per rectum before starting treatment. In the past I have invariably been presented with a *fait accompli*—a diseased prostate the origin of which was open to conjecture. Furthermore, it may appear clinically either before treatment is begun or shortly after treatment, when the gonococcus is to all intents and purposes destroyed. It is much more common than folliculitis, which occurs characteristically in untreated cases of gonorrhoea of at least three weeks' duration; or in inadequately treated cases, as with small infrequent doses of a sulphonamide. In urethritis due to chronic anterior folliculitis or litritis the urethral discharge is usually teeming with mixed organisms, and

urethral smears show myriads of secondary organisms—usually small Gram-negative bacilli—even though there may be relatively few pus cells. Occasionally also in chronic anterior folliculitis large clumps of gonococci may be seen lying close to or upon squamous epithelial cells. Such a picture never occurs in the urethral discharge associated with the prostatitis under consideration.

This early involvement of the prostate suggests that the prostatitis in question might be a purely secondary effect. The question is, Of what nature? If it be of an allergic nature, one would expect the whole of the genital tract to participate in the phenomenon. Further, if it be allergic, it is selective, not only as regards the prostate as a whole, but actually within the prostate, for it very often happens that one prostatic lobe is enlarged and tense while the other is normal in size and consistence. The same argument applies to a purely "toxic" theory. Again, a prostatitis of this nature responds, both when treated and when untreated, like any other closed infection elsewhere: when regularly drained it resolves; when untreated it leads to fibrosis. Furthermore, the severity of this type of prostatitis is definitely related to the stage at which treatment of the primary infection is begun and to previous infection. It is, indeed, to be expected theoretically, and is found in practice, much more often in cases which give a history of repeated infections, and in delayed or inadequate treatment. Again, epididymitis occurring in association with a urethritis of venereal origin is invariably preceded by a prostatitis, and gives rise to very acute symptoms, whereas the concomitant and antecedent prostatitis does not. If the prostate is palpated per rectum in cases of epididymitis, it is usually found that the prostatic lobe corresponding to the side of the affected testis is more abnormal than its fellow on the unaffected side; and prostatic smears obtained after the acute symptoms and signs of the epididymitis have subsided reveal pus cells in large numbers. Lastly, cases of prostatitis do occur in which gonococci are present in sufficiently large numbers to be detected microscopically in prostatic smears, although the history and physical signs in such cases should lead one to suspect the presence of gonococci in the prostate.

The sum total of clinical evidence, therefore, seems to indicate that the prostatitis under consideration is a true infection, due to invasion of the gland by gonococci or other organisms, or both. If that conclusion be the correct one, the following questions immediately suggest themselves: (1) Why does the posterior urethra become infected simultaneously with the anterior urethra in some cases of acute primary gonorrhoea at its very inception? (2) In those cases in which the prostate becomes infected subsequently to the administration of penicillin, why should a few gonococci survive the general and rapid destruction of the organisms which occurs, and invade the depths of the prostate, leaving the anterior urethra without evidence of infection? (3) Why is the gonococcus so difficult to recover from the prostate in cases of this kind?

Summary and Conclusion

The main object of this article is to stress the prevalence of symptomless subacute and chronic prostatitis discovered in the Tropics following routine treatment of acute gonorrhoea with penicillin (or the sulphonamides), in doses generally accepted as adequate, after the acute signs and symptoms of the disease have subsided. It embodies the practical experience of 4½ years' continuous V.D. practice in the Army.

Six cases have been chosen to illustrate the main features of the condition, and to prove that it can and does originate very early in the course of acute primary gonococcal infections, appearing sometimes before, and sometimes very soon after, apparently successful penicillin therapy.

The type of prostatitis encountered is described in detail, and its aetiology is discussed. No theory of its causation is advanced. Further careful and more comprehensive investigations, with the use of controls, will have to be undertaken before the problem is finally solved and a more efficient and rapid form of treatment of the condition is evolved.

I am indebted to Dr. R. M. Dowdeswell for his kind help and voluntary co-operation in what promised to be a very interesting series of investigations (I was posted outside the Command before they had progressed very far); and to Lieut. E. S. Machell, R.A.M.C., for helpful criticism and suggestions. I also wish to thank Brig. G. M. Denning, one-time D.M.S., East Africa Command, for permission to publish this article, which has been abridged from the original written at No. 87 (Nairobi) British Military Hospital in June, 1946.

THIOPENTONE-NITROUS-OXIDE-OXYGEN ANAESTHESIA WITH CURARE FOR HEAD AND NECK SURGERY

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My purpose here is to describe a way of using thiopentone ("pentothal")-gas-oxygen anaesthesia to cover the whole field of surgery of the head and neck, including ear, nose, and throat, in adult patients. The method employs curare, the passing of endotracheal tubes, and the performance of artificial respiration in patients who may be apnoeic for many minutes. The article is therefore intended only for specialists in anaesthetics who are familiar with these techniques and not for the "occasional anaesthetist," who is recommended to continue to use the better-known methods with ether.

Many anaesthetists now agree in placing thiopentone-gas-oxygen, where their use is applicable, in merit above all other agents for speed of induction, ease and safety in maintaining anaesthesia, and freedom from unpleasant sequelae. Used together, they provide light general anaesthesia suitable for surgery of skin, fascia, muscle, bone, joint, and nerve—suitable, in fact, for all operations on the limbs and the body wall. They would also cover operations in the ear, nose, and throat, on the face, scalp, and neck, and on the skull and its contents, were it not for the difficulties of intubating, packing the pharynx, and deadening the cough reflex when they alone are used.

To overcome these difficulties the common practice has been to deepen the anaesthesia with ether until the jaw and larynx are relaxed for intubating and then to continue anaesthesia with ether at a level where the cough reflex is deadened, aided perhaps by spraying the larynx with cocaine. The objections to this are threefold: (1) It is time-consuming: 15 minutes or more are usually needed to provide conditions for easy atraumatic intubation through the mouth, and attempts to intubate earlier often result in greater delay. (2) An ether anaesthesia of this depth is nearly always followed by nausea and malaise of considerable duration. (3) Under certain conditions there is a risk of explosion.

It was to eliminate these disadvantages and to gain those of the thiopentone-gas-oxygen combination that the method to be described was evolved. In this method curare replaces ether as the relaxing agent. The profound relaxation which it provides is quick and certain. The larynx and trachea can be very thoroughly "cocainized" by spraying, so that the cough reflex remains deadened, and intubating and pharyngeal packing are easy. The time taken is

greatly reduced, the patient is spared the unpleasant after-effects of ether, and no inflammable agent is used.

Method

In outline the sequence is as follows: (a) Initial injection of thiopentone, injection of curare, injection of maintenance dose of thiopentone. (b) Insufflation of the lungs with oxygen, using the Boyle's machine and mask, for two to three minutes until the full curare effect has developed. (c) Laryngoscopy, "cocainization," intubation. (d) The machine is now connected to the tube and the gas-oxygen flow started. The larynx is packed and gas-oxygen anaesthesia continued with "assisted" respiration until spontaneous respiration has recovered to a normal depth.

Consider these points in detail. The initial dose of thiopentone varies according to the principles well understood by anaesthetists, but should be on the generous side. For a robust young adult it is 12 to 14 ml. of 5% solution. The dose of curare is 20 mg. of pure crystalline *d*-tubocurarine chloride made up in 1% solution and called "tubarine" (Burroughs Wellcome). This is given quickly in one injection immediately after the thiopentone, and as the solutions of thiopentone and curare are incompatible it is better injected through another needle into a different vein.

At first smaller doses of curare were used and found insufficient in some cases where intubating through the mouth was necessary. But if intubating through the nose is required for an operation of short duration—as, for example, dissection of the tonsils by a quick surgeon—the smaller dose of 15 mg. is preferable. Unlike thiopentone, it is difficult to predict the approximate dose of curare that is required for any individual. What is important is that it should be sufficient. With a relative overdose, artificial respiration is, by the very nature of the action of curare, extremely easy to perform. With too small a dose intubation is difficult and the merits of the method are largely lost.

The maintenance dose of thiopentone is for the purpose of providing continual basal narcosis throughout the operation. What remains in the 20-ml. syringe is usually enough. It may be given immediately after the curare or intermittently over the next few minutes according to the reaction of the patient to the initial dose. In robust young patients the whole dose is generally given at once. If the operation is a long one, further small doses of thiopentone may be added from time to time when necessary, the ankle veins being chosen as conveniently remote from the surgical field.

Insufflation of the lungs with oxygen is most simply done by holding the mask firmly on the face, turning on the oxygen bypass, and alternately squeezing the bag to inflate the lungs and lifting the mask a little to allow the expired gases to escape. This is continued for two or three minutes, when the full effect of the curare will have developed. At this stage apnoea is complete, or nearly so, but the concentration and quantity of oxygen in the lungs is high enough to provide full oxygenation of the blood, under the conditions, for many minutes.

During these minutes laryngoscopy, "cocainization," and intubation are performed with care, with ease, and without hurry. There is inevitably some accumulation of carbon dioxide. It is likely that this develops slowly, as not only is the metabolism of the patient depressed by the premedication (omnepon 1/6 gr.=11 mg.; scopolamine 1/150 gr.=0.45 mg.) and by the thiopentone but also muscle tone is abolished by the curare. In any case it is a common practice for the anaesthetist deliberately to raise the concentration of alveolar CO₂ in the early stages of an anaesthetic without apparent detriment to the patient.

"Cocainization" is performed by spraying the larynx, under direct vision, with the usual type of Rogers spray. The exposure is so good that there is no difficulty in directing a cloud of fine spray not only over the larynx but down the trachea. If the operation is a long one, 2% amethocaine is used liberally, but for a short operation, especially one in which blood may accumulate in the pharynx when it is finished, 10% cocaine solution is used, and sparingly.

Oral is preferred to nasal intubation whenever the surgical procedure allows, and the largest tube which will pass com-