MEDICAL GRAND ROUNDS

Parkland Memorial Hospital

"THE CLINICAL SPECTRUM OF CRYOGLOBULINEMIA"

October 21, 1971

Case 1. [redacted]: This 73 YO [redacted] woman was well until [redacted], 1967 when she developed vesicular ulcerating lesions on the feet and lower portions of both legs which healed with hyperpigmentation. She had previously been seen in medical clinic because of hypertension, which was controlled by Naqua and Guanethidine. Two weeks before, she noted reddened areas of her nails and fingers; this was followed by gangrene of the tips of the right 2nd & 3rd digits. Splinter hemorrhages developed in the nails of the left hand. There was a recent history of pain, numbness and discoloration on exposure to cold water or cold environmental temperature. Physical examination showed a blood pressure of 130/90. There was gangrene of the distal end of the right 3rd finger to the middle of the second phalanx and earlier similar changes of the tip of the second finger of the right hand. Many splinter hemorrhages were present in all fingernails. The arterial pulses of both arms and legs were strong. There were large areas of hyperpigmentation and ulceration extending from the lower third of the legs to the lateral aspects of the feet and soles. There had been only one joint involved, the right second MCP, with arthralgia but no evidence of arthritis.

A cryoglobulin of the IgG type was identified by testing of serum at 4°C and was further shown to be a 7S globulin on ultracentrifugation and specific immune precipitation. It was present in the serum in a concentration of 100-200 mg% with a low solubility curve. Cryocrit was 4%. Evaluation for an underlying collagen disease was unrewarding (except that one L.E. prep initially read as "positive" upon re-evaluation, actually showed cryoglobulin inclusions) but an IVP and renal arteriogram showed a mass occupying much of the left kidney. Surgery was recommended but she refused. Four months later a left nephrectomy was performed at St. Paul Hospital and review of the slides confirmed the presence of a clear-cell renal carcinoma.

She was re-admitted here six months after the initial evaluation because of extension of the peripheral gangrene as well as lethargy, nausea and vomiting. Soon afterward, she developed an episode of severe substernal pain followed by biventricular congestive failure; an electrocardiogram showed signs of anterolateral myocardial infarction. She was digitalized and responded. Despite several unsuccessful attempts at plasmapheresis (due to marked venospasm), her gangrene progressed and she underwent three amputations over a short period of time (a B-K amputation of left leg, an A-K amputation of right leg, and amputation of digits 2 & 3 of right hand). Postoperatively she was febrile, oliguric and probably had a micro-angiopathic hemolytic anemia. She died approximately 10 months after the onset of her initial symptoms. Permission for an autopsy was denied.

Comment. This patient illustrates the prominent cold-dependent symptoms associated with single component IgG cryoglobulin present in relatively low concentration (100-200 mg%) but with a low solubility curve. Cryoglobulin-inclusion polymorphonuclear leukocytes were originally misdiagnosed as L.E. cells.

Case 2. [redacted]). The patient was a 32 YO [redacted]. In 1955, he noted the onset of recurrent, episodic purpura of the feet and ankles. These episodes occasionally were accompanied by a feeling of coldness and numbness of the left foot, but at first there was no relation to exposure to cold. Two years later when the patient was working in and out of a cold storage vault, the purpura became worse and ulcers appeared at the purpuric sites. Left lumbar sympathectomy and splenectomy were performed in [redacted], 1957, with a subsequent short remission in purpura and healing of the ulcers.

During 1958, the episodes of purpura increased in frequency and severity, especially during the winter. Severe, recurrent epistaxis also became a problem. About this time, the patient began to have a persistent four plus proteinuria. A percutanous liver biopsy showed no pathologic alterations.

In [redacted], 1960, the patient experienced an acute episode of chills, fever, vomiting, and low back pain which radiated into the posterior portions of the thighs. Urinalysis at this time showed four plus protein, gross hematuria, 10-15 white blood cells, and many waxy, granular, and hyaline casts per high power field. He was thought to have a urinary tract infection and was treated with antibiotics. The symptoms cleared in 72 hours but recurred about two weeks later. Blood and urine culture tests were negative on both occasions. A percutaneous renal biopsy showed "subacute and chronic glomerulonephritis consistent with cryoglobulinemia." A bone marrow aspiration contained 14 per cent plasma cells with features suggesting a dysproteinemia but not multiple myeloma. A radiologic bone survey revealed no lesions. Cryoglobulins were present in the serum and these were of the 7S gamma globulin type. The cryocrit was 2 per cent on admission and following five plasmaphereses the cryocrit was zero at discharge. Subsequent to the plasmaphereses the purpuric lesions of the lower extremities cleared rapidly. Shortly after discharge, the patient noted the development of a painful nodule in the third right intercostal space adjacent to the sternum. The pathologic diagnosis upon biopsy in February, 1961, was "nonspecific chronic inflammation." Cryocrit at this time was 4.5 per cent.

Later in [redacted] the patient again had chills, fever and low back pain. For the first time, purpura with ulceration occurred at sites other than the feet and ankles. They were now present on both ears and on the scrotum. Diagnoses of pneumonia, septicemia, and meningitis due to *Diplococcus pneumoniae* were established, but with antibiotic therapy the patient slowly recovered. Plasmapheresis was again performed and the ulcers of the feet, ears, and scrotum healed.

The patient remained relatively well for several months; but in [redacted], 1961, he began to have severe frontal headaches. The blood pressure which had always been normal, became intermittently elevated to 140/110 mm of mercury. In [redacted], 1961,

he began to have severe "asthma attacks." Increasing azotemia was noted, and the headaches became more frequent and severe. Urinalysis at this time showed one plus to four plus proteinuria and varying red blood cells and casts. Beginning in [redacted], 1961, the patient's condition deteriorated rapidly. Cryoglobulins again increased despite prednisolone therapy, headaches became continuous despite the administration of narcotics, the blood pressure remained elevated and the blood urea nitrogen (BUN) remained around 50 mg per 100 cc. Urine protein fell to one plus with numerous waxy, hyaline and granular casts.

In [redacted], 1962, the patient was admitted for the last time. During this admission, the syndrome of malignant hypertension was present, with diastolic pressures as high as 148 mm of mercury. The patient was administered hypotensive agents, plasmapheresis, and 6-mercaptopurine therapy in an attempt to control the cryoglobulin levels. This therapy was not successful and the patient died one month after the last hospital admission.

Comment. A young male with "essential" IgG cryoglobulin and a clinical picture characterized by purpura, gangrene and glomerulonephritis.

Case 3. [redacted]H. was a sixty-six year old [redacted] woman, was well until [redacted], 1958, when she noted the onset of pain and stiffness in the lower extremities. This was followed by gradual darkening of the skin over the lower extremities. In [redacted], 1958, she complained of a persistent "cold" and was given a penicillin injection by her private physician. This was followed one day later by a generalized macular rash which cleared spontaneously. Several days later the patient sustained hip and leg bruises and a fractured rib in an automobile accident. She was observed in the hospital and discharged. She remained well for ten days when she was admitted to another hospital in shock, having fainted while working at home. Physical examination revealed acute respiratory distress, bilateral moist rales and bilateral costovertebral angle tenderness.

Laboratory studies on admission revealed a sodium concentration of 159 mEq. per L.; chloride 118 mEq. per L.; carbon dioxide, 42 volumes per cent; potassium, 2.5 mEq. per L.; and blood urea nitrogen, 8 mg per cent; non-fasting blood sugar, 236 mg per cent. There was 1+ albuminuria. Electrocardiogram showed supraventricular arrhythmia and evidence of recent subendocardial injury. Roentgenograms revealed pleural effusions and hiatus hernia.

The patient was given respiratory assistance and intravenous fluids containing potassium. She rapidly became more alert and strength gradually returned during the next twelve days. At the time of discharge the lungs were clear and the electrocardiogram was normal. The serum electrolyte pattern also was normal.

After discharge the patient continued to feel well for two months and then noted increased thirst, weakness and urinary frequency. This was followed by nausea and vomiting, which led to her admission to [redacted] in [redacted], 1958.

At that time physical examination revealed an elderly, pale and lethargic white woman with a blood pressure of 160/90 mm Hg; pulse rate, 68; respirations, 24; and oral temperature of 97.4°F. The only significant physical findings were the presence of right costovertebral angle tenderness, hyperactive bowel sounds and a brownish pigmentation over the legs.

The laboratory data on admission showed hemoglobin, 8.5 gm per cent; hematocrit, 27 per cent; leukocyte count, 15,400 per cu mm; polymorphonuclear leukocytes, 92 per cent; monocytes, 2 per cent; and lymphocytes, 6 per cent; platelet count, 388,000 per cu mm; urinalysis, pH 7.5; specific gravity, 1.002; albumin, sugar, cells and casts absent. The urine was negative for Bence Jones protein. Significant aminoaciduria was absent. Urine culture revealed more than 500,000 Escherichia coli per ml. The reaction to the Kline and serologic tests for syphilis was weakly reactive; the Wassermann test anticomplementary; Treponema pallidum immobilization test, negative. The fasting blood urea nitrogen was 18 mg. per cent; creatinine, 3.5 mg. per cent; blood sugar, 126 mg. per cent; carbon dioxide, 23.3 volumes per cent; arterial pH, 7.33; chloride, 107 mEq. per L.; sodium, 140 mEq. per L.; potassium, 2 mEq. per L.; calcium, 9.5 mg. per cent; and phosphorous, 3.3 mg. per cent. The serum total protein was 10.2 gm. per cent with 4.2 gm. per cent albumin and 6 gm. per cent globulin. The result of the cephalin flocculation test was 2 plus; thymol turbidity, 26.7 units; alkaline phosphatase, 3.4 Bodansky units; and bromsulfalein retention, 4 per cent. Glucose tolerance test revealed a mildly diabetic curve. The prothrombin time was 100 per cent. A lupus erythematosus cell test result was negative. The serum was strongly positive for cryoglobulins. Paper electrophoresis showed albumin, 3.7 gm. per cent; α-globulin, 0.37 gm. per cent; α-2 globulin, 1.2 gm. per cent; β-globulin, 1.07 gm. per cent; and γ-globulin, 3.7 gm. per cent. The γ-globulin peak was relatively non-disperse but showed no discrete component. Multiple aspirations of sternal and iliac crest marrow showed approximately 5 per cent plasma cells. Roentgenograms revealed only generalized osteoporosis.

The diagnosis of renal tubular acidosis with cryoglobulinemia was made. Therapy consisted of sedation, the administration of intravenous fluids, supplementary potassium and antibiotics for the infection of the urinary tract. The patient responded well and the electrolyte pattern reverted to normal. Recovery was uneventful except for the passage of a renal stone.

Comment. This case represents the first report of a mixed, IgM-IgG cryoglobulin. The only feature compatible with the syndrome of essential mixed cryoglobulinemia was the presence of hyperpigmentation in the lower extremities. This patient also represents one of the two known cases with concomitant renal tubular acidosis.

Case 4. [redacted]): This 49 year-old [redacted] from Dallas was admitted on [redacted]/69 with symptoms of CHF which became symptomatic about 1 week prior to admission. She denied any previous hypertension, renal disease and heart disease. She had never had arthritis, arthralgias, Raynaud's phenomena, purpura or recent febrile episodes.

Past History: Penicillin allergy. Hysterectomy for "tumor" in 1965 at Baylor.

Review of Systems: No history of lymphadenopathy, anemia or malignant disease, i.e., leukemia, etc. She had had an erythematous rash on her feet in 1955, treated in the EOR.

Her SH and PH are non-contributory.

On admission, her exam revealed BP 210/110, P 90 and regular, afebrile. She had no rash, urticaria, purpura or lymphadenopathy. Her fundi revealed an exudate in OD without hemorrhages. JVP increased at 45° with bilateral dullness and rales at the bases. She had cardiomegaly with S_3 gallop and ii/vi apical systolic murmur. She had 8 fb hepatomegaly without palpable spleen. The extremities revealed 2+ pitting edema with intact peripheral pulses. Her neurological exam was normal.

X-ray: Generalized cardiomegaly with increased pulmonary vasculature and bilateral pleural effusions.

EKG: Borderline 1° AV block. NSSTT changes.

Laboratory: Hgb 9.9 to 7.1, Hct 28.6 to 22.7. WBC 5900. ESR 85, retics 2.3, 3.5, 1.8. Platelets 198,000. Sickle prep negative. Peripheral smear revealed mild polychromasia, schistocytes, burr cells and helmet cells. Bone marrow: erythrocytic hyperplasia with stainable iron with mild plasmacytosis. Pro time, PTT and thrombin time, within normal limits. Urinalysis: pH 5.0, sp.gr. 1.021, 300 mg% albumin without sugar or acetone. 30-40 RBC, 5-10 WBC and 5-10 hyaline casts, RBC casts. 24-hour urine protein 2 gm and 1 gm with creatinine clearance of 63-68 cc/min. Urine culture, sterile. IVP, decreased excretion bilateral, left >right. VDRL 2 dilutions, FTA positive. Stool guaiac negative X3. BUN 35 to 55 to 24. Creatinine 1.5 to 1.9 to 1.0. Electrolytes WNL. CT 10 seconds, VP 20. LFTs WNL. Coombs negative X2. Serum protein electrophoresis, albumin 2.20, gamma G 0.70. No monoclonal spike. ANA negative X4. ASO titer >50. Reactive latex fixation. Renal biopsy: Increased mesangial cellularity with isolated glomerular capillary fibrinoid necrosis which stained positive for trichrome subendothelially. Basement membrane WNL. Vessels, unremarkable.

Diagnosis: Diffuse glomerulonephritis compatible with capillary loop fibrinoid necrosis with a connective tissue disorder.

Course in Hospital: She responded rapidly to digitalization and diuresis with compensation of her CHF. She was thought to have a connective tissue disorder, specifically SLE, and was treated with Cytoxan 100 mg q.d. but leukopenia forced withdrawal of this drug.

After discharge, the rheumatology group noted her high SSCA of 1:3584, latex 4+ positive and consistently low serum complements beta-1-C in the 60-80 mg% range. Hemolytic complements are also consistently low. She was found to have an IgG-IgM cryoglobulin with a serum concentration of 200 mg%.

Comment: A patient with essential mixed IgM-IgG cryoglobulinemia. Renal disease, hypertension and congestive heart failure were the presenting features but several months later she developed the typical purpuric rash of the lower extremities. She also had "autoimmune" features such as circulating antibodies directed against her own leukocytes, perhaps accounting for the leukopenia.

Case 5. [redacted] This was one of many [redacted] admissions for this 53 year-old [redacted] woman. This patient had an extremely long and complicated course covering 13 years and 1400 pages of medical records. A brief chronological summary follows:

In 1958 the patient had a total gastrectomy and splenectomy for lymphosarcoma at a local hospital. The patient received post-op. irradiation and no evidence of recurrence was found.

In 1960 the patient had a total thyroidectomy for thyrotoxicosis.

In [redacted], 1969, the patient was found to have a gram-negative RML and RLL pneumonia. The pneumonia was treated with Keflin and kanamycin. The patient developed a neurosensory hearing loss secondary to kanamycin. She was found to have a mixed B_{12} and iron deficiency anemia treated by Fergon and Vitamin B_{12} IM. Her PBI was 1.9 and she was treated with thyroxine.

In [redacted], 1969, the patient was admitted for her second episode of gram-negative pneumonia. She was found to have leg ulcerations compatible with a vasculitis suggestive of cryoglobulinemia. Cryocrit was 5%.

In [redacted], 1969, the patient was admitted for workup of recurrent lymphosarcoma. An extensive workup was negative including negative bone marrows, liver scan, bone survey, IVP, UGI, BE, and node biopsies.

In [redacted], 1969, the patient again had leg ulcerations and superficial phlebitis. Cryoglobulins were identified as mixed IgM and IgG.

In [redacted], 1969, the patient was found to have positive latex fixation, sensitized sheep cell agglutination, a cold area on liver scan and was considered for treatment with Penicillamine, Cytoxan, or steroids.

In [redacted], 1969, the patient was admitted with RML pneumonia with bulging of the fissures; Klebsiella was isolated and the patient was treated with Keflin and chloramphenicol. Immunoglobulins were quantitated: IgG - 320 (nl 800-1600), IgM 26.5 (nl 50-200), and IgA 170 (nl 340). Complement was 155. Anergy to all skin tests including mumps was found. She failed to respond with antibody to repeated typhoid injections.

In [redacted], 1970, the patient was admitted with a RML and RLL pneumonia which responded to erythromycin. No organism was grown.

In [redacted], 1970, she was admitted with RUL pneumonia and was treated with erythromycin and plasmaphoresis. The immunoglobulins were unchanged but the complement was 30 U. T_4 was 0.6 mcgm% while on 0.3 mg thyroxine/day. She was begun on gamma globulin q three weeks.

In [redacted], 1970, she was admitted for bronchitis and Klebsiella and Pseudomonas were isolated. Antibiotics used are not known.

In [redacted], 1971, the patient received her last gamma globulin shot and failed to return. She had no episodes of pneumonia during the eight months she was on gamma globulin.

In [redacted], 1971, the patient was admitted with RML pneumonia and the cultures were positive for pneumococcus. Immunoglobulins revealed IgG 300, IgA 125, IgM 123. The patient's pO_2 was consistently around 40. T_4 was 2.4 and her thyroxine was increased to 0.4 mg/day. Her pneumonia was treated with Keflin and chloramphenicol.

Last admission, [redacted], 1971: The patient was admitted on [redacted] 1971, with progressive shortness of breath, orthopnea, and pedal edema. She denied cough, sputum production, hemoptysis, fever, chills, or anorexia. She has gained 4-1/2 lbs. since discharge three weeks previously. A chest film performed in clinic on the day of admission, revealed a persistent RML infiltrate and a new LLL infiltrate and left pleural effusion.

Physical exam revealed T 98^2, P 80, R 24, BP 106/60. There were skin ulcerations on the right leg. Head, eyes, ears, nose and throat were all normal. Examination of the lungs re-

vealed no dullness. There were tubular breath sounds in the right axilla and rales in the left base. The heart was not enlarged with no murmur or gallop. Abdominal exam revealed no organomegaly or masses. There was 3+ pedal edema.

The hospital course was marked by a falling hematocrit, a rising BUN, and a rising WBC. No evidence of blood loss could be found. Peripheral blood smears revealed burr cells and fragmented red blood cells. The BUN progressively rose with a urine output of 500-1500 cc/daily. A renal biopsy was interpreted as proliferative glomerulonephritis. Peritoneal dialysis was performed in the last week. The patient remained afebrile until the last 48 hours. Though afebrile, the patient had a progressively rising WBC from 8,000 on admission to 32,000, five days before death and fell during the last five days in response to Cytoxan and steroids. Numerous blood cultures, biopsy cultures, urine cultures, throat cultures, and sputum cultures grew only normal flora. Terminally the patient developed a LUL pneumonia with Gram positive cocci in lumps on smear and was treated with Staphcillin and gentamycin. The patient also had a recurrent left pneumothorax requiring chest tubes. A liver biopsy was reported with "changes consistent with lymphoma." She failed to respond to antibiotics, dialysis and oxygen and expired on the 38th hospital day.

Comment: A patient with mixed IgM-IgG cryoglobulinemia with leg ulcers and skin vasculitis as the only manifestation of her disease for two years. She developed severe hypogammaglobulinemia and rapidly progressive glomerulonephritis in the last two months of her life.

TABLE I

THE CRYOPATHIES (2)

1. Cryoglobulinemia
2. Cryofibrinogenemia
3. Cold agglutinin syndrome
4. Cold hemolysin syndrome

} Paroxysmal cold hemoglobinurias

5. Cold urticaria
6. Raynaud's disease
7. Occlusive arterial disease
   - Arteriosclerosis
   - Thromboangiitis obliterans
   - Arterial embolism
8. Connective tissue diseases
   - Systemic lupus erythematosus
   - Rheumatoid arthritis
   - Scleroderma
   - Polyarteritis nodosa
   - Dermatomyositis
   - Sjögren's syndrome
9. Skin disorders
   - Perniosis (chillblains)
   - Cold panniculitis
   - Idiopathic acrocyanosis
   - Erythrocyanosis
   - Cold erythema
   - Livedo reticularis
   - Neonatal cold injury
10. Neurologic and neurovascular lesions
    - Pituitary and hypothalamic tumors
    - Diencephalic epilepsy
    - Post-sympathectomy syndrome
    - Shoulder-girdle compression syndromes
11. Occupational diseases
    - Raynaud's phenomenon in pneumatic drill operators, pianists, typists, creamery workers
12. Others
    - Heavy metal poisoning (lead, arsenic)
    - Ergotism
    - Familial periodic paralysis
    - Myxedema
    - Primary pulmonary hypertension

TABLE II

CRYOPROTEINS

1. Plasma fraction I-1 (6)
2. C-reactive protein-albumin complex (7)
3. Cryofibrinogens (8-10)
4. Cryoglobulins

TABLE III

CRYOFIBRINOGENEMIA (2)

1. Primary
2. Secondary to or associated with
   a. Malignancy
   b. Myeloproliferative disorders
   c. Infections
   d. Normal pregnancy
   e. Pre-eclampsia
   f. Connective tissue diseases
   g. Myocardial infarction
   h. Miscellaneous

TABLE IV

	Cryoglobulin	Cryofibrinogen
Serum	+	-
Plasma	+	+

TABLE V

INCIDENCE OF CRYOGLOBULINEMIA (11)

	Number	Per cent Positive
Blood donors	623	1.3
Various diseases*	281	4.0

*All adult patients admitted to the hospital during February, 1969.

TABLE VI

COMPOSITION OF CRYOGLOBULINS

A. Pure or single component
   1. IgG
   2. IgM
   3. Bence-Jones protein (L chains)

B. Mixed
   1. IgM + IgG
   2. IgA + IgG
   3. IgM + IgA + IgG

TABLE VII

DISEASES ASSOCIATED WITH CRYOGLOBULINEMIA

A. Essential or Idiopathic

B. Dysproteinemias
   1. Multiple Myeloma
   2. Macroglobulinemia
   3. Chronic Lymphatic Leukemia and Lymphoma
   4. Chronic Liver Diseases

C. Abnormal Immunity
   1. Systemic Lupus Erythematosus
   2. Rheumatoid Arthritis
   3. Ankylosing Spondylitis
   4. Sjögren's Syndrome
   5. Thyroiditis
   6. Sarcoidosis

D. Intense Antigenic Stimulation
   1. Subacute Bacterial Endocarditis
   2. Acute Glomerulonephritis
   3. Syphilis
   4. Leprosy
   5. Infectious Mononucleosis
   6. Cytomegalovirus Infection

TABLE VIII

SINGLE COMPONENT CRYOGLOBULINEMIA (18)

Diagnosis	Cryoglobulin		Symptoms
	Type	Concentration gm%	
Multiple Myeloma	IgG	1.5	0
Multiple Myeloma	IgG	1.7	0
Multiple Myeloma	IgG	1.1	0
Multiple Myeloma	IgG	0.3	0
Essential	IgG	2.8	3+
Essential	IgG	1.5	3+
Liver Cirrhosis	IgG	0.04	1+
Purpura	IgG	0.03	1+
Lymphatic Leukemia	IgM	1.7	0
Lymphosarcoma	IgM	2.0	2+
Lymphosarcoma	IgM	0.8	0
Lymphosarcoma	IgM	1.4	0
Lymphosarcoma	IgM	1.2	0
Lymphosarcoma	IgM	0.5	0
Lymphosarcoma	IgM	2.5	0

TABLE IX

SYMPTOMS

A. Cold Dependent Phenomena

1. Raynaud's phenomenon
2. Peripheral gangrene
3. Cold urticaria
4. Livedo reticularis, cutis marmorata

B. Hyperviscosity Syndrome

1. Mucosal bleeding
2. Thrombosis
3. Congestive heart failure
4. Deafness
5. Vertigo
6. Loss of vision
7. Cerebrovascular accidents

C. Immune Complex Disease

1. Vasculitis (purpura, leg ulcers)
2. Arthritis, arthralgia
3. Glomerulonephritis

D. Other Manifestations

1. Renal tubular acidosis
2. Nephrotic syndrome
3. Hypogammaglobulinemia

TABLE X

INCIDENCE OF CRYOGLOBULINEMIA (11)

	Number Tested	Per Cent Positive
Blood donors	623	1.3
Various diseases	281	4.0
Suspected "autoimmunity"	4130	19.0
S.L.E.	28	68.0

TABLE XI

DISEASES ASSOCIATED WITH MIXED CRYOGLOBULINEMIA (11)

Diagnosis	Number
Purpura-Arthralgia Syndrome	19
S.L.E.	20
Juvenile Rheumatoid Arthritis	13
Connective Tissue Diseases	13
False-positive Serology	11
Syphilis	9
Infectious Mononucleosis and CMV	8
Bacterial Infections	9
Other Diseases	18
Total	120

TABLE XII

CORRELATION BETWEEN PRESENCE OF CRYOGLOBULINS AND SERUM C3 LEVEL IN PATIENTS WITH SLE (55)

Cryoglobulins	No.of Patients	Serum C3 (mg%)		
		0-69	70-99	100-300
Present	11	8	2	1
Absent	25	1	2	22

TABLE XIII

CLINICAL FEATURES OF NINE PATIENTS WITH MIXED CRYOGLOBULINEMIA (41)

Age and Sex	Cryoglobulin Concentration mg%	Arth-ralgia	Pur-pura	Hepato/ Splenomegaly	Renal Disease Onset Prior To Death
49, F	140	3+	3+	+	6 months
43, F	80	2+	2+	+	-
48, F	130	3+	3+	+	3 weeks
45, F	90	2+	3+	+	-
63, M	120	1+	3+	+	3 weeks
54, F	110	2+	3+	+	-
61, F	90	2+	3+	+	-
29, F	90	3+	3+	+	-
55, F	80	3+	3+	+	-

TABLE XIV

THE SYNDROME OF MIXED CRYOGLOBULINEMIA

Purpura

Arthralgias, Arthritis

Glomerulonephritis

Hepatosplenomegaly

Lymphadenopathy

Rheumatoid Factor

Hypocomplementemia

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