carcinoma in the gastric stump—the occurrence of such cases 3½, 7, and 17 years after a partial gastrectomy for cancer suggests a new malignancy.

In addition there were cases with a double pathology such as gastric or duodenal ulcer with carcinoma; chronic gastritis, simple polyp and cancer; simple and malignant polyp; and malignant polyp and infiltrating carcinoma. These lend force to the dictum of Hurst that gastric carcinoma never develops on a normal mucosa.

Conclusion

The emphasis in an earlier clinical diagnosis is upon symptoms, and the taking of a careful clinical history is the first step. Once the suspicion of malignancy is aroused in the mind of the surgeon and investigations are begun, he must be wary of the negative report, for this in the past has led to disaster. Fortunately he can now rely upon three lines of scientific investigation—namely, radiology, gastroscopy, and cytology—and by sifting the evidence they provide he may reasonably hope to advance the detection of this disease and thereby to improve the prospect of cure which only surgery can offer.

PROSTATITIS AND ANKYLOSING SPONDYLITIS

BY

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As part of a study of the radiological appearances of Reiter's disease two groups of patients, one with ankylosing spondylitis and one with rheumatoid arthritis, have been used for comparison. Since it has been argued that (1) Reiter's disease is a variant of rheumatoid arthritis (Littler, 1951), (2) ankylosing spondylitis is a variant of rheumatoid arthritis (Committee of American Rheumatism Association, 1953), (3) ankylosing spondylitis is a complication of Reiter's disease (Ford, 1953), and (4) ankylosing spondylitis is due to genital infection (Romanus, 1953), it was clearly necessary to determine the incidence of genital inflammatory disease in the two latter groups. All cases were therefore examined for signs of chronic prostatitis. We were impressed with the frequency with which patients with ankylosing spondylitis were found to have this condition when compared with those suffering from rheumatoid arthritis, the incidence being almost as high as that found in patients with Reiter's disease. We have therefore examined the data with particular care to ensure that this finding is not due to some other unrelated factor or to misdiagnosis. The present report covers this part of the investigation alone, and the radiological findings are discussed only to the extent that they relate to this aspect.

TABLE I.—Clinical Material—Age at Time of Study

	Age in Years												Total	Mean Age (Years)	Mean Duration (Years)	Mean Age of Onset (Years)
	15-		25-		35-		45-		55-		65-					
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%				
Ankylosing spondylitis ..	9	17	10	19	25	46	6	11	4	7	0	0	54	37.4	10.1	27.3
Rheumatoid arthritis ..	0	0	5	6	15	17	29	34	26	30	11	13	86	52.7	6.7	46.0
Reiter's disease ..	6	10	12	20	11	19	25	42	4	7	1	2	59	42.2	8.4	33.8

Clinical Material

Fifty-four cases of ankylosing spondylitis were studied and compared with 86 cases of rheumatoid arthritis and 59 of Reiter's disease, all males, a total of 199 cases. Those with ankylosing spondylitis and rheumatoid arthritis presented to the Department of Physical Medicine and Regional Rheumatism Centre of the London Hospital, and those with Reiter's disease mostly to the Whitechapel Clinic. We have included in the ankylosing spondylitis group only those cases in which a confident clinical diagnosis had been made, and have excluded all those in which reasonable doubt existed—for example, cases which might be classified as atypical spondylitis by Sharp and Easson (1954) and Sharp (1957). All the patients with rheumatoid arthritis were well-established typical cases. The diagnosis of Reiter's disease was based on the finding of a non-gonococcal urethritis associated with an arthritis of acute onset and a variable, often chronic, relapsing course. Conjunctivitis occurred in 24 of the 59 cases (40%) and uveitis and keratoderma blennorrhagica in 6 cases (10%) each.

Age Distribution and Disease Duration.—Each group presented a distinct frequency distribution of age at the time of study (Table I), the mean age of the ankylosing spondylitis group being 37.4 years, with a mean duration of disease of 10.1 years; the rheumatoid arthritis group had a mean age of 52.7 years, with a mean duration of 6.7 years; and the Reiter's disease group a mean age of 42.2 years, with a mean duration of 8.4 years. Disease duration was estimated from the first joint or spinal symptom in all categories.

Rose-Waaler Test

A Rose-Waaler test was carried out in 80% of the ankylosing spondylitis group, in all but one of the patients with rheumatoid arthritis, and in 34% of those with Reiter's disease. The technique used was that originally described by Waaler (1940) and Rose *et al.* (1948). Later modifications have given a higher degree of sensitivity to this test, but were not used for this study because of the additional time required for these techniques, time which a laboratory in a general teaching hospital could not allocate. The results (Table II) do, however, show a clear distinction

TABLE II.—Results of Rose-Waaler Test

	Positive		Negative		Test Not Done	
	No.	%	No.	%	No.	%
Ankylosing spondylitis ..	0	0	43	80	11	20
Rheumatoid arthritis ..	30	35	55	64	1	1
Reiter's disease ..	0	0	20	34	39	66

between the rheumatoid arthritis group on the one hand and the ankylosing spondylitis and Reiter's disease groups on the other. 35% of the rheumatoid arthritis group (38% of those with a history of one year or more) gave a positive Rose-Waaler test at the 1/16 level, while there were no positive titres in the other two groups. The incidence of positive tests in the rheumatoid group is comparable to that of Miller *et al.* (1949), who obtained 33%, using a similar technique. An analysis of the sample of ankylosing spondylitis and of Reiter's disease on which the test was done shows that these were reasonably homogeneous samples in terms of disease duration, the mean duration of the ankylosing spondylitis sample being 10.0 years and of Reiter's disease 6.2 years.

Sacro-iliitis

As part of the radiological survey the sacro-iliac joints of all patients were radiographed. Seven of the films (four Reiter's disease, two rheumatoid arthritis, and one ankylosing spondylitis) were not available at the time of reading, leaving 192 x-ray films for analysis. All were read "blind"—that is, without knowledge of the clinical diagnosis—by two of us, one a clinician, the other a radiologist. Only those findings referring to the sacro-iliac joints are reported on here. Equivocal changes were recorded, since we felt that early or slight changes might be missed if they were not. In the event these do not appear to alter the picture significantly. The three disease categories are distinctive (Table III).

TABLE III.—Incidence of Radiological Sacro-iliitis

	Ankylosing Spondylitis	Rheumatoid Arthritis	Reiter's Disease
Unequivocal bilateral sacro-iliitis	49 (94%)*	7 (8%)*	19 (32%)*
Equivocal bilateral sacro-iliitis	1	6	2
Unequivocal unilateral sacro-iliitis	1	12	6
Equivocal unilateral sacro-iliitis	0	9	4
No sacro-iliitis	2	50	24
X-ray films not available	1	2	4
	54	86	59

* These percentages are calculated assuming that the non-available films were normal.

Unequivocal bilateral sacro-iliitis was recorded in 49 of the 54 (91%) of patients with ankylosing spondylitis, normal sacro-iliac joints being found in only 2 cases. This is approximately the expected incidence (Thompson, 1957), bearing in mind the fact that, for reasons of economy, special techniques (Grainger, 1957) were not used. In the rheumatoid arthritis group unequivocal bilateral sacro-iliitis was present in 7 of 86 cases (8%) of those radiographed, an incidence similar to that found by Sharp (1957). In Reiter's disease the figures are intermediate, bilateral sacro-iliitis being recorded in 19 of 55 cases (35%).

Prostatitis

All the patients in the rheumatoid arthritis and ankylosing spondylitis groups (with the exception of one patient with rheumatoid arthritis who refused examination) were examined by one of us (J.K.O.) for the presence of chronic prostatitis, using a standard technique. Five samples of the fluid obtained by prostatic massage were scrutinized by dark-field microscopy for the presence of polymorphonuclear leucocytes in clumps. The diagnosis of chronic prostatitis (or more correctly "prostatitis-vesiculitis," as the expressed fluid is usually a mixture of vesicular and prostatic fluids) was made only on the finding of pus cells in clumps, with a minimum of 10 pus cells per high-power field. In nearly all cases very many more than 10 pus cells per field were found; indeed, the average clump usually comprised between 30 and 50 cells (Fig. 1). No distinctive features were found in the pathological appearances of the prostatic fluids in positive cases, whichever group the specimen was

FIG. 1.—Typical positive prostatic smear (portion of 1/12 field).

the specimen was

obtained from. These criteria for the diagnosis of chronic prostatitis are generally accepted (Hinman, 1935; Pelouze, 1939); also, as repeated massage was not practicable, our results represent the minimum incidence, and the true figures are probably higher. In the patients with Reiter's disease all except four had non-specific urethritis. These four gave a clear history of urethral discharge which had ceased at the time of examination. The prostatic fluid, which was examined in each case after the acute phase of the disease was over, was found to be normal in all four patients.

Table IV gives the overall incidence of prostatitis in the three groups.

TABLE IV.—Incidence of Prostatitis

	Prostatitis		No Prostatitis	
	No.	%	No.	%
Ankylosing spondylitis	45	83	9	17
Rheumatoid arthritis*	28	33	57	67
Reiter's disease	56	95	3	5

* One refused.

The difference between the ankylosing spondylitis group, with an incidence of 83% prostatitis, and the rheumatoid arthritis group, with 33%, is highly significant ($P < 0.01$). The high incidence in the Reiter's disease group is not surprising. The incidence in the ankylosing spondylitis group is similar to that reported by Romanus (1953), who, in a very careful study of 117 cases without, however, any controls, found an incidence of "prostatitis-vesiculitis" in 102, or 91%. His slightly higher figures may be accounted for by the very detailed investigation carried out in each case.

The difference between the rheumatoid arthritis and ankylosing spondylitis groups in respect of the incidence of prostatitis requires further analysis and consideration of whether this could be due to differences other than the disease process itself. Is it possible, or likely, that the difference in the ages of the two groups is the operative factor? The mean age of the rheumatoid arthritis group is some 15 years more than that of the spondylitis group (Table I), with a maximum incidence in the 45-64 decades, while the ankylosing spondylitis group has a maximum incidence in the 35-44 decade. Can it be argued that prostatitis in the younger and more sexually active male is commoner than in the older age group? Other control studies—for example, Parrino (personal communication)—suggest the opposite. He found an incidence of 38% prostatitis in a group of 411

FIG. 2.—Clinical material—incidence of prostatitis. (N.B. Cases of Reiter's disease with frank non-specific urethritis are included in the positive massage group.)

recruits, and he also examined 129 normal civilians. Of the latter, 30% had chronic prostatitis and there was a positive correlation with increasing age.

Table V and Fig. 2 show the correlation between age and prostatitis in the present material. It will be seen that the pattern of prostatitis in the ankylosing spondylitis group follows almost exactly the pattern of age distribution of the group. Moreover, the incidence in the rheumatoid arthritis group shows no trend in favour of the younger decades. On the contrary, of the 15 cases of rheumatoid arthritis in the 35-44 decade, only 4 had prostatitis, an incidence of 27%, or less than the incidence for the whole group; whilst in the same decade in the ankylosing spondylitis group 24 of the 25 cases (96%) had prostatitis. It seems unlikely, therefore, that the difference results from differences of age.

A similar examination of the relation of prostatitis to disease duration revealed no trend in favour of any relationship between duration of disease and prostatitis such as could account for this finding.

Prostatitis in Rheumatoid Arthritis

Control data, to be valid, must be obtained from a population of the same age and by using the same technique—indeed, the same individual carrying out the examination, since skill will be a variable. Adequate figures are thus hard to obtain. Ambrose and Taylor (1953) found 25% of young normal males to have chronic prostatitis. Oates (1957) found 20% of 63 males between the ages of 18 and 45 similarly affected. The rheumatoid arthritis group may, however, form a fairly satisfactory control group. It is necessary to be sure that it does not contain cases of Reiter's disease or of ankylosing spondylitis misdiagnosed as rheumatoid arthritis, since these will tend to give a falsely high incidence of prostatitis. If, however, there were a number of cases of Reiter's disease or ankylosing spondylitis in this group then we should expect to find a higher incidence of prostatitis in the cases with a negative serology.

In the event an exactly similar incidence was found in both groups (33%), which would support the supposition that no substantial error arises from this cause. It seems probable that the incidence of prostatitis, as judged by our criteria, in the rheumatoid arthritis group represents a fair approximation of that to be found in the general population of similar age distribution from which the clinical material was drawn.

Sacro-iliitis and Prostatitis

The incidence of sacro-iliitis is higher in Reiter's disease than in rheumatoid arthritis (Table III). In the present series, 35% had unequivocal bilateral sacro-iliitis. In those with a history of over five years it reached 61%. This has been commented on previously by others (Marche, 1950, 1954; Sharp, 1957), although Harkness (1949, 1950) found an incidence of only 5%. We have therefore examined our material to see whether there could be any association between sacro-iliitis as such and prostatitis. The number of cases with no evidence of prostatic disease is small, except in the rheumatoid arthritis group, where the incidence of sacro-iliitis was not significantly different whether prostatitis was present or not. All 11 cases of ankylosing spondylitis with a normal prostatic fluid had unequivocal bilateral sacro-iliitis, but none of the four cases of Reiter's disease with a normal prostatic fluid had changes in the sacro-iliac joints.

Alternatively, is it possible that prostatitis follows or results from sacro-iliitis? If so, one would expect the incidence of prostatitis to be higher amongst cases with sacro-iliitis. Of the 49 cases of ankylosing spondylitis with unequivocal bilateral sacro-iliitis, 38 (79%) had prostatitis, compared with an incidence in the whole group of 83%. In the rheumatoid arthritis group two out of six (33%) had prostatitis, compared with 33% in the whole group. If prostatitis resulted from sacro-iliitis one would have expected a higher incidence in these cases; the figures do not suggest that this is likely.

Age of Onset of Symptoms

Five cases of ankylosing spondylitis, or 9%, had their first joint or spinal symptom at the age of 14 or before—three at the age of 14, one at 13, and one at 12. A pre-pubertal onset has been noted by others (Polley and Stocumb, 1947; Lennon and Chalmers, 1948; Simpson and Stevenson, 1949; Lucchesi and Lucchesi, 1950; Romanus, 1953; Baird *et al.*, 1955). Hart's (1955) series of 184 cases contained 16 males whose onset was between the age of 10 and 15 years—an identical incidence of 9%.

These figures are clearly of some importance when considering the relationship of genito-urinary infection to ankylosing spondylitis. It must be noted that the date of onset in these cases may well be from the beginning of peripheral joint involvement rather than sacro-iliitis, which is difficult to observe at this age; and Ziff *et al.* (1956) draw attention to the incidence of spondylitis in post-pubertal patients with rheumatoid arthritis of juvenile onset. Of the five cases in the present series, three had prostatitis. These were those with long-standing disease—20, 20, and 21 years—whilst the two with five and seven years' duration had normal prostates.

Past History of Venereal Disease

In view of the possibility that the higher incidence of prostatitis in the ankylosing spondylitis group was due to a higher incidence of previous venereal infection, all patients were questioned closely about previous venereal disease. As might be expected, this was high in the Reiter's disease group: 27 of the 59 cases (46%) had had a previous attack of gonococcal urethritis, while the incidence in the ankylosing spondylitis group and rheumatoid arthritis group was low—5 of 54 (9%) in the former, and 4 of 86 (5%) in the latter. All the ankylosing spondylitis with a past history of urethritis had chronic prostatitis. In the rheumatoid arthritis group only two had prostatitis.

Discussion

The association between prostatitis and ankylosing spondylitis is not a new finding. The literature has been very fully reviewed by Romanus (1953), who points out that it goes back at least to 1926, when Marie amended his original paper of 1898 to the effect that the gonococcus was responsible for spondylitis; and many other workers since then—for example, Forestier (1935, 1939) and Volhard (1938)—have reported on the association between venereal infection and spondylitis. Others—for example, Watson-Jones and Osmond-Clarke (1955) and West (1949)—have contested this view. Much of the work is, however, obscured by a failure to distinguish between Reiter's disease with a subsequent spondylitis and ankylosing spondylitis itself, a distinction which is often by no means easy in

TABLE V.—Age Distribution of Prostatitis

	Age in Years												Total	Mean Age (Years)	Mean Duration of Arthritis (Years)
	15-		25-		35-		45-		55-		65-				
	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%			
Ankylosing spondylitis	6	11	8	15	24	44	4	8	3	5	0	0	45	37.8	10.7
Rheumatoid arthritis	0	0	2	2	4	5	11	13	7	8	4	5	28	52.5	6.8
Reiter's disease	5	8	12	20	10	18	25	42	3	5	1	2	56	42.1	9.0

individual cases. We have, however, been impressed by the contrast between Reiter's disease occurring in a slightly older age group—presenting with what is often, although not always, a florid urethritis and acute peripheral arthropathy and with a slowly developing, clinically silent sacro-iliitis—and ankylosing spondylitis with early sacro-iliitis, and, usually, an asymptomatic genital infection.

The evidence regarding whether prostatitis is an associated phenomenon or aetiologically related to ankylosing spondylitis is still not clear, and the interpretation of the data remains difficult. It is well recognized that chronic prostatitis may exist even when examination of a specimen of prostatic fluid may show few or no inflammatory cells. The explanation usually offered is that fibrosis or pocketing of inflammatory exudate takes place and that these areas may not be opened and drained by a first massage. This could explain some of the negative findings in the nine patients with ankylosing spondylitis. The finding of a normal prostatic fluid in the four patients with Reiter's disease who also had normal sacro-iliac joints is of little significance, since it is clear that the disease is quite often cured and no evidence of genital disease remains. In the rheumatoid arthritis group there is no correlation between sacro-iliitis and genital inflammatory disease. The opposite is the case when the findings in ankylosing spondylitis are considered. There is, however, no proof that the genital inflammation causes sacro-iliitis as postulated by Romanus, although it must be admitted that this is a seductive hypothesis, and the high incidence of sacro-iliac disease in male paraplegics (Abramson and Kamberg, 1949; Abel, 1950), nearly all of whom can be expected to have chronic prostatitis (Prather, 1949), adds support to such a theory. That many patients have apparently identical genital inflammatory disease in the form of chronic prostatitis and never develop sacro-iliitis is obvious. Many explanations could be offered for this—for example, the prostatitis producing sacro-iliitis may be due to a specific, so far unidentified, organism. This might cause sacro-iliitis in all patients so infected, or perhaps in only those genetically predisposed. Conversely, the cause of the prostatitis may be a single one which operates to produce sacro-iliitis only in those patients with a suitable genetic background. The importance of genetic factors in ankylosing spondylitis is, of course, well recognized (Tegner and Lloyd, 1949; West, 1949; Hersh *et al.*, 1950; Mason, 1951; Graham and Uchida, 1957). Genetic studies of Reiter's disease have not, so far as we are aware, been carried out, although a few families have been reported (Koster and Jansen, 1946; Trier, 1950; Fabregoule, 1951; Csonka, personal communication, 1957). One of our series with the full syndrome had a brother who appeared to have suffered an identical attack, but he refused to attend for examination. It seems clear, therefore, that until the organism responsible for non-specific urethritis is identified, cause and effect cannot be distinguished, and no more than an association between ankylosing spondylitis and inflammatory disease of the genital tract can be established.

Summary

The incidence of chronic prostatitis in 54 cases of ankylosing spondylitis is described and compared with the findings in 59 cases of Reiter's disease and 86 of rheumatoid arthritis.

The high incidence of chronic prostatitis in ankylosing spondylitis is discussed.

It is concluded that there is a real association between ankylosing spondylitis and inflammatory disease of the urogenital tract.

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The Government of India has published a report by S. C. Seal and L. M. Bhattacharji on a health survey undertaken in Sikkim State by the section of epidemiology of the All India Institute of Hygiene and Public Health, Calcutta. The main purpose of the survey was to obtain an integrated picture of health and sickness in the community studied, and the work consisted of physical examination of individuals, the recording of family data and medical and social histories, the collection and examination of laboratory specimens, insects, and rodents, and the assessment of environmental and socio-economic conditions. Sikkim lies between Tibet in the north and Darjeeling District in the south and has a population of nearly 150,000. The majority of the people are ignorant about the causes or prevention of disease, being demonistic or deistical in outlook on health matters. They are reluctant to keep themselves clean, and pediculosis, scabies, and worm infestation are very widespread. The almost universal drink of the people is rakshi, a kind of alcohol prepared from fermented millet or buckwheat. Next to alcohol the common addiction is tobacco; even among children 12% indulge in alcohol and 15% in tobacco. In addition, 1.2% of the population indulge in opium. The rate of marriage was least among the Christians and highest among the Hindus, with the Buddhists occupying an intermediate position. There are no official vital statistics, but those carrying out the survey estimated the crude birth rate to be 28.8 per 1,000 and the crude death rate 15.9 per 1,000. The abortion and stillbirth rates were 9.1% and 3.6%, respectively. The infant mortality rate was 208 per 1,000. As a result of the survey, certain measures have been suggested to overcome the main health problems that were found to be seriously affecting the economy of the State.