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Clinical application of synovial fluid change

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CLINICAL APPLICATION OF SYNOVIAL FLUID CHANGE.

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The presence of a viscous fluid in the articular cavities was first noted by Paracelcus (1493-1541). The fluid was described as being contained in the space formed by the opposing cartilage covered epiphyses and the surrounding joint capsule.

Joint components are mesodermal in origin. A joint cavity forms by the liquefraction of the mesenchymal tissue which separates the chondrified skeletal elements. The perichondrium, later periosteum, is continued over this cavity while the lining of the capsule appears on the end of the bones, articular cartilage and capsule. This last structure is known as the synovial membrane. In some regions, as the knee and temperomandibular joints, the intervening mesenchyme forms the meniscus. The capsule, like the periosteum, is composed of tough, inelastic, white fibrous tissue. Synovial membrane, on the other hand, is a thin, soft, freely movable elastic membrane, richly supplied with pain fibers and an abundant blood supply. The membrane covers all the joint surfaces except the cartilage covered weight bearing areas. It covers the edges of the articular cartilages to which it is very adherent and terminates gradually without sharp demarcation. Normally the synovial membrane is very thin and its internal surface is characterized by a variable number of delicate villi and folds. The surface is cellular, but no cells similar to goblet cells are found (1).

It is possible to consider the articular cavities as large tissue spaces lined by somewhat modified connective tissues. Syno-

vial fluid may be considered as a matrix of the connective tissue with the mucin being similar to that found in other connective tissues (2). This fluid is formed by a dialysate of blood plasma, so-called ultra-filtrate, with the addition of mucin (3). The nature of the rich subsynovial vascular supply is in accord with this concept. In some instances the capillaries are separated from the interior of the joint by no more than one or two layers of synovial lining cells. The presence of mucin distinguishes synovial fluid from other body fluids that are dialysates of plasma and is responsible for its viscosity (4). The mucin is formed by the surrounding connective tissue cells (5) and carried into the joint cavity by the diffusing dialysate of plasma water.

Normal human synovial fluid is a relatively clear, pale yellow, viscous fluid that doesn't clot (6). It has four main functions: (1) lubrication; (2) it has a high molecular weight so it maintains the fluid in the joint; (3) mucin acts as a buffer and maintains the alkalinity of the joint; (4) nutrition of the avascular cartilage. Since the nutrition and lubrication are most important the fluid contains few cells. The amount of fluid varies from 1.3 to 3.5 cc. (7). This volume is determined by two forces, capillary pressure and the difference in osmotic pressure between synovial fluid and plasma.

Values for non-electrolytes and electrolytes in synovial fluid as compared with plasma indicate that the non-electrolytes are distributed in accord with the Donnan theory of membrane equilibrium (3).

Albumin and globulin are found in synovial fluid in an average total concentration of 1.72 gm. per 100 cc. (6) and an individual concentration of albumin of 1.02 gm. per 100 cc. and globulin of 0.05 gm. per 100 cc. (7). Their presence is presumably explained on the basis of slight capillary permeability to protein. The marked difference between albumin and globulin indicates a greater permeability to albumin than to globulin.(9). This might well be explained by the difference in molecular weights. The normal albumin and globulin concentrations in synovial fluid result in a high albumin globulin ratio (8). There is no fibrinogen in normal fluid, therefore it doesn't clot (7).

As previously mentioned, the mucin content in synovial fluid is responsible for its viscosity and distinguishes it from the other fluids that are dialysates of blood. Mucin is a protein-polysaccharide complex sometimes called hyaluronic acid. This highly polymerized acetic molecule is built from units of glucuronic acid and N-acetyl glucosamine linked together to form a long chain (10). There is some disagreement as to the existence of mucin as a true product. Ropes and Bauer consider the protein polysaccharide molecule to be a real product with the protein portion consisting of at least an albumin and several globulin fractions. Sundblad considers hyaluronic acid to be in no way connected with protein, thus the mucin formed by the addition of acetic acid to synovial fluid is an artificial product. In any event, the mucin or hyaluronic acid is responsible for the high viscosity of synovial fluid. The

The fluid viscosity approaches that of water after the mucin has been destroyed enzymatically (7). Incubation of synovial fluid with hyaluronidase also produces a fluid with a viscosity similar to that of water (10). A reliable indication as to the state of mucin in any fluid is obtained by the addition of acetic acid. This results in a precipitation of normal mucin as a tight, ropy clump in a clear solution. The mucin concentration can also be measured as grams of nitrogen or mucin glucosamine concentration. The average normal mucin concentration is 0.104 gm. nitrogen per 100 cc. and mucin glucosamine is 0.087 gm. per 100 cc. The normal relative viscosity is 235 at 38° C (7).

Cytologic examination of normal synovial fluid reveals it to be relatively cell poor. Normally the erythrocyte count will not exceed 160 per cu. mm. Total leukocytes average 63 per cu. mm. with a differential count of 7 percent polymorphonuclears, 25 percent lymphocytes, and 63 percent monocluclear phagocytes (6) (11).

Examination of synovial fluid begins with its aspiration. The type of examination done depends upon the amount of fluid obtained. Only a few drops are necessary for gross appearance, total nucleated cell count, differential, viscosity and type of precipitation with acetic acid. Approximately 8 cc. is necessary for sugar, total protein, albumin and globulin concentrations, mucin concentration, bacterial and immunological studies. Determinations of non-protein Nitrogen, uric acid and electrolytes are of no diagnostic or prognostic value (6). At the time of joint aspiration, blood should

also be withdrawn for sugar and protein fractions. This will provide the necessary finding for comparison with synovial fluid.

The gross appearance should be recorded as to the degree of turbidity, color, apparent viscosity and presence or absence of clotting. If the fluid contains blood it should be determined if this was present before the tap or a result of needle trauma. Xanthocromic blood pigment in the supernatant fluid after centrifuging indicates the bleeding occurred before the tap. Blood streaks on aspiration with clotting localized to the streaks means that the blood is a result of the tap.

Bacteriological examination includes a smear with gram strain and cultures on appropriate media. Occasionally guinea pig innoculation may be necessary to determine the presence of tubercule bacilli.

Cytological examination can be done in a standard hemocytometer. using saline as a diluent. Addition of methylene blue aids in the recognition of cell types. Differential counts are made with Wright's stain.

An indication as to the degree of polymerization of mucin can be obtained very simply by the addition of acetic acid to synovial fluid. Normal mucin precipitates a tight, ropy clump in a clear solution (7). As depolymerization of mucin occurs (with disease), the precipitate changes. Occasionally in some pathological fluids only small flecks will precipitate in a cloudy solution. Viscometer readings are done at a constant temperature (usually 38^{o}C) with either a Hiss viscometer

or an Oswald viscosity pipette. A decreased viscosity found in pathological conditions may be due to one or two factors or both: (a) dilution with extra cellular water as in edema; (b) depolymerization of the highly complex hyaluric acid molecule with disease processes (12). Sugar and protein determinations are done as standard laboratory procedures.

Indications for joint aspiration are as follows: (a) relief of massive effusion usually aids in relaxation of tissues and speeds recovery by increasing circulation; (b) drainage of infectious arthritis; (c) injections of air or lipiodol with subsequent x-ray examination to reveal any communication of the joint with surrounding bursae or pouches; (d) diagnosis of unexplained joint effusion by examination of synovial fluid. Aspiration of a joint can be considered as a benign procedure. One series of 2,200 such examinations have been done without a single resulting joint infection (7). The only danger of serious bleeding exists in hemophilia.

Pathologic synovial fluids can be divided by etiology and synovial fluid findings into two large groups. The following classification and material are taken from the work of Ropes and Bauer (7) unless otherwise numbered.

Group I diseases are inflammatory reactions of traumatic origin. There is a disorder of permeability, circulation and metabolism from any tissue injury. This group includes all types of traumatic arthritis, osteochondritis dissecans, degenerative joint disease, neuroarthropathy (Charcot Joint), and osteochondromatosis.

Group II contains all types of infectious arthritis of known origin. Included are streptococci, staphlococci, pneumococci and E. coli. Also found in this group is Reiter's syndrome and rheumatoid arthritis.

There is a third group which has fluids resembling Group 1 or Group II. They are considered as a separate group because of their varying etiology. Members in this group are lupus erythymatosis disseminatus, hypertrophic pulmonary osteoarthropathy, hemophilia, gout and hemorrhagic villous synovitis. Synovial fluid effusion as a result of peripheral edema will be considered as a separate topic.

The findings under the various diseases can best be presented in an outline form.

Fluids from Group I - Diseases of traumatic origin.

1. Traumatic Arthritis. These effusions usually occur within several hours after injury and subside in no longer than three months. As a rule the joint is not red, hot or acutely tender. There are two types of traumatic effusion, hemorrhagic and non-hemorrhagic.
   (A) Non-hemorrhagic traumatic fluids show slight change from normal:
      (1) Fluid is clear and doesn't clot.
      (2) Total erythrocyte count averages 2,250 per cu. mm.
      (3) Total leukocyte count averages 1,250 per cu. mm. with an absolute polymorphonuclear count below 100 per cu. mm.
      (4) Protein concentration (less mucin) was 2 or 3 times above normal, averaging 3.75 gm. per 100 cc. Most of this in-

crease is in the albumin fraction which results in a high average albumin-globulin ratio of 4.9:1. Electrophoretic patterns show that the albumin fraction is always higher in synovial fluid than in serum. Alpha-1 and beta globulins are essentially the same in fluid and serum. Alpha -2 and gamma globulins are lower in synovial fluid than in serum (14).

(5) Viscosity is reduced from normal (average of 29). Mucin glucosamine averages 0.098 gm. per 100 cc. and mucin nitrogen is 0.076 gm. of nitrogen per 100 cc.

(6) Mucin is precipitated with acetic acid as a tight, ropy clump in a clear solution.

(B) Hemorrhagic traumatic effusions:

(1) Fluids appear turbid and red with occasional very soft clot formation.

(2) Total erythrocyte count averages 1,305,000 per cu. mm.

(3) Total leukocytes average 1,540 cu. mm. with absolute polymorphonuclear count of 315 per cu. mm.

(4) Total protein is essentially the same as non-hemorrhagic fluids, but there is an increase in globulin concentration which results in an average albumin-globulin ratio of 2.8:1.

(5) The viscosity is approximately equal to non-hemorrhagic fluids, but the mucin nitrogen and mucin glucosamine concentration is less (0.050 gm. nitrogen per 100 cc. and

0.019 gm. glucosamine per 100 cc.). The mucin precipitate is normal.

(6) The sugar content in the majority of fluids is lower than in serum because of the increased glycolytic enzyme with the blood.

2. Osteochondritis dissecans effusions are usually limited to one joint (more often the knee). The joint is normally not red, warm or tender.

(1) Fluids are clear to slightly turbid and usually form a small clot on standing.

(2) The average erythrocyte count is 15,310 per cu. mm.

(3) The total leukocyte count averages 750 per cu. mm. with absolute polymorphonuclear counts in the range of traumatic fluids.

(4) The average total protein (less mucin) is 3.31 gm. per 100 cc. Albumin is 2.81 gm. per 100 cc. and globulin is 1.16 gm. per 100 cc. (similar to traumatic).

(5) Viscosity is 23 at 38° C, and the mucin precipitate with acetic acid is normal.

3. Osteochondromatosis effusions are not uncommon. They usually involve only one joint which is not red or tender.

(1) The fluids are clear, do not clot and are extremely viscous.

(2) Total erythrocyte counts average 1,590 per cu. mm.

(3) Total leukocyte counts average 510 per cu. mm. with absolute polymorphonuclear counts of 5 per cu. mm. per 100 cc.

(4) The average total protein (less mucin) is 2.23 gm. per 100 cc.

(much lower than traumatic fluids).

(5) The viscosity averages 499 at 38° C with an extremely high mucin glucosamine of 0.099 gm. per 100 c.c. These values are the highest found in any type of joint disease. The mucin precipitate is normal.

4. Neuroarthropathy (Charcot Joint) shows marked degenerative changes, joint destruction and loss of pain sense. Usually one or more joints are involved which are not warm, red or tender. These effusions are usually large and persist for years.

(1) The fluids are very similar to traumatic types in that they may be clear or hemorrhagic, but do not clot.

(2) The total erythrocyte count averages 91,330 per cu. mm.

(3) The average total leukocyte count is 750 per cu. mm. (15).

(4) The total protein (exclusive of mucin) is 3.36 gm. per 100 cc. (same as traumatic fluids). The globulin concentration is slightly higher than other Group I fluids with an average albumin-globulin ratio of 2.2:1.

(5) Viscosity averages 31 at 38° C. Mucin is precipitated as a soft mass in a clear or slightly cloudy solution.

(6) Wasserman reactions vary with different authors. Keefer (16) has two cases where it is negative in fluid and positive in serum. Chesney (17) has one case where the reaction is positive in fluid and negative in serum. Ropes and Bauer had a positive reaction in fluid and serum in 6 out of 8 cases.

5. Degenerative joint disease effusions are usually small when they occur. They are most often caused by excessive use of the joint. Clinical findings are a joint which is not hot or red, but tender.
   (1) Fluids are clear, very viscous and do not clot (18).
   (2) The average erythrocyte count is 11,930 per cu. mm.
   (3) The total leukocyte count is 720 per cu. mm. (18) which a low number of absolute polymorphonuclears.
   (4) The total protein (exclusive of mucin) is 3.08 gm. per 100 cc. The albumin-globulin ratio is 4.8:1 which is similar to other traumatic fluids.
   (5) The viscosity is 41 with an average mucin of 0.090 gm. nitrogen per 100 cc. and 0.088 gm. of glucosamine per 100 cc. The mucin precipitate is normal.

Fluids from Group II - Rheumatoid arthritis and disease of infectious origin. The barrier between blood and joint cavity is permeable to diffusible substances like protein and bacteria (2). Joint symptoms in this group vary markedly from arthralgia to severe joint involvement. In most specific infections, the organisms reach the fluid, but the degree of involvement is determined by the number, type and virulence of the organism in relation to the general resistance of the patient.

1. Septic arthritis due to specific organisms such as streptococci, staphlococci, pneumococci and E. coli form large effusions of short duration. The joint is hot, red and acutely tender. Swelling often extends beyond the limits of the joint structures. This

type of arthritis will be considered under two groups.

(A) Specific infectious arthritis with negative cultures:

(1) The fluids are turbid, viscous and form large, firm clots.

(2) The average erythrocyte count is 12,570 per cu. mm.

(3) The total leukocyte count is 62,210 per cu. mm. with the polymorphonuclear cells in the average differential being 92%. Similar results were found by Keefer (16).

(4) Total protein (less mucin) is high, averaging 4.55 gm. per 100 cc. with a globulin concentration of 1.21 gm. per 100 cc. This last value results in a low albumin-globulin ratio.

(5) The viscosity is very low, 10.7 at 38° C (18). Mucin nitrogen is reduced. The mucin precipitates as small flecks in a cloudy solution.

(6) The average sugar concentration in synovial fluid is 48 mgm. percent with the average level in serum being 97 mgm. percent. Similar low sugar levels were found by Allison (19).

(B) Specific infectious arthritis with positive cultures:

(1) The appearance is very turbid with firm clot formation.

(2) The erythrocytes average 33,660 per cu. mm.

(3) The leukocytes average 73,370 per cu. mm. with a differential of 90% polymorphonuclear cells.

(4) The total protein is slightly above negative culture fluids with increased globulin up to 1.63 gm. percent.

This results in an albumin-globulin of 1.7:1.

(5) The viscosity averages 16.1 at 38° C. Mucin nitrogen is increased slightly above negative culture fluids. Mucin precipitates as small friable masses in a cloudy solution.

(6) The average synovial fluid sugar was 21 mgm. percent with an average serum level of 112 mgm. percent.

2. Gonococcal arthritis effusions may occur in one or many joints. Symptoms vary from redness, heat and tenderness to only slight warmth and tenderness. These fluids are also divided into two groups by negative or positive bacterial cultures.

(A) Gonococcal arthritis with negative cultures:

(1) Fluids appear turbid and form a firm clot.

(2) Total erythrocytes average 1,400 per cu. mm.

(3) Average leukocyte count is below 300,000 per cu. mm. with an average polymorphonuclear differential of 67 percent. Similar results were obtained by Myers (20).

(4) Total protein (less mucin) is 5.31 gm. per 100 cc. with a globulin concentration of average 2.02 resulting in an albumin-globulin ratio of 1.7:1. Myers found similar findings (20).

(5) Viscosity is 13 at 38° C. Mucin precipitates as small friable masses in a cloudy solution.

(6) The average fluid sugar is 83 mgm. percent with serum levels of 100 mgm. percent.

(B) Gonococcal arthritis with positive cultures:

(1) Fluids are very turbid and form firm clots.

(2) The average erythrocyte count is 730 per cu. mm.

(3) The total leukocyte count averages above 300,000 per cu. mm. with an average differential of 95% polymorphonuclear cells. Similar results were obtained by Myers (20).

(4) Total protein less mucin is approximately equal to that found in negative cultures, but the globulin concentration is elevated resulting in an albumin-globulin ratio of 1.4:1.

(5) The viscosity is 4 at 38° C. Mucin nitrogen is decreased from levels found in negative cultures. Mucin precipitates as small friable masses in a cloudy solution.

(6) Complement fixation examinations of fluids with both positive and negative cultures were reflections of that found in serum (16).

3. Meningococcal arthritis usually involves one or more joints. Clinical symptoms vary from arthralgia to severe swelling. Effusions ordinarily last several weeks and subside with varying degrees of joint damage. Positive cultures are very difficult to obtain.

(1) All fluids are turbid, viscous and usually form a firm clot.

(2) The average total erythrocyte count is 12,400 per cu. mm.

(3) The total leukocyte count is 132,360 per cu. mm. with average polymorphonuclear differential of 93 percent.

(4) Total protein (less mucin) averages 4.3 gm. per 100 cc. resulting in an albumin-globulin ratio of 0.9:1.

(5) Viscosity averages 15 at 38° C. The average glucosamine is 0.027 gm. per 100 cc. and the average mucin is 0.061 gm. nitrogen per 100 cc. The mucin precipitate varied from a fairly cohesive material in a clear solution to shreds in a cloudy solution.

(6) The average sugar in synovial fluid was 48 mgm. percent with serum level of 92 mgm. percent.

4. Tuberculous arthritis may be limited to the synovial tissue or involve the bone. Effusions occur in either case. Untreated, these effusions last for months or years. Most often only one joint is involved. These joints are usually cold.

(1) Fluids are turbid and do not clot.

(2) The average erythrocyte count is 28,310 per cu. mm.

(3) The total white count is usually around 19,470 per cu. mm. There is a tendency toward a predominance of lymphocytes in early cases and an increase in polymorphonuclear cells as the case becomes chronic.

(4) The total albumin and globulin is around 5.31 mgm. percent. Average albumin-globulin ratio is 1.9:1.

(5) Viscosity is very low (21). The average at 38° C is 7.7. Mucin precipitates as small friable masses in a cloudy solution.

(6) The average synovial fluid sugar was 27 mgm. percent with

serum level of 97 mgm. percent. Allison (19) found moderately lowered fluid sugar levels as compared to serum.

(7) Guinea pig innoculation was negative in only 8 cases of 29 innoculations (19). Another author had 85 percent positive results with guinea pig innoculation (22).

5. Syphilitic arthritis (congenital) effusions usually occur in both knees, but may involve other joints. These effusions may persist for years and are usually painless (23).

(1) The fluids are turbid, not viscous, and may clot.

(2) The total erythrocyte count is 16,660 per cu. mm.

(3) The average leukocyte count is 15,600 with a polymorphonuclear differential of 46 percent. Similar results were found by Kling (23) and Chesney (17).

(4) Total protein (less mucin) is 4.67 gm. percent.

(5) Viscosity is 11 at 38° C. Mucin precipitates as soft clumps of shreds in a cloudy solution.

(6) Sugar levels in synovial fluid are approximately equal to serum levels.

(7) The Wasserman reaction in serum and fluid varies with different cultures. Ropes and Bauer had 3 cases where the reaction was positive in fluid and serum, one case where it was negative in fluid and positive in serum, and one where it was negative in both. One author found 9 out of 10 fluids had positive reactions along with serum (17).

6. Reiter's syndrome (non-gonococcal urethritis, arthritis and conjunctivitis) involves one or more joints in varying degrees of

severity. Effusions last longer than gonococcal arthritis and the residual damage is usually less than gonococcal.

(1) The fluids are turbid, not very viscous and do not clot.

(2) The average total erythrocytes are 9.800 cu. mm.

(3) The total leukocyte count is 18,890 per cu. mm. with a 61 percent polymorphonuclear differential.

(4) Total protein (less mucin) is slightly below Group II levels (4.49 gm. per 100 cc.) with a relatively low globulin level.

(5) Viscosity is approximately 11 at 38° C with mucin precipitation as soft clumps or shreds in a cloudy solution.

(6) Pleuro-pneumonia like organisms can occasionally be cultured from genitourinary tract and synovial fluid.

7. Rheumatoid arthritis presents joint symptoms of stiffness and aching pain of dull or moderate intensity. Fluids in this disease vary more than any other group. In general the variations could be correlated grossly with the severity of the disease, degree of inflammation and duration of effusion (24).

(1) The fluids range from clear to turbid - 58 percent clotted.

(2) The total erythrocyte count varied from 200 to 4,890 per cu. mm.

(3) The total leukocytes ranged from 450 to 66,000 averaging 15,310 per cu. mm. with polymorphonuclear cells averaging 65 percent (24).

(4) Total protein (less mucin) ranged from 3,30 gm. per 100 cc. to 8.89 gm. per 100 cc. (this last value is the highest recorded

by Ropes and Bauer). Globulin concentration is high, resulting in an albumin-globulin ratio of 1.5:1. This is below most Group II fluids. Electrophoretic patterns resemble traumatic effusions (14). In effusion of several years duration there is a marked increase of gamma globulin above that of serum (13).

(5) Viscosity varies from 2.8 to 59 with an average of 11 at 38° C. Mucin concentrations are approximately the same as other Group II fluids, but the range is much greater. The majority of fluids from active rheumatoid arthritis precipitate poorly with acetic acid, but occasional mild or early cases have a good precipitate (25).

(6) The average sugar concentration in fluids is 65 mgm. percent. This is slightly lower in cases of long standing (26).

(7) Numerous bacterial cultures taken in rheumatoid fluids have all been negative (27) and (7).

8. Intermittent hydrarthrosis is a periodic joint effusion at regular intervals whose etiology is unknown. In rheumatoid arthritis effusions can occur at intervals. It is possible that the disease is an atypical form of rheumatoid arthritis.

(1) Fluids are slightly turbid in appearance and usually form clots.

(2) Total erythrocyte count averages 570 per cu. mm.

(3) The total leukocytes average 2,220 per cu. mm. (27) with an average differential for polymorphonuclear cells at 7 percent.

(4) Albumin-globulin ratio, total protein and albumin and globulin fractions are similar to average rheumatoid fluid.

(5) Relative viscosity is 9.5 at 38° C with mucin precipitating as a tight, ropy clump in a clear solution. The mucin concentration is 0.050 gm. nitrogen per 100 cc.

(6) Sugar levels are equal in serum and fluid.

The last diseases to be considered will be those that have fluids resembling both Group I and Group II.

1. Hypertrophic pulmonary osteoarthropathy effusions may occur and present symptoms of a painful joint that is not red or hot.

   (1) Fluids are clear, viscous and form firm clots.

   (2) The erythrocyte counts average 5,330 per cu. mm.

   (3) The average total leukocyte count is 1,830 per cu. mm. with percent of polymorphonuclear cells averaging 15.

   (4) Total protein (less mucin) is 3.07 gm. per 100 cc. with an albumin-globulin ratio of 2.1:1.

   (5) Viscosity is 15.3 at 38° C. Mucin precipitates as a soft mass in a clear to cloudy solution.

2. Hemophilic arthritis presents joints that are usually swollen, painful and warm.

   (1) The fluid is grossly bloody and forms small clots.

   (2) The average erythrocyte count is 2,482,000 per cu. mm.

   (3) The total leukocyte count averages 5,320 per cu. mm. with a polymorphonuclear differential of 38 percent.

   (4) Total protein (less mucin) is 5.94 gm. per 100 cc. The aver-

age albumin-globulin ratio is 2.4 gm. percent.

(5) The average viscosity is 21 at 38° C with a mucin precipitate of small masses in a cloudy solution.

3. Lupus erythematosus disseminatus effusions are not too uncommon. They usually remain small and subside with remissions in the disease.

(1) Fluid is clear to turbid, very viscuus and does not clot.

(2) The average erythrocyte count is 38,490 per cu. mm.

(3) The total leukocyte count is 2,860 per cu. mm. with the average differential for polymorphonuclear cells being 2 or 3 percent.

(4) The total protein (less mucin) is 2.51 gm. per 100 cc. with average globulin concentration of 1.8 gm. percent. Albumin-globulin ratio is 1.3:1.

(5) Viscosity is slightly decreased from normal (21). Mucin concentration is 0.092 gm. nitrogen per 100 cc. Mucin precipitates as ropy clump in a clear solution.

4. Gout effusions are often large and usually subside in a few days. In the acute attack the joint is red, hot and extremely tender. Swelling often extends beyond the limits of the joint cavity.

(1) The fluids are turbid, not viscous, and form large clots.

(2) The total erythrocyte count averages 38,490 per cu. mm.

(3) The total leukocyte count averages 13,317 per cu. mm. with an average polymorphonuclear differential of 71 percent.

(4) The total protein (less mucin) is 4.18 gm. per 100 cc. with

an average albumin-globulin ratio of 1.8:1.

(5) The average viscosity at 38° C is 17. Mucin precipitates as shreds in a cloudy solution.

(6) Sugar and uric acid levels in synovial fluid are similar to those found in blood (6).

5. Rheumatic fever effusions may occur in one or more joints simultaneously. Ordinarily the effusions last only a few days with symptoms of a swollen, red, tender joint.

(1) Fluids are viscous, slightly turbid, and usually clot.

(2) The total leukocyte count averages 64,840 per cu. mm.

(3) The average leukocyte count is 17,820 per cu. mm. with an average differential for polymorphonuclear cells being 50 percent. Higher counts are found in the first few days of effusion. Then the polymorphonuclear cells are gradually replaced by lymphocytes as the effusion ages (28).

(4) Total protein (less mucin) is 3.74 gm. percent with an average albumin-globulin ratio of 3.1:1. Globulin concentration is 1.07 gm. percent.

(5) The viscosity at 38° C is 22. Mucin precipitates as a tight, ropy clump in a clear solution.

(6) Sugar levels are approximately equal in fluid and serum.

6. Hemorrhagic villous synovitis (pigmented villo-nodular synovitis) usually involves only one joint which is tender, but not warm or red.

(1) Fluids appear bloody, not very viscous, and they may or may

not clot.

(2) The total red cells average 682,270 per cu. mm.

(3) The total leukocyte count averages 3,110 per cu. mm. with average polymorphonuclear cells being 15 percent.

(4) Total protein (less mucin) is 4.23 gm. percent with albumin equal to 2.92 gm. percent and globulin equal to 1.31 gm. percent.

(5) Viscosity is low (5.4 at 38° C). Mucin precipitates as a soft mass in a clear to cloudy solution.

Synovial fluid from patients with edema, but no joint disease, has characteristic changes from normal. These effusions are usually large with findings that indicate normal fluid has simply been diluted.

(1) The appearance is that of a clear fluid with a pale yellow color, which is not very viscous.

(2) The total nucleated cell count averages 32 per cu. mm. (29).

(3) Total protein (less mucin) is 0.63 gm. per 100 cc. Globulin and albumin concentrations are also markedly decreased from normal (29).

(5) Average viscosity is definitely decreased from normal (30). The mucin content averages 0.061 gm. of nitrogen per 100 cc. and the precipitate with acetic acid is normal. The lowered mucin content in association with increased diffusion of water into the joint suggests the formation of mucin is not accelerated to the rate of the transudation of water. This supports the theory that synovial fluid is a dialysate of blood plasma

with the addition of mucin by cells surrounding the joint.

SUMMARY

A survey of the findings in synovial fluid from various joint diseases is presented. The classification of these diseases and findings as presented by Ropes and Bauer seemed to be the most valuable. Generally, joint diseases can be divided into two large groups by etiology and synovial fluid changes. Group I contains diseases in which an inflammatory reaction of traumatic origin is present. Included in this Group are effusions of traumatic arthritis, osteochondritis dissecans, degenerative joint disease, Charcot Joint, and osteochondromatosis. Group II fluids are the result of all types of infectious arthritis of known origin such as streptococci, staphlococci, pneumococci, gonococci, meningococci, E. coli, tuberculosis, Reiter's syndrome and rheumatoid arthritis. In between these two Groups are a number of other joint diseases which have varying etiology and synovial fluid findings. Effusions from lupus erythematosis disseminatus, hypertrophic pulmonary osteoarthropathy and hemophilia resemble Group I fluids. Rheumatic fever, gout and hemorrhagic villous synovitis have fluids resembling both Group I and Group II.

Generally, in a pathological effusion, if an aspirated fluid is fairly clear, viscous and does not clot, its cause can be found in Group I or occasionally the cause may be rheumatic fever and mild atypical rheumatoid arthritis. All specific infectious and most rheumatoid fluids are turbid, less viscous and often form firm clots.

All members of Group I show slight changes from normal. The total leukocyte count is usually below 3000 per cu. mm. with an absolute polymorphonuclear count below 500 per cu. mm. Total albumin and globulin is increased above normal, but remains below 5 gm. per 100 cc. The albumin-globulin ratio is above 2. Concentrations of mucin and sugar tend to be normal or only slightly decreased in osteochondromatosis where mucin is greatly increased. The viscosity is normal except again in osteochondromatosis where it is greatly increased. Mucin precipitates with acetic acid as a tight, ropy clump in a clear solution.

Group II fluids demonstrate a marked deviation from normal in some findings. The total nucleated cell count is usually above 3000 per cu. mm. with an absolute polymorphonuclear cell count above 500 per cu. mm. Total protein (less mucin) is above 4 gm. per 100 cc. and the albumin-globulin ratio is usually below 2:1. Concentration of mucin is often below normal and the mucin precipitate with acetic acid is poor. Often no precipitate will occur. These findings indicate a severe inflammatory process in association with loss of or abnormal mucin synthesis or abnormal mucin destruction. The sugar content is usually below normal, but varies with the specific disease and presence or absence of positive bacterial cultures. Sugar levels in rheumatoid arthritis can be normal. Levels found in infected fluids with positive cultures and in most tuberculous fluids are low or completely absent.

CONCLUSION

Synovial fluid changes can be used to differentiate traumatic arthritis from non-traumatic effusions. They may further act as a guide to separate individual members of each group. A specific combination of fluid changes may make the diagnosis of one joint disease, but should be correlated with clinical, laboratory and roentgenographic findings. Therefore, the real value of synovial fluid lies in the fact that it is an additional tool for the diagnosis and treatment of joint disease.

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