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SOME VIEWS ON THE PATHOLOGY OF SYNOVIAL FLUID

By

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In contrast to the numerous and detailed morbid anatomical descriptions in existence concerning diseased conditions of the tissues which surround and form the joints themselves, it is surprising to find how lacking we are in investigations on pathological exudates. Bichat's statement of 1799 still holds good that no part of the physiology of the human body consists of a greater number of theories and fewer true facts than the synovial system. And yet diseases of joints still constitute to-day the chief cause of invalidity.

A question like the following naturally arises: can investigations into the morphology, biochemistry and physiology of a synovial fluid really give us any information as to the character of the underlying process of a hydrops? On the basis of our present knowledge of synovial fluids are we able and justified in drawing any conclusions?

We have heard here a discussion of different aspects of synovial fluid. However from the patho-anatomical and clinical standpoints it is best for us at present to stick to those factors which are definitely found to vary in pathological conditions. For the time being we are forced to consider mere fragments of the pathological progress —pending a deeper knowledge of pathological physiology.

Synovial fluid is a dialysate of the blood plasma to which mucin has been added. This statement is based upon the distribution of electrolytes and non-electrolytes between serum and synovial fluid. We have no knowledge as to how the mucin is added. There is much to support the view that mucin might emanate from the peri- or subsynovial connective tissue.

A pathological exudate shows a composition in many respects

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different from the normal. This has been supposed to be due to the change in permeability of the synovial membrane. How this mechanism works is not known. There is no doubt that many factors govern the exchange between the serum and the synovial fluid. Edlund has recently given valuable contributions to the solution of this problem.

The amount of *protein* passing into the joint varies with the degree of inflammation. The "protein rate" is low in traumatic conditions without haemarthrosis but is considerably raised in severe rheumatoid and septic conditions. See figs. 1 and 2. The way in which the protein conditions vary will be dealt with by Olhagen.

Mucin is perhaps the factor that more than any other is responsible for the viscosity of the synovial fluid. On precipitation of mucin the viscosity of the synovial fluid approaches that of water. The relative viscosity in normal synovial fluid varies greatly in different joints in one and the same individual. The underlying causes of such great variations are unknown. Joints with the same function may present different values, e.g. the right and left ankle joint. This may conceivably be explained by chemical variations in the viscosity-determining substance.

It has not been found possible to decide with certainty whether a traumatic irritation stimulates the connective tissue cells to form more mucin, or whether in certain cases it helps the mucin to enter the joint. A traumatic exudate has a relatively high viscosity. Infected synovial fluid holds a lower concentration of mucin and shows a reduced viscosity. There are reasons to assume that this is due to an increased destruction of mucin through bacterial enzymatic action and not due to any reduced formation. It may be that bacterial production of hyaluronidases plays some part. Clinical observations entitle us to assume that a closer study of the factors determining the viscosity of the exudate will give us valuable information regarding the nature of the process causing the exudation. From clinical quarters we must therefore welcome the activities of our fellow-biochemists. Without their help we shall never be able to understand the pathophysiology of exudative conditions.

Regarding the *cytology* of normal synovial fluid, data in medical literature is very scanty. It is really primarily through works of Key, Kling and Bauer that light has been thrown on the cell contents of normal synovial fluid—and this happened only during the latter half of the nineteen thirties. In a healthy joint the total number of cells varies between 13 and 180 per mm^3 with an average of 63. The cells of the synovial fluid bear no relationship to those of the blood. The types of cells normally occurring have been found to be as follows:

Fig. 1.

Exudate from Kneejoint

Number of cases	Etiology	Diagnosis	Number of white bl. corp./mm³
	Infection	Acute arthritis	14,800
		„ „	15,000
		„ „	2,400
		„ „	38,000
7		„ „	122,000
		„ „	32,700
		„ „	13,100
	Trauma	Acute distortion	8,400
		„ „	12,000
5		„ locking (osteochondritis)	2,000
		Acute locking (meniscus)	6,000
		Contusion (1 month)	1,200
2	Chronic irritation	Arthrosis deformans	300
		„ „	300
	Uncertain	Non-specific synovitis	1,400
		„ „	2,000
		„ „	3,000
7		„ „	3,000
		„ „	4,000
		„ „	3,000
		„ „	1,700

Fig. 2.

Comparison between number of white bl. corp./mm³ and amount of total protein in gm/100 ml exudate of kneejoint.

White bl. corp.	Total protein
13,100	5.50
6,000	4.26
3,100	4.26
1,200	4.35
1,100	5.53
500	3,18
300	4.98
200	3.44

Monocytes	47.9 %
Clasmatocytes	10.1 %
Non-classifiable phagocytes	4.9 %
Lymphocytes	24.6 %
Polynuclear leukocytes	6.5 %
Synovial cells	4.3 %
Non-classifiable cells	2.2 %
Eosinophils and basophils	0 %
	100 %

Mononuclear phagocytes make up the predominant type of cell and their chief task seems to be to dispose of the products of wear and tear in the joint, the result of the continuous minor traumata to which every joint is exposed.

Experiments have been carried out by Bauer and his co-workers which show in what manner synovial fluid reacts even to minor traumata. An injection of normal saline into the knee-joint of a rabbit immediately brings about an increase of the polynuclear leukocytes. Gradually the picture alters in character and the mononuclear phagocytes increase in numbers. A very mild irritation is in itself sufficient to produce changes in the subsynovial capillaries with the result that polynuclear leukocytes immediately enter the joint. This then is the first cytological reaction one has been able to observe. It is only later that the mononuclear phagocytes appear. This is clinically an important and valuable piece of information because it gives us a chance, by early examination in a case of hydrops, to decide whether an acute trauma has been the cause of the exudation, or whether a slowly progressing irritation has gradually led to an increased amount of synovial fluid. It would seem fair to assume that the variations occurring in the total number of cells, or types of cell, correspond with the nature of the intra-articular affection present. It can be seen how in joints not acutely damaged or not infected, i.e. in so-called healthy joints, the highest cell figures are to be found in cases where there are degenerative changes in the cartilages, i.e. in such cases where the strain has become greater on using the joint owing to the changes present on the joint surfaces. These conditions are found in elderly people.

It is always difficult to conclude merely from the cytological conditions in an exudate what is the cause of the exudation. The nature and strength of irritation and the time of onset are the factors that determine the cell picture. Without having this clearly in mind,

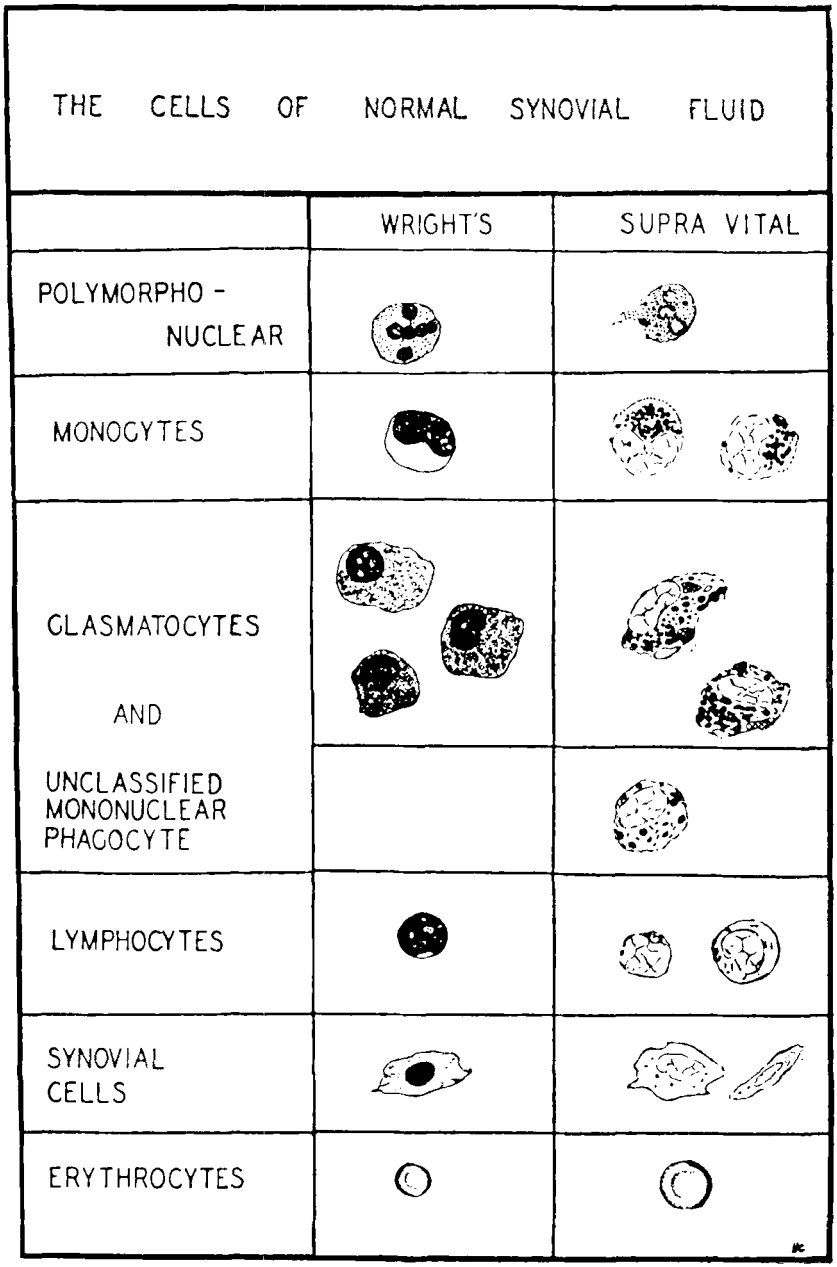
THE CELLS OF NORMAL SYNOVIAL FLUID
WRIGHT'S
SUPRA VITAL
POLYMORPHO - NUCLEAR
MONOCYTES
GLASMATOCYTES AND UNCLASSIFIED MONONUCLEAR PHAGOCYTE
LYMPHOCYTES
SYNOVIAL CELLS
ERYTHROCYTES

Fig. 3.

the value of the total cell count or the determination of the type of cell becomes slight. A careful anamnesis combined with a cytological examination affords us information not only on the ætiology but also on the present stage of the exudation.

For the clinician it is often exceedingly important to be able to decide, definitely, whether a hydrops is of a post-traumatic nature or of some other genesis. From the point of view of insurance the question is also of course important. Naturally it is generally held that a haemorrhagic fluid is a sign of a traumatic ætiology. Although this is true in most cases, exceptions occur. Sarcoma and haemophilia may lead to haemarthrosis or a vessel may be damaged on puncture. On the other hand, if the puncture is carried out a long time after an injury, the blood may have been absorbed and the exudate again become clear. After bleeding has taken place in a joint the red blood cells are broken down. The hemoglobin undergoes changes of which bilirubin is the final product. The amount of bilirubin formed in the exudate depends upon the number of red cells broken down and on the time passed since the onset of the haemarthrosis. Small haemorrhages yield small amounts of bilirubin even if all the red cells have been destroyed. Large haematomata present during the first few days a picture of intact blood cells and little bilirubin. It is clear therefore that the determination of the bilirubin content in an exudate can give us information as to whether bleeding has occurred or not. In the individual case it is a question of comparing the value obtained with the patient's blood values. Up to four weeks after a trauma increased values may be obtained if bleeding has taken place. The shorter the time lapse between trauma and puncture the more blood cells and the less bilirubin will be found, and the longer one delays the puncture, the more bilirubin and the fewer blood cells will be observed. Some idea of the intensity of the bleeding can be obtained by a haematocrit determination or a direct count of the number of red cells. The value obtained should be compared with that of the circulating blood. If the figures obtained are higher than those of the blood serum it is a sign in favour of haemarthrosis, which as stated above is generally due to trauma.

In cases of intra-articular fractures, venous blood, rich in bilirubin, may enter the joint from the bone marrow and immediately yield a high icteric index. A high bilirubin value of this nature, obtained on immediate puncture or during the first twenty-four hours after the injury, constitutes a characteristic feature of intra-articular fractures.

Under normal conditions synovial fluid contains no *fat*. On centrifugation of the punctate after certain traumatic conditions with hae-

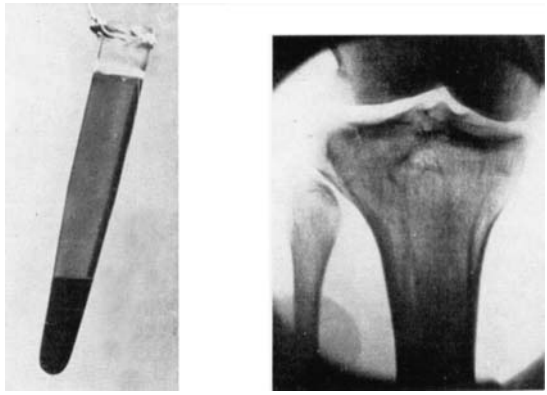

Fig. 4.
Fracture of lateral tibial condyle.

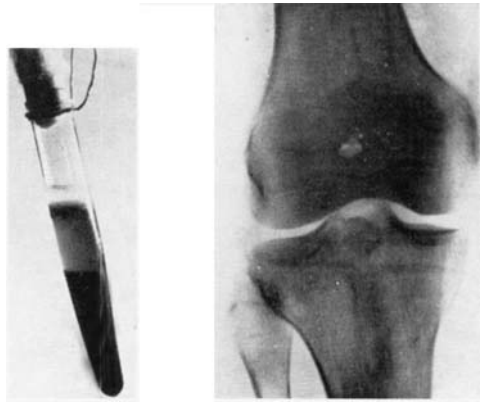

Fig. 5.
Fracture of lateral tibial condyle with slight depression.

marthrosis a layer of fat may be perceived on the surface of the centrifugate. This fatty layer may vary considerably in size. In intra-articular fractures fat is obtained, which is liquid in room temperature and chiefly consists of oleates. In cases of contusion of the patella or the subpatellar pad of fat, macerations of the latter may sometimes occur. Such subpatellar fat is of firm consistence in room temperature and consists mainly of stearates.

SUMMARY

Summarising it may be said:
that *traumatic exudates* show high viscosity and high mucin contents but lower protein contents and a relatively small number of cells;
that *inflammatory exudates* show low viscosity and low mucin contents and a great number of cells;
that *exudates* from osteoarthritis show high viscosity, high mucin contents but low protein contents and a very small number of cells.

The introduction of chemotherapy and antibiotics, the discovery of hyaluronidase and the experiments with cortisone and ACTH will undoubtedly make greater claims on our knowledge of the synovial system. Adequate and searching tests of these new measures can scarcely be entertained without a close study of the morphology, biochemistry and physiology of joint exudates. It is to be desired that exudate investigations be undertaken at different clinics with a view to gaining further experience. With such experience behind us we shall no doubt be standing on much firmer therapeutic ground.

RESUME

En résumé, il est dit
que *les exsudats traumatiques* ont une viscosité plus grande et une teneur en mucine plus élevée, mais une teneur en protéine plus faible et un nombre de cellules relativement bas;
que *les exudats inflammatoires* ont une faible viscosité et une teneur en mucine peu élevée, mais une teneur élevée en protéine et un grand nombre de cellules;
que *les exsudats d'arthrose déformante* ont une grande viscosité et une teneur relévé en mucine, mais une faible teneur en protéine et un très petit nombre de cellules.

L'introduction de la chémothérapie et des antibiotiques, la découverte de l'hyaluronidase et les expériences réalisées quant au cortison et à l'ACTH poseront certainement de nouvelles exigences en ce qui concerne notre connaissance du système synovial. On ne peut guère procéder à de nouveaux essais avant d'avoir entrepris une étude approfondie de la morphologie, de la biochimie et de la physiologie des exsudats articulaires. Il serait désirable que des recherches sur les exudats fussent entreprises dans différentes cliniques pour acquérir de l'expérience. Cela permettrait alors d'avoir une base thérapeutique plus ferme.

ZUSAMMENFASSUNG

Zusammenfassend kann man sagen:

Dass traumatische Exsudate hohe Viskositet und einen hohen Mucingehalt, aber niedrige Proteinwerte und eine relativ geringe Zellanzahl zeigen;

dass entzündliche Exsudate eine geringe Viskositet und niedrigen Mucingehalt, aber hohe Proteinwerte und eine grosse Anzahl von Zellen zeigen;

dass Arthrosis deformans Exsudate hohe Viskositet, hohen Mucingehalt, aber niedrige Proteinwerte und eine sehr kleine Zellanzahl aufweisen.

Die Einführung von Chemotherapie und Antibiotica, die Entdeckung der Hyluronidase und die Experimente mit Cortison und ACTH werden zweifellos grössere Forderungen an unsere Kenntnis des synovialen Systems stellen. Adequate Untersuchungen und Schätzungen dieser neuen Massnahmen können kaum gemacht werden ohne genaues Studium der Morphologie, Biochemie und Physiologie von Gelenksexsudaten. Es wäre wünschenswert dass Exsudatuntersuchungen an verschiedenen Kliniken durchgeführt werden könnten um weitere Erfahrungen zu sammeln. Mit solchen Erfahrungen würden wir zweifellos auf viel festerem therapeutischen Boden stehen.