DIAGNOSIS OF CHRONIC PROSTATITIS*

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Prostatic infection or inflammation is a subject to which little attention has been paid in the last 15 years. This neglect is probably attributable to the development and widespread use of antibiotics during this period which has enabled the symptoms of bacterial invasion of the genito-urinary tract to be rapidly allayed. Evidence is now accumulating that chronic prostatitis may be concerned in the development of ankylosing spondylitis (Romanus, 1953; Mason, Murray, Oates, and Young, 1958) and the chronic forms of Reiter's disease (Weinberger, Dienes, and Bauer, 1952; Romanus, 1952; Csonka, 1958; Oates, 1958). It seems timely therefore to review the methods of diagnosis of chronic prostatitis.

The criteria for the diagnosis of this condition are by no means universally agreed upon. The patient's complaints may frequently suggest that prostatic involvement is present, but it is well known that prostatitis may exist without any symptoms whatsoever. Few accurate studies of the incidence of chronic prostatitis in otherwise healthy men have been carried out. Where they have been undertaken, their authors frequently do not specify the criteria by which the diagnosis has been made. Hinman (1935) stated that 35 per cent. of men had chronic prostatitis, with the highest incidence between the ages of 35 and 50 years. Pelouze (1921) thought that probably 35 per cent. of normal males were so affected, and Wilde (1949) estimated that 40 per cent. of men over 40 years of age had chronic prostatitis. Visher (1929), who studied 500 consecutive admissions of male patients to a hospital, found that 17 per cent. showed definite evidence of prostatitis. All these figures with the exception of those of Wilde relate to patients seen in the pre-antibiotic era when one might perhaps expect to

find a higher number of cases of chronic genital infection. In two recent studies carried out in the United States by Ambrose and Taylor (1953) and Parino (1958), it was found that 32 and 38 per cent. respectively of "normal" men had evidence of prostatitis. Parino found that there was some evidence that the number of men with evidence of disease of the gland was higher in the older age groups. The men examined were all young men who had recently completed 2 years of military service. The criteria adopted for the diagnosis were given as "fifteen to fifty pus cells per high-power field, or the presence of clumps of pus" in the expressed prostatic secretions. They found 38 per cent. of 411 men were so affected. To meet the criticism that such a group of men represented a selected sample, they examined a group of young male civilians and found that 30 per cent. of 129 such men had chronic prostatitis.

In general, however, symptomatic chronic prostatitis has two main forms of presentation. In the first and larger group the patients complain of perineal discomfort, and aching sensations referred to the inner side of the thighs, the suprapubic region, the groin, and sometimes the lumbosacral region. There is frequently a sensation of discomfort on micturition which the patient finds difficult to describe but about the existence of which he is quite definite. Many patients notice a little urethral discharge before passing the first urine of the day. Some of these symptoms are met with in neurotic patients in whom there is no demonstrable organic genital disease.

The second group usually presents with repeated urinary infections, the onset often being acute with malaise and some fever. Actual urinary symptoms may be very slight and the cause of the attacks may pass unnoticed. Indeed they are often diagnosed as influenza (Hinman, 1935; Badenoch, 1953). After a few days the fever subsides only to recur after a few days or weeks. Pyrexia is often present and the

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coliform bacillus is cultured from the urine. Thus the patient's symptoms do not often help in making the diagnosis.

Palpation of the gland may reveal tenderness, induration, boggy swelling, or nodular thickening of the gland, but these findings are uncommon and frequently of little significance as they may be found in patients where microscopic examination of the expressed fluid reveals a complete absence of inflammatory cells. Tenderness on rectal palpation of the prostate is frequently complained of by the patient but such complaints require careful interpretation. It can usually be demonstrated by further questioning that no true feeling of pain is present but rather a sensation of generalized rectal discomfort resulting from the rectal manipulation rather than from the pressure on a tender gland. Patients who have never previously experienced rectal examination are very prone to this complaint. Induration, however, is an important physical sign when present and is not often found in normal men. Considerable experience is required to differentiate between "induration" and the small, firm, flat prostate which is a common variant of the normal. "Boggy" swelling well describes the sensation experienced on palpating some chronically inflamed glands, but its value as a physical sign is very slight as it also may be found in normal subjects. Attempts have been made to find biochemical tests which may indicate prostatic inflammation. Huggins and McDonald (1944) estimated the quantity of two enzymes produced by the prostate, namely acid phosphatase and fibrinolysin, in patients suffering from chronic prostatitis. They found no correlation between the level of acid phosphatase in the prostatic fluid and the presence or degree of prostatitis. They found, however, that prostatic fluid which contained a higher number of pus cells (indicating, presumably, a severe degree of prostatitis) contained larger amounts of fibrinolysin. This test is of little clinical value because it involves the use of difficult laboratory techniques which are time-consuming. It does however suggest possible fields for further investigation which may lead to the development of simple accurate tests for prostatic function. Some other workers (Hansen and Jensen, 1946) have, however, claimed that there is a correlation between the level of acid phosphatase in prostatic fluid and the presence of prostatitis.

Thus it is clear that the diagnosis of chronic prostatitis can only be made accurately by the microscopic examination of the expressed prostatic secretion for the presence of polymorphonuclear leucocytes. Unfortunately, the technique of prostatic massage and individual variations in size and

position of the seminal vesicles and prostate render it inevitable that most specimens of secretion obtained by massage are a mixture of urethral, prostatic, and vesicular fluids. If urethral contamination can be excluded the presence of any inflammatory cells should, strictly speaking, be regarded as evidence of "prostatic-vesiculitis" rather than just prostatitis. Romanus (1953) has described a technique of "differential stripping" whereby the vesicular and prostatic fluids can be separately examined. This method is not suited to routine clinic practice.

Criteria for Diagnosis by Microscopy

All authorities agree that the presence of numbers of polymorphonuclear leucocytes in the prostatic secretion is evidence of disease, though no agreement exists on the number of cells which should be considered abnormal. It should also be noted that, with one exception (*vide infra*), no attempts to count these cells accurately have been carried out, most authors relying on the number of cells seen per microscopic field. This clearly can give no more than a very rough estimate and as previously pointed out few authors give details of the lens objective, etc., employed.

Pelouze (1939) stated that the fresh secretion of the normal prostate contained from two to six polymorphs per 1/6th microscopic field, and that any figure above this should be interpreted as evidence of prostatitis. Romanus (1953) regarded more than five to ten cells per high-power field (size of objective not given) as indicating prostatitis. He also quoted Hinman as stating that the normal vesicular fluid contains only an occasional white cell. Romanus also drew attention to the importance of clumping of the leucocytes in chronic prostatitis and to the necessity of immediate microscopic examination of the fresh material in order to appreciate this phenomenon. The exact cause of leucocytic clumping is unknown, but Pelouze (1939) suggested that it might indicate poor drainage of sites of prostatic inflammation. If the leucocytes are not present in clumps then drainage is assumed by Pelouze to be good. Huggins and McDonald (1944) estimated by means of a counting chamber the number of leucocytes per c.mm. in the prostatic fluid of "25 patients with chronic prostatitis, abscess being excluded". They found totals ranging from 1,200 to 13,000 leucocytes per c.mm., the majority falling between 2,000 and 8,000. They stated that the normal prostatic fluid contained between 200 and 1,000 cells per c.mm. but gave no experimental data in support of their statement.

A trial of the chamber method of counting leucocytes in prostatitis was made as follows:

Samples of prostatic fluid obtained by massage from patients with chronic prostatitis were collected into narrow cylindrical wax containers and placed in an incubator at 37°C. for 30 minutes in order to allow lysis of any vesicular contents to take place. The fluid was then agitated with a small glass rod, 0.01 c.mm. was withdrawn into a standard haemoglobin pipette, and diluted with Hayem's solution to 0.02 c.mm., and a sample of the mixture was counted in a Jena cell-counting chamber. Twenty patients were examined with the following results:

Cells (per c.mm.)	Patients
2,000 and Under	4
2,100-4,000	6
4,100-5,000	1
5,100-7,000	5
7,100-10,000	2
15,000 and Over	2

There are many objections to this technique which possibly gives an illusion of that accuracy so lacking in other methods. There exist no standard normal levels for comparison and the compilation of such a series would be an arduous task. Also, even if great care is taken to allow the secretions to liquefy before taking the pipette sample, it is a common finding that many of the leucocytes are still present in clumps and strings which prevent accurate counting and demonstrate that the cells are not homogeneously suspended throughout the specimen. In addition, it is a time-consuming procedure.

In view of the failure of this method, attention was directed to the more conventional form of diagnosis by direct microscopy of the expressed fluid. The usual method employed in venereal disease clinics for the examination of the prostatic secretions is for a heat-dried spread to be prepared and then stained by Gram's method. Owing to the high protein content of the secretions they fix extremely badly to the slide, and a great deal of material is lost during the fixing and staining processes. In addition, any leucocytes present tend to marginate during the drying of the specimen, and the clumping of these cells cannot be properly appreciated.

It seemed likely, therefore, that examination of fresh wet specimens would offer the best chance of seeing the number and disposition of these cells. The technique adopted was as follows:

The patient passed urine after having refrained from micturition for a minimum period of 2 hours. It was considered that this was sufficient to cleanse the urethra of

any debris, pus, or other exudates. The prostate was then massaged and the first drops of fluid appearing at the meatus were discarded to avoid the possibility of any significant urethral contamination. A drop of the remaining fluid was placed on each of five glass slides and was immediately examined by dark field microscopy, the following features being noted:

- (1) Average number of pus cells per 1/12th microscopic field.
- (2) Appearance of clumping of leucocytes.
- (3) Quantity of lecithin bodies or granules present.

The test can be carried out quite successfully using a normal microscope with direct lighting rather than a dark field, but the latter instrument was preferred as it was found to be easier to identify the various elements present.

Results

This "five-slide" test was applied to a large number of routine clinic patients, including treated cases of both gonococcal and non-specific urethritis. Many of these patients had routine stained single prostatic smears taken at the same time. After 2 years' experience of this method the following conclusions were reached:

(1) Normal prostatic fluid rarely contained more than two or three polymorphonuclear leucocytes per 1/12th microscopic field, and in most men many such fields had to be examined before even a single leucocyte was seen.

(2) Leucocytic clumping was almost invariably found in chronic prostatitis. However, a few cases were seen where ten or more pus cells per 1/12th field were present with no signs of clumping.

(3) It was not found possible to correlate the number of lecithin bodies present with the number of pus cells and in later studies they were disregarded.

(4) It was frequently found that two or three slides would show no pus cells whilst the remainder would reveal large clumps of inflammatory cells. At the same time the single dry-stained film was often reported as showing prostatic fluid only.

Thus this method permits the examination of five separate specimens of prostatic fluid from a single prostatic massage and it is likely that many cases of prostatitis are found which would otherwise escape diagnosis.

The number of polymorphs present per 1/12th microscopic field upon which a diagnosis of prostatitis was based was ten or more. This is, as already indicated, higher than most authorities regard as necessary. The field covered by the 1/12th objective and eyepiece of the microscope employed in the

investigation was approximately 1/400 mm. square. Assuming a film thickness of 1/12 mm. a very rough approximation of the number of cells per c.mm. could be obtained by multiplying the average number of cells to each field by 4,000. Thus five cells per field $\approx$ 20,000 cells per c.mm., a figure much higher than those found by Huggins and in the series here reported—and ten cells per field $\approx$ 40,000 cells per c.mm.

All these calculations assume of course that each field of the entire specimen contains roughly the same number of cells—a state of affairs which rarely, if ever, obtains since prostatic fluid is not a homogeneous suspension of cells. The indications are enough, however, to show that the criteria adopted for the diagnosis of chronic prostatitis are reasonable and in accord with previous experience.

Summary

- (1) The diagnosis of chronic prostatitis is briefly reviewed and the "five-slide" test is described.
- (2) The presence of ten or more pus cells per 1/12th microscopic field in the expressed

prostatic secretions should be regarded as evidence of chronic prostatitis.

- (3) Leucocytic clumping is nearly always present in chronic prostatitis.

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