

Synovial Fluid Lipids in Normal Individuals and Patients with Rheumatoid Arthritis

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Normal human synovial fluid contains trace amounts of phospholipids and cholesterol. Phospholipid composition is similar to that in serum. Rheumatoid synovial fluid contains increased amounts of phospholipid, cholesterol, and neutral lipids. In most cases the concentration is 40 to 60 per cent of that found in simultaneously collected serum specimens. A direct relationship appears to exist between total synovial fluid protein and lipid concentration. No relationship could be established between lipid content in rheumatoid synovial fluid, and total cell content, hyaluronic acid, severity or duration of synovitis in the involved joint.

Normal liquido synovial in humanos contine quantitates tracia de phospholipidos e de cholesterol. Iste phospholipidos es simile in composition a illos del sero. Le liquido synovial ab patientes rheumatoide contine augmentate quantitates de phospholipido, de cholesterol, e de lipidos neutre. In le majoritate del casos, le concentration es 40 a 60 procento de illo trovate in simultaneemente colligite specimens de sero. Un relation directe pare exister inter le proteina total e le concentration lipidic in le liquido synovial. Nulle relation poteva esser establite inter le contento de lipidos in liquido synovial ab patientes rheumatoide e le parametros del total contento cellular, de acido hyaluronic, e del severitate o del duration de synovitis in le afficite articulation.

INTEREST in further studies on the lipids of rheumatoid synovial fluid was prompted by increasing evidence that a variety of cells synthesize both neutral lipids and phospholipids. Of considerable importance is the suggestion that several types of cells can contribute to extracellular lipid concentration. Recent investigations by Buchanan,¹ and Marks² have shown that leukocytes possess this capacity. Preliminary reports by Jackson³ indicate the cells of the carrageenin granuloma synthesize lipids, and studies in this laboratory⁴ indicate that the cells of the polyvinyl granuloma will incorporate glycerol-C¹⁴ into phospholipids and neutral lipids. By comparing the lipid composition of serum with that of the cells, and the cell poor fraction of synovial fluid, it was hoped that additional information as to the source of these lipids might be obtained.

Over a century ago Frerichs⁵ reported that traces of fat were present in bovine synovial fluid. Ropes and Bauer⁶ found no lipid in bovine fluid, but did report the presence of cholesterol in rheumatoid joint fluid. It was their impression that synovial lipids accumulated in joints where excessive tissue destruction had occurred. This observation was in agreement with earlier work by

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Kling⁷ indicating that fat occurred only in traumatic effusions or at the nidus of "rice bodies" resulting from inflammatory degenerative changes in the synovium.

Recently, Schmid and McNair^{8,9} have reported detailed studies of the protein composition of synovial fluid. They found α_1 - and β_1 -lipoproteins, identified by their cholesterol content, present in traumatic synovitis and a pooled specimen of rheumatoid fluid, and trace amounts in synovial fluid obtained postmortem from patients without apparent joint disease. Most recently, Chung and associates¹⁰ have reported on the lipid composition of fluids obtained from patients with rheumatoid arthritis and osteoarthritis. These investigators have suggested that synovial cells may synthesize some of the lipids found in synovial fluid.

METHODS AND MATERIALS

Clinical

Three pools of human synovial fluid (2 to 3 cc. each) obtained from the knee joints of normal volunteers were available for study.* Synovial fluid was also obtained from 24 patients with classical rheumatoid arthritis,¹¹ two patients with juvenile rheumatoid arthritis (19 and 24 years of age at the time of study), one patient with psoriatic arthritis and one with monoarticular rheumatoid arthritis. Simultaneous blood specimens were obtained in most cases. Eleven of the patients had received intra-articular hydrocortisone tertiary-butylacetate 1 to 2 months prior to aspiration of the specimen used in this study. Six of the patients were receiving maintenance gold therapy, and one patient was on 2.5 mg. of prednisone per day. Acute synovitis characterized by recent increase in effusion, definite erythema, local heat, pain, and tenderness was present in 15 of the nonsteroid treated patients. Two-thirds of these individuals had had synovitis in the aspirated joint for less than 24 months. Four of the steroid treated patients had acute synovitis. The remainder had chronic indolent effusions, all but one of these having been present for 2 to 15 years.

Analytical

An aliquot of fluid was removed for routine laboratory studies and the remainder of the joint fluid and simultaneously collected serum were then subjected to low speed centrifugation. The cell-poor fraction of synovial fluid was promptly removed and stored with the cell pellet, and serum at -20°C . until analysis. Seven of the synovial fluid specimens were lyophilized and weighed aliquots subjected to chloroform-methanol extraction.¹² The extract was washed with 0.2 volume of water and the aqueous phase discarded. The organic layer was dried by vacuum desiccation and its weight determined. The remainder of the specimens were extracted by the method of Sperry and Brand.¹³ The methods used in this laboratory for phosphorus, cholesterol, total ester, nitrogen, and ninhydrin nitrogen have been reported previously.¹⁴ The method of calculation of the several lipid groups is in agreement with that of Phillips¹⁵ and has been reported.¹⁴ Details of the procedure for quantitative silicic acid paper chromatography and qualitative detection of phospholipids by rhodamine, choline, and ninhydrin staining have recently been reviewed by Marinetti.¹⁶ Silicic acid column chromatography utilizing step-wise gradients of chloroform and methanol combined with paper chromatography was employed as described by Marinetti and co-workers.¹⁷ Cholesterol and cholesterol ester were determined by the method of Kingsley and Schaffert.¹⁸ Total protein in the serum and synovial fluid was measured by

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Table 1.—Normal Human Synovial Fluid

Pool	Milligrams per cc.				
	Protein	Hyaluronic Acid	Total Phospholipid	Cholesterol	Neutral Lipid
1	21.7	3.18	0.130	—	—
2	16.3	2.64	0.150	0.075	0
3	16.1	2.66	0.135	0.066	0
Mean:	18.0	2.83	0.138	0.071	0

ultraviolet absorption at 215 and 225 $m\mu$ as described by Waddell.¹⁹ Total mucopolysaccharide content of the synovial fluid specimens (hyaluronate, as uronic acid) was determined as follows: a 1:25 dilution of the specimen was carried out, 1 cc. of the diluted material was extracted with an equal volume of 20 per cent trichloroacetic acid. This was brought to 100 C. in a boiling water bath to precipitate protein. A measured aliquot was centrifuged at 10,000 rpm and an aliquot of the supernatant was utilized for carbazole reaction.²⁰

RESULTS

Normal Human Synovial Fluid

Two of the normal human synovial fluid pools were extracted by the method of Sperry, the third by the method of Folch. The values for total protein, hyaluronic acid, and lipids are given in table 1. Satisfactory agreement was obtained between the three pools. Hydroxamate reactive ester was detected in two pools, and all of it could be accounted for as phospholipid ester. Based upon this determination, no neutral ester was present. The data for quantitative silicic acid paper chromatography of phospholipids are included in table 3 and will be discussed in reference to the other specimens analyzed. Qualitatively the choline spot test indicated the presence of three components corresponding to lecithin, sphingomyelin, and lysolecithin. Ninhydrin reactivity was limited to a faint spot at the origin of the chromatograms.

Rheumatoid Synovial Fluid

a. *Total lipids:* In four patients who had never received intra-articular steroids, total lipids constituted 4.2 per cent of the total solids in two patients, 4.1 per cent in another, and 8.8 per cent in the fourth. In three patients who had received intra-articular steroids, total lipid expressed as per cent of total solids was 9.0, 9.5, and 10.9 per cent respectively.

b. *Total phospholipid, cholesterol, and neutral lipids:* Serum values for these substances were determined in this laboratory for a small number of normals, using the analytical procedures employed in this study. They were in general agreement with those recently published by Phillips,¹⁵ and Mellinkoff and associates²¹ for the major lipid groups. In figure 1A, data for total phospholipid, cholesterol, and neutral ester are given in mg./cc. of rheumatoid synovial fluid. In figure 1B, values for the cell-poor fraction of rheumatoid synovial fluid are expressed as per cent of simultaneously determined serum values for the same constituents. Specimens obtained from patients untreated with intraarticular steroids (o) have been segregated from those that had received intra-articular medication(s). The combined mean value for total

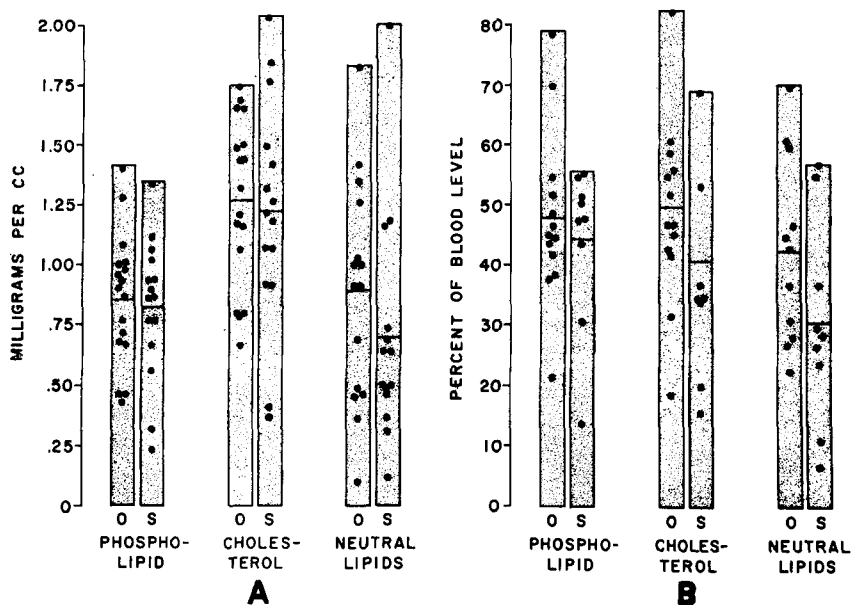


Fig. 1.—A. Mean and range of values for total phospholipid, cholesterol, and neutral lipid in the cell-poor fraction of individual specimens of rheumatoid synovial fluid from the knee joint. B. The same components expressed as a percentage of the concentration found in simultaneously obtained serum specimens. O—patient had never received intra-articular steroids, S—previous treatment with intra-articular steroids.

phospholipid was 0.84 mg./cc.; total cholesterol, 1.25 mg./cc.; and neutral lipid, 0.80 mg./cc. In 14 untreated patients, total phospholipids, cholesterol and neutral ester constituted 47.8, 49.6, and 42.4 per cent of the simultaneously determined serum value. In nine of the steroid treated cases the mean value for total phospholipid, cholesterol, and neutral ester was 43.3, 40.8, and 30.4 per cent, respectively. Again, the range of values is extremely broad. In all patients, the value for each lipid group was lower than that for serum. In most instances, the value was 40 to 60 per cent of the serum level.

Total phospholipid, cholesterol, neutral ester, and total lipid determinations on the extract from the cell pellet accounted for less than 10 per cent of the value obtained on the cell-poor fraction of synovial fluid. Total cell counts per cu. mm. on these specimens ranged from 3500 to 47,500 with a mean of 14,000. From the volume of synovial fluid utilized the total number of cells extracted was calculated, and it was evident that total lipid present exceeded the amount that could be accounted for intracellularly. Cholesterol and neutral lipids contributed most to this discrepancy. Values for pellets that were washed repeatedly with cold physiologic saline prior to extraction were definitely lower but still exceeded those given for red cells.²² Total phospholipid phosphorus approximated that in human synovial cells.²³ Qualitative silicic acid paper chromatography of this fraction of synovial fluid demonstrated the presence of both phosphatidylethanolamine and phosphatidylserine (cephalin

Table 2.—Percentage Composition—Pooled Specimens of Rheumatoid Synovial Fluid

	Total Phospholipids	Ester Cholesterol	Free Cholesterol	Ester* Fraction	"Triglyceride"
Blood					
Mean	37.5	33.5	14.7	0.70	17.8
Range	(34.1–43.9)	(27.8–38.0)	(11.3–18.7)	(.67–.77)	(11.8–24.2)
Synovial Fluid					
Mean	38.3	41.5	15.1	0.73	6.4
Range	(35.0–42.5)	(21.7–54.0)	(3.5–28.3)	(.43–.82)	(0–14.5)

*Corrected ester ÷ corrected total cholesterol concentration (18).

Table 3.—Percentage Composition of Phospholipids Rheumatoid Serum, Synovial Fluid, Cell Pellets, and Normal Synovial Fluid

	Lecithin	Sphingo- myelin	Lyso- lecithin	Phospho- inositide	"Cephalins"	Uniden- tified	No. De- termi- nations
Serum							
Mean	51.3	28.9	9.8	1.8	2.4	7.2	5
Range	(45.3–59.8)	(21.4–33.7)	(4.4–14.4)	(0–7.7)	(0–6.4)	(0–14.2)	
Synovial Fluid							
Normal							
Mean	61.2	19.4	6.8	3.0	1.2	8.3	3
Range	(57.9–64.5)	(13.1–25.6)	(4.2–9.3)	(0–6.0)	(0–2.4)	(6.9–9.8)	
Rheumatoid							
No steroid							
Mean	52.7	25.3	9.8	2.9	1.8	10.0	5
Range	(45.6–58.6)	(11.8–39.0)	(5.6–16.8)	(0–5.4)	(0–4.5)	(0.1–16.8)	
Rheumatoid							
Steroid							
Mean	60.9	22.8	9.0	1.0	5.0	1.1	5
Range	(54.1–68.2)	(19.1–27.6)	(5.2–10.5)	(0–2.0)	(1.3–7.9)	(0–5.4)	
Synovial Pellet							
Mean	49.1	24.9	0.9	8.3	3.7	11.3	5
Range	(38.8–60.0)	(13.6–41.8)	(0–3.4)	(5.7–10)	(0–6.0)	(5.4–18.5)	(4.7–9.5)

phospholipids). The quantitative data for the individual phospholipids are given in table 3.

c. *Esterified cholesterol and "triglyceride" constituents:* Total lipid extracts of serum and of the cell-poor fractions of synovial fluid from several of the patients were combined and studied in duplicate. In addition, the chloroform eluate from two similar specimens from serum and synovial fluid were analyzed following silicic acid column chromatography. Mean percentage composition and range of four separate determinations for the major lipids of blood and synovial fluid are given in table 2. Values obtained on the two pooled total extracts were in agreement with those obtained on the chloroform eluate from silicic acid columns. Only the neutral lipid content (cholesterol ester and triglycerides) appeared to differ from that found in serum. Esterified cholesterol was higher, while the ester fraction of total cholesterol in synovial fluid varied more than that for serum. The derived value for triglyceride in blood of 17.8 per cent contrasts with that of 6.4 per cent for synovial fluid. In one of the synovial fluid pools, no triglyceride was present. However, the range of values for triglyceride in serum and synovial fluid overlapped. This study on

the pool specimens would indicate that the major proportion of neutral lipid in the cell-poor fraction of synovial fluid was esterified cholesterol.

d. *Chromatography of phospholipids:* In table 3, values are given for percentage composition of individual phospholipids as determined by quantitative silicic acid paper chromatography. For comparative purposes, phospholipid composition of five rheumatoid cell pellets and three normal synovial fluid pools are included with values for rheumatoid serum and synovial fluid. Unidentified phosphorus is recorded at the extreme right of the table. This value expresses the efficiency of recovery of total phospholipid phosphorus applied to the chromatograms. It can be seen that recovery varied between 84 and 100 per cent, and was greater than 90 per cent for most of the analyses. The mean concentration of individual phospholipids was similar for rheumatoid serum and the cell-poor fraction of synovial fluid. The range of observed values overlapped in each instance. In normal fluid the mean values for sphingomyelin and lysolecithin were definitely lower, while the monophosphoinositide value was slightly higher than that for the pathologic specimens. The composition of phospholipids in the cell pellets of five synovial fluid specimens demonstrates: an extremely low content of lysolecithin, a moderate cephalin phospholipid level, and a relatively high level of phosphoinositide which has been segregated into mono- and di-phosphate components. This refers to material chromatographing with characteristics of these two species of phosphoinositide.¹⁶ The amount of material available did not allow more definitive identification of these inositide fractions.

Silicic acid column chromatography done on a pooled specimen of lipid extract from the cell-poor fraction of synovial fluid of seven rheumatoid patients and on a similar pool from serum is shown in figure 2. Striking similarity of the elution pattern for each is evident. Results of rechromatography of aliquots from each of the fraction tubes on silicic acid impregnated paper is also given. The early small cephalin peak contains both phosphatidylethanolamine and phosphatidylserine, as well as monophosphoinositide. It is evident that the analysis of total phosphorus from column fractionation may include more than one individual phospholipid in several of the column peaks. This finding is in agreement with the reports of Wallach²⁴ and Reed.²² By repeat chromatography of phospholipids obtained from these columns, percentage composition of the individual phospholipids can be obtained and is also given in figure 2. These values are similar to those of Nye¹⁷ for plasma using combined silicic acid column and paper chromatography. Total phosphorus in the synovial fluid cephalin peak was 0.5 μ mole of which 0.31 μ mole was ninhydrin reactive. This was in agreement with repeat determination by paper chromatography which demonstrated that "cephalins" constituted 0.33 μ mole of this peak. The remainder was monophosphoinositide. The elution pattern for major phospholipids and the percentage composition of individual phospholipids from serum and synovial fluid are very similar.

e. *Sequential studies of the lipid content in rheumatoid synovial fluid:* Follow-up analysis on synovial fluid lipids was carried out in four patients (table 4). Patient 1 had never received intra-articular steroids. In this joint with syn-

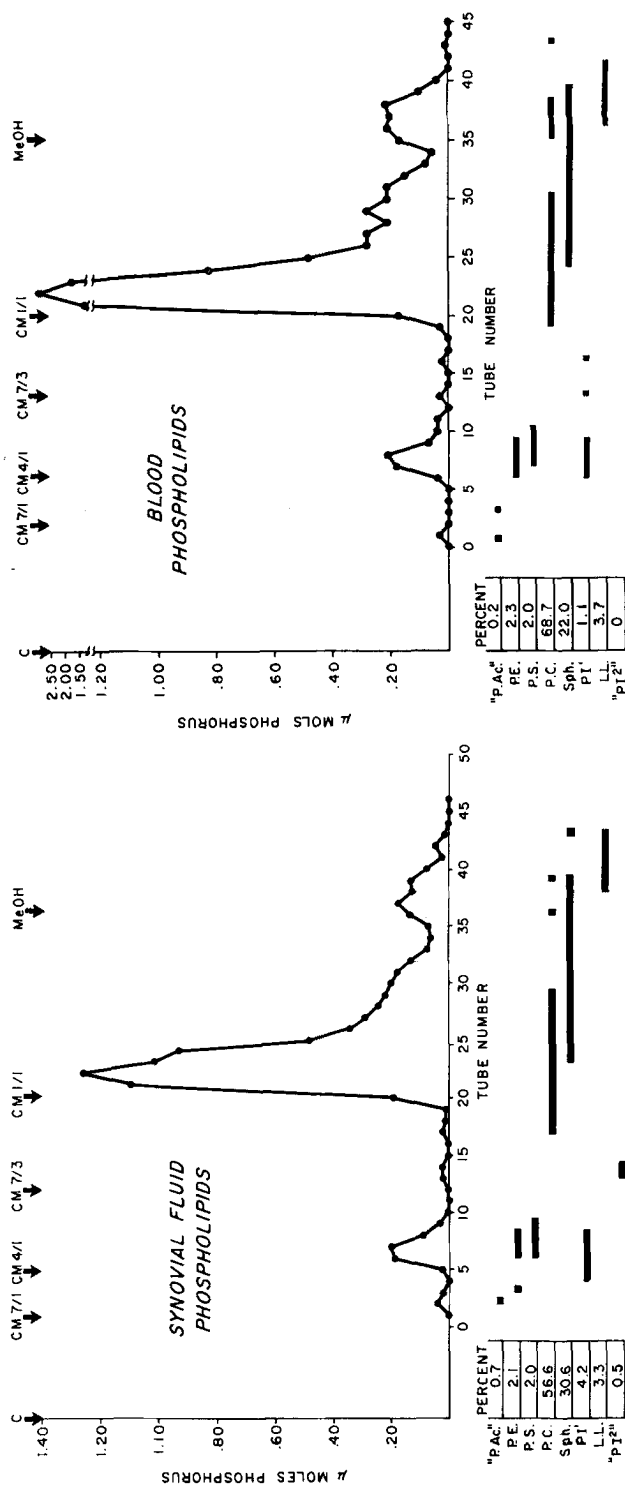


Fig. 2.—Silicic acid column chromatography of pooled total lipid extracts of serum and cell-poor fraction of rheumatoid synovial fluid. At the bottom of each figure the results of qualitative and quantitative re-chromatography on silicic acid impregnated paper are shown. All of the major column peaks were found to contain mixtures of individual phospholipids: "P.Ac.," phosphatidic

acid or polyglycerylphosphatide; P.E., phosphatidylethanolamine; P.S., phosphatidylserine; P.C., phosphatidylcholine (lecithin); Sph., sphingomyelin; PI¹, monophosphoinositide; L.L., lysophosphatidylcholine (lysolecithin); "PI²," Diphosphoinositide, tentative. Column loads 10 μ moles total phosphorus, recovery 94.9 and 99 per cent.

Table 4.—*Sequential Analyses of Synovial Fluid Lipids in Rheumatoid Arthritis*

Pt.	Date	mg. per cc.						Clinical Status:		
		Phospho- lipid	Choles- terol	Neutral Lipid	Total Lipid	Hyal- uronic Acid	Total Protein	Cells cu. mm.	Jt.	Interval Since Last I.A. Steroids
1	8/4/61	.87	1.49	.91	3.20	—	—	2,800	RK*	0
	8/11/61	.43	.78	.36	1.57	.56	59.6	4,700	RK	0
2	8/30/61	.90	1.21	.64	2.76	—	59.1	6,850	RK	12 days
	9/6/61	.76	1.07	.50	2.47	1.31	49.5	3,550	RK	7 days
3	9/6/61	.93	1.32	.68	3.00	—	44.1	41,900	RK	2 mo.
	10/6/61	.86	1.44	.73	3.03	.96	40.9	24,000	LK	1 mo.
4	3/30/60	.67	1.77	1.19	3.63	—	—	23,600	LK	4½ mo.
	7/8/60	.77	1.85	.50	3.12	—	—	—	LK	1½ mo.
	11/10/61	.86	1.27	.49	2.62	1.48	36.3	15,000	RK	16 mo.

*RK and LK—right and left knee.

ovitis of 6 months' duration, lipid content decreased significantly in 7 days, while the total cell count had doubled. Patients 2 and 3 with classic rheumatoid arthritis of long duration (7 and 13 years) had received intra-articular steroids on multiple previous occasions. Lipid content was remarkably stable in the same, and the opposite knee during the time intervals indicated in table 4. In patient 4, with classic rheumatoid arthritis of 4 years' duration, gold therapy was initiated after the first fluid analysis. At that time the patient was experiencing a severe flare of her disease. Four months later, a second analysis revealed decreased neutral lipid content; during this interval the signs of acute synovitis had regressed. Sixteen months later this patient was clinically in remission, although a chronic asymptomatic effusion persisted in the opposite knee. The lipid content in the right knee was similar, with low neutral lipid, to that found months previously in the left knee. No consistent pattern

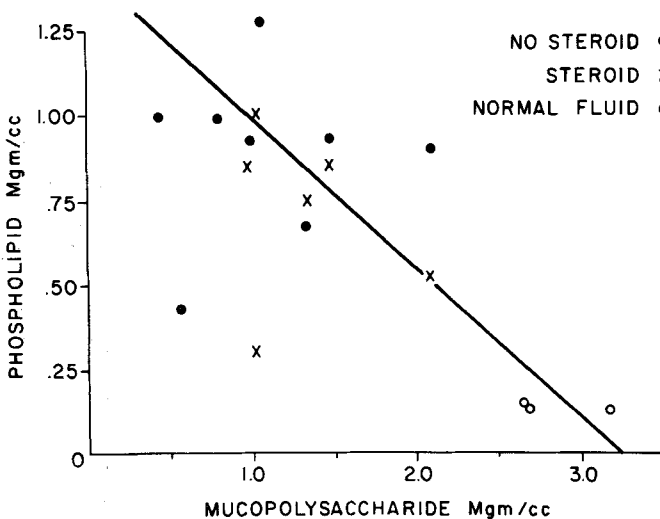


Fig. 3.—Concentration of total phospholipid and hyaluronic acid determined simultaneously in 14 rheumatoid patients, and three pools of normal human synovial fluid. Patients who had received prior intra-articular steroid (x), and non-steroid treated (●) patients.

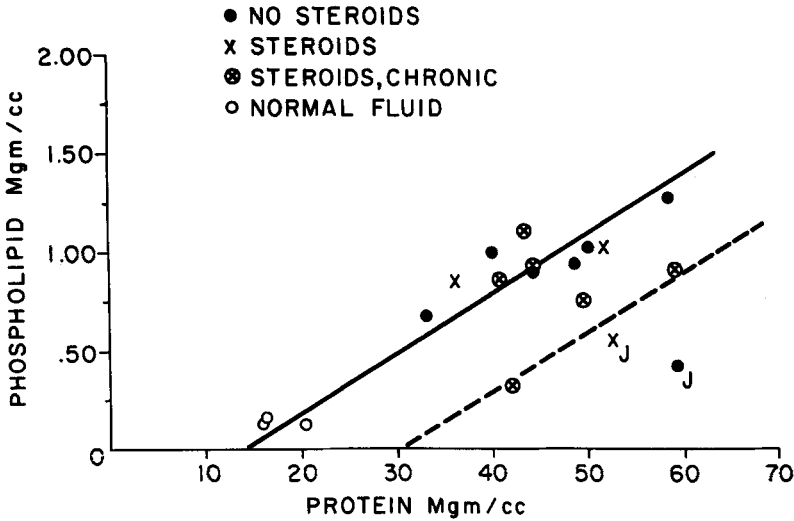


Fig. 4.—Concentration of total phospholipid, and total protein determined simultaneously in 15 rheumatoid patients, and three pools of normal human synovial fluid. The clinical status of the patient at the time of aspiration of the knee is indicated in the figure. See text for details. J—juvenile rheumatoid arthritis.

of response is apparent from these few sequential studies. Stability of the lipid values is evident in steroid treated patients, except perhaps for neutral lipid content. In the single untreated patient with acute synovitis, the level of lipids changed during an interval of 1 week.

f. *Non-lipid constituents: cells, hyaluronic acid, and proteins:* The total cell count in synovial fluid was unrelated to the level of any of the lipid constituents in the cell-poor fraction of synovial fluid.

In figure 3, concentration of total phospholipid is plotted against the concentration of hyaluronic acid in 14 patients in whom it was simultaneously determined. The data have been segregated for those patients treated with steroids and those that had never received intra-articular steroids. The three normal pools are also included. Very little, if any, correlation existed between concentration of total phospholipid and mucopolysaccharide in the synovial fluid from these patients. No relationship could be established between total cholesterol or total neutral lipids and hyaluronic acid concentration in synovial fluid.

In figure 4, total protein is plotted against total phospholipids found in the cell-poor fraction of synovial fluid. At the extreme lower left of the figure, values for the three normal fluid pools are shown. Taking this as an arbitrary point of reference, some relationship between total protein and total phospholipid concentration appears to exist. The five points that appear to be most divergent in this plot include two patients with juvenile rheumatoid arthritis (J), and two with advanced rheumatoid arthritis of long duration. Two determinations were done on one of these patients. Both had received repeated injections of intra-articular steroid. Plotting total cholesterol or total neutral

ester against protein gave a comparable relationship. The same five specimens appeared most divergent from the other determinations. In general, the level of protein was highest in those having the highest total lipid content.

DISCUSSION

It is evident from table 1 that the lipid concentration is extremely low in normal human fluid. The presence of only trace amounts of phospholipid in normal fluid, even smaller quantities of total sterol, and the absence of neutral lipid contrasts sharply with the concentrations found in serum. It is significantly different from the increased content found in the cell-poor fraction of rheumatoid synovial fluid. The content of cholesterol in normal fluid agrees well with that reported by Schmid and McNair.⁹ The small quantities of phospholipid present in normal synovial fluid has a qualitative distribution very similar to that of human plasma.¹⁷ In the normal state, lipids (lipoproteins) appear to be prevented from freely entering the synovial cavity. In rheumatoid arthritis, the level of all lipids in synovial fluid increases significantly. In most cases triglyceride content increases less than that for phospholipids and cholesterol.

No attempt has been made to relate these data in rheumatoid patients to various classes of lipoproteins segregated by electrophoresis, Cohn fractionation, or ultracentrifugation. Difficulties inherent in making such a comparison have been discussed by Bragdon,²⁵ Hillyard,²⁶ and Phillips.²⁷ Chung, Shanahan, and Brown¹⁰ concluded from their recent study of lipids of serum and synovial fluid from 12 rheumatoid and eight patients with degenerative arthritis that phospholipid composition and ratio of total cholesterol to phospholipid in synovial fluids differed from serum, and were characteristic of serum lipoproteins of density < 1.063 . In two patients with degenerative joint disease they studied the phospholipid composition of α - and β -lipoproteins separated by starch block electrophoresis, and felt that the differences were even more significant. They suggested that these differences might result from "absorption rate differences for different classes of lipoproteins," or be contributed by the synovial membrane itself.

In the present investigation a concentration difference for lipids persists between serum and the cell-poor fraction of rheumatoid synovial fluid. The ratio is similar to that reported by Chung.¹⁰ The composition of lipids found in the blood and synovial fluid is similar qualitatively (table 2). The percentage composition of phospholipids in serum, normal joint fluid, and rheumatoid synovial fluid before or after intra-articular steroids, as determined by silicic acid paper chromatography, is comparable (table 3). The range of variability observed for each phospholipid might account for this apparent similarity. However, variance of this degree does not occur when a single specimen is subjected to replicate analyses. Using comparable technics, Nye and Waterhouse²⁸ reported levels for the three major phospholipids of serum in a group of chronic nephrotics which varied as widely as the values for our rheumatoid patients. This has also been found true for patients with liver disease.²⁹ The values for phospholipids in pooled lipid extracts (fig. 2) of serum and synovial

fluid determined by combined silicic acid column and paper chromatography differ slightly from those discussed above. All of the values fall within the range observed for the individual specimens, but make it evident that moderate differences in concentration require cautious interpretation.

From these data it is impossible to assess the significance of these changes in relation to the physical state of native lipoproteins. In most of our patients the concentration of the major lipid groups in rheumatoid synovial fluid appeared to relate grossly to the total protein concentration. This has been reported to be the most consistent relationship observed by Nettelbladt,³⁰ and Pigman³¹ for sialic acid containing glycoproteins identified in pathologic synovial fluid. Whether the protein to lipid relationship noted for the two juvenile rheumatoids and two chronic, intra-articular steroid treated patients reflects a true difference from that for the majority remains undetermined. Although speculative, one explanation for this could be that in pathologic synovial fluid different lipoproteins occur than are found in serum. Proof of this hypothesis is not yet available.

If cell degeneration and breakdown contributed in any major way to the lipid content of rheumatoid fluid, it would be anticipated that the "cephalin" level should approximate 20-30 per cent as found for a variety of intact cells.^{22,24,32} The value was consistently less than 5 per cent for the cell-poor fraction of synovial fluid. The cell pellets separated by initial centrifugation contained less than 10 per cent of the total lipid, and no correlation between lipid concentration and total cell count in synovial fluid could be established. In addition, the lipid concentration in most of the rheumatoid synovial fluids studied was unrelated to duration of disease or degree of local inflammation.

The present study and Chung's data¹⁰ would indicate that most of the lipid in synovial fluid must in some way be derived from the blood; however, a gradient of difference in total concentration exists in all of the patients included in this study. By contrast, studies of experimentally induced granulation tissue^{3,4,33} have shown that local synthesis, as well as presumed changes in vascular permeability, contribute to tissue lipid concentration. Both of these factors may effect the concentration and composition of lipids present in pathologic synovial fluids. Based upon current observations, changes in permeability would appear to be the more important in human disease.

SUMMARY

The composition of the lipids in normal human fluid and in 28 patients with rheumatoid arthritis have been described. The lipid concentration in normal fluid was extremely low, while concentration of the major lipid groups in the cell-poor fraction of rheumatoid synovial fluid constituted in most cases 40-60 per cent of the level in the serum. Pleocytosis in the fluid contributes only to a minimal degree to the total concentration. A direct relationship between total protein concentration and the major lipid constituents found in synovial fluid appeared to exist. No clear association between the use of steroids, severity of disease or total mucopolysaccharide content could be established.

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