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SYNOVIAL pH IN RHEUMATOID KNEE-JOINTS

I. *The Effect of Synovectomy*

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Inflammatory reactions are among other characteristics distinguished by a local acidosis. This varies in relation to the intensity of the inflammatory state. For example, in the initial stages when there is a predominance of polymorphonuclear leucocytes the hydrogen ion concentration is relatively low and the pH ranges around 7.4. With further development of inflammation and correlated to this a change in the cellular morphology towards the mononuclear phagocytic type, the alkalinity subsides and there is a drop in pH to levels around 6.5 (Menkin & Warner 1937). This progressive acidity which parallels inflammation in duration of time depends on a number of factors, e.g., the influence of protein split products such as amino acids (Ropes & Bauer 1953) or, as Menkin & Warner (1937) and Menkin (1956) suggest, on the result of increased glycolysis with conversion of sugar into lactic acid ultimately resulting in an uncompensated acidosis as there is no corresponding increase in the alkali reserve.

It can then be expected that a chronic inflammatory condition like rheumatoid arthritis might exhibit a certain degree of acidosis in the articular exsudates. Ropes & Bauer (1953) determined the pH in normal human synovial fluid obtained at autopsy and found it to be 7.39. In 8 cases with rheumatoid arthritis the pH averaged 7.22. The determinations were made extracorporeally after aspiration. In a comparative study of pH in normal and rheumatoid synovial fluids Cummings & Nordby (1966) found a pH of 7.43 in 7 normals with a range of 7.31–7.64. In 8 rheumatoid patients the pH of the synovial fluid was 7.22 with a variation from 7.08 to 7.28. In neither of the above-men-

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tioned works has the duration of the rheumatoid disease before the pH determination been stated.

It is apparent that in synovial fluids of rheumatoid arthritis there is an increased hydrogen ion concentration, though of little degree. According to Dingle & Page Thomas (1956) this is part of the glycolytic metabolism in the diseased synovial tissue. The proposed destructive action of this metabolism may be counteracted by the administration of anti-inflammatory drugs (Dingle & Page Thomas 1956). In consequence it appears plausible that the surgical removal of inflamed synovial tissue, a common method of treatment in rheumatoid arthritis, should alter the hydrogen ion concentration of the synovial fluid.

In this study we have investigated the pH of articular fluid by an intra-articular measuring method in normal knee-joints and rheumatoid knee-joints before and after synovectomy.

MATERIAL

Three groups were selected, one representing normal knees (10), another rheumatoid knees (12), and the third rheumatoid knees subjected to synovectomy (10) prior to this investigation.

Table 1. Hydrogen ion concentration of synovial fluid in normal knees

Age	Sex	Diagnosis	pH
51	♂	Multiple sclerosis	7.2
53	♀	Femoral neck fracture	7.2
46	♂	Distorsion talocrural lig.	7.1
44	♂	Ganglion	7.1
23	♂	Talipes	7.3
26	♂	Arthritis wrist	7.4
57	♂	Arthritis hip	7.2
53	♂	Arthritis hip	7.7
24	♂	Granuloma lower limb	7.4
48	♂	Talipes	7.4
			Mean 7.3

Normals. Patients who were admitted to hospital for ailments not involving the knee-joints were measured. Permission was granted by the patients. The diagnoses of the patients measured are seen in Table 1. The ages varied from 23 years to 73 years.

Rheumatoid arthritis. Only patients selected for synovectomy were measured. All had a swelling of the knee with a bulging, oedematous synovial tissue and increased

articular exsudate. The duration of disease from onset until time of measurement varied from 2–6 years. The ages of the patients were from 48 to 74 years. All patients fulfilled the criteria of the American Rheumatology Association. Some of the patients were subjected to cortisone treatment, which will be commented upon in the discussion of results. These pH readings (2) were excluded from the statistical analysis. Thus 10 patients were evaluated.

Rheumatoid arthritis after synovectomy. The time between synovectomy and measurement ranged from 5 to 36 months (mean 14 months). Of these 3 were also measured before synovectomy (Table 3) but 1 was still receiving cortisone treatment at the time of measurement and the value was therefore not included in the statistical analysis. One more patient was excluded for the same reason which thus left 8 patients for statistic analysis. The operative procedure was the same as described by Goldie (1968).

Table 2. Hydrogen ion concentration in synovial fluid of rheumatoid knee-joints. Steroid-treated patients excluded in the statistical calculations

Age	Sex	Duration of illness (yrs)	pH	Comment
48	♂	3	6.0	Also measured after synovectomy
74	♂	5	6.4	Also measured after synovectomy
62	♀	7	6.2	
69	♀	10	6.1	
73	♀	20	6.8	Fibrotic synovial tissue
54	♀	4	7.3	Fibrotic synovial tissue
58	♀	4	7.3	Fibrotic synovial tissue
56	♀	8	6.5	
64	♀	6	6.6	
36	♂	5	6.9	
			Mean 6.6	
73	♀	10	7.8	Massive *steroid* treatment
53	♀	5	7.3	Also measured after synovectomy Osmium and *steroid* treated

Table 3. Hydrogen ion concentrations in synovial fluid of synovectomized rheumatoid knee-joints. Steroid-treated patients excluded in the statistical calculations

Sex	Age	Time between operation and measurement (mths)	pH	Comments
48	♂	13	6.3	Measured before synovectomy
74	♂	6	6.8	Measured before synovectomy
58	♀	30	6.6	
58	♀	5	7.1	
59	♀	36	6.6	
64	♀	9	6.7	
36	♂	14	6.9	
57	♀	18	7.3	Fibrotic tissue
			Mean 6.8	
53	♀	6	7.1	Measured before synovectomy *steroid* treated
59	♀	9	7.0	*steroid* treated

METHOD

All patients were measured under general fluothane anaesthesia with a needle-type pH-electrode, especially constructed* for measurement in deep somatic tissues like intervertebral discs (Nachemson 1969). The length was 145 mm, diameter 1.2 mm. The electrode consists of purest antimony and, as a reference, a calomel electrode was used which was placed together with the patient's finger in a solution of physiological saline. The advantages and disadvantages of an antimony electrode have previously been described by Bates (1964). Recordings were made from Radiometer pH Meter 25-25SE-27. The calibration of the pH-electrode was made from different standard buffer solutions immediately after taking the reading inside the knee-joints, and the values obtained were corrected according to the calibration-curves obtained.

The electrode was chemically sterilized in diglutaraldehyde 2.5 per cent for at least 2 hours prior to measurement (Borick, Dondershine & Chandler 1965).

The knee-joint cavity was reached by a larger needle (diameter 2.1 mm) with a pointed mandrin, which was then extracted and the electrode inserted. Care was always taken to place the tip of the electrode in free joint cavity. Reading was taken after 2 min stabilization time. In some cases the electrode was then moved to another part of the knee joint cavity without noticeable change in pH.

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RESULTS

In the group of normals it became evident very soon that it was most essential to perform the measurements in patients who had no injurious involvement of their knees. Thus patients with a previous history of knee affliction were excluded as it was shown among other things that such an ailment as, e.g., habitual dislocation of the patella apparently affected synovial tissue and fluid in a way that increased hydrogen concentration ensued. This was thought to be due to a low-grade chronic synovitis which also was verified at operation. In Table 1 a summary of the results of normals is given.

The pH measurements coincide with those reported elsewhere (Ropes & Bauer 1953, Howell 1965, Cummings & Nordby 1966).

Rheumatoid knees. In this group it was obvious that the pH was decidedly lower than that reported in other series. The only exceptions were those who had been subjected to corticosteroid treatment where a slight elevation was noted but still below or near normal. The mean value was 6.6 with a lowest registration of 6.0 and a highest of 7.8. The latter had not only received intra-articular injections of corticosteroid but also had systemic cortisone treatment at the time of surgery (Table 2).

Table 4

	Normal knees	Rheumatoid knees	Rheumatoid synovectomized knees
Mean	7.30	6.61	6.79
SD^2	0.033	0.214	0.098
T-statistics	←$t_{diff.}$ = 4.42→	←$t_{diff.}$ = 0.95→	
	←————	————$t_{diff.}$ = 4.01→	

Rheumatoid knees after synovectomy. In this group as well as in the previous, small variations were noted especially in those receiving corticosteroid treatment (Table 3). The overall results, however, disclosed a marked high hydrogen ion concentration with a pH around 6.8 with a lowest registration of 6.3 and a highest of 7.1. Also in this group the highest pH values were obtained in those knee-joints into which hydrocortisone had been injected.

A statistical evaluation of the differences between these three groups revealed that there was a highly significant difference between the pH values obtained in the normal knees compared with both the non-

synovectomized ($t_{diff.} = 4.42$) and the synovectomized ($t_{diff.} = 4.01$) group (Table 4).

There was no difference between the two latter groups.

As mentioned above those patients who received corticoid therapy at the time of measurement were excluded from this statistical calculation.

COMMENTS

Previous investigations on the pH of synovial fluid have been carried out on samples aspirated from the joints (Ropes & Bauer 1953, Dingle & Page Thomas 1956, Howell 1965, Cummings & Nordby 1966). The values obtained have ranged around 7.4. In our investigation the method employed has permitted the registrations to be made intra-articularly *in vivo*. This, however, has not caused any greater difference in the estimation of the pH values in apparently normal knee-joints, all of which have fallen in the range of 7.3.

There is, on the other hand, a conspicuous difference in the readings obtained in the group with rheumatoid arthritis. In this investigation the hydrogen ion concentration has been more pronounced than in other reported series. The values obtained have been in the range of 6.7 as compared to 7.2–7.3 in other communications (Ropes & Bauer 1953, Cummings & Nordby 1966). The reason for this is uncertain but could depend on changes occurring in the aspirated samples where, for instance, oxygenation may influence the hydrogen ion concentration. This assumption was to some extent verified in three cases where the aspirated fluid showed pH 7.6, 7.6, and 7.4, whereas the pH in the knee-joint cavity was 6.6, 6.7, and 6.8, respectively.

The pH recordings in the rheumatoid knees of this investigation coincide with earlier observations of acidity in inflamed tissues by Menkin & Warner (1937). This has been confirmed by others (Hamerman, Stephens & Barland 1961).

The pathomorphology of rheumatoid arthritis discloses in synovial tissues features all of which are indicative of a chronic non-specific inflammation. It thus appears that the pH determinations in this study depict the local intra-articular acidosis which parallels the cytologic picture of the synovial tissue.

If then these tissues are removed as is done in synovectomy, the question arises whether there will be any change in the pH. Our investigation has disclosed that there remains a pronounced acidity long after the time for regeneration, which is 60–90 days (Stevens & White-

field 1966, Preston 1967). Some state (Marmor 1967, Preston 1967, McEwen 1967) that the synovial tissue which regenerates after synovectomy is quite normal. Own investigations (Goldie 1967) have shown, however, that the new synovial tissue replacing the old contains features similar to those found in the tissue removed at first synovectomy and have, like these, been classified by pathologists as "chronic" non-specific inflammation. With this in mind it might then not be astounding that the hydrogen ion concentration remains high in rheumatoid articulations after synovectomy.

The normal or near normal readings which have been registered in the corticosteroid-treated cases may be explained by the anti-inflammatory action of these drugs.

It is at the present time impossible to ascertain the different factors causing the high hydrogen ion concentration. In spite of the fact that this concentration remained unaltered after synovectomy the patients claimed clinical improvement. Other objective tests (Goldie 1968) have, however, indicated a normal function of the regenerated synovial tissue, These investigations have included intra-articular temperature recordings and thermographic registrations, which depict the circulatory conditions, whereas the test of hydrogen ion concentrations may be based on the activity of the synovial cellular elements.

SUMMARY

Using an intravital method the hydrogen ion concentration has been estimated in synovial fluids of normal (10), rheumatoid (12), and synovectomized (10) rheumatoid knee-joints.

Normal knee-joints showed a pH of 7.3, rheumatoid of 6.6, and rheumatoids at varying time after synovectomy a value of 6.8 with a statistically significant difference between the first and the two latter groups. The observations are in alignment with current ideas of an increased hydrogen ion concentration being paralleled with tissue changes of the chronic inflammatory type which characterized the synovial tissues in rheumatoid arthritis before and after synovectomy.

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