MEDICAL GRAND ROUNDS

PARKLAND MEMORIAL HOSPITAL

March 18, 1965

THE KIDNEY IN POLYARTERITIS

Case No. 1 - [redacted]

A 31-year old [redacted] woman was admitted complaining of a rash on her leges of a days duration. A week prior to admission she experienced a mild sore throat accompanied by a chill and fever, all of which subsided spontaneously without specific therapy in several days. She felt well until the day prior to admission when the nonpruritic rash over her legs and ankles began. The onset of the rash was quickly followed by intermittent cramping periumbilical pain. These symptoms were accompanied by vomiting, slight swelling of the lower extremities, together with pain in the shoulders, elbow and knee joints.

Past History: There had been a transient urticarial skin rash 6 months prior to admission.

Examination: The patient was complaining of abdominal pain, but was not otherwise in distress. Physical examination revealed a blood pressure of 115/70, pulse of 100, respirations 16, and a temperature of 99°F. The fundi were not remarkable. There was no neck-vein distention. The chest was clear. The heart was not enlarged. There was a mild generalized tenderness of the abdomen, but no organs were palpable. The right shoulder and elbow were slightly tender but were neither red nor swollen. A purpuric and ecchymotic, discrete and confluent, skin eruption was noted over the legs, posterior aspects of the thighs, and buttocks. There was slight ankle edema.

Laboratory Results: Hgb 11.4 gm%; HCT 35%; WBC 13,850 with 84% segs; 14% lymphs, 2% monos. The platelet count, bleeding, and clotting times were normal.

Urinalysis: Specific gravity 1.022; protein trace; sediment; 5-10 WBC and 200 RBC/HPF. There were occasional granular and red blood cell casts. BUN was 13 mg%. All other blood chemistries (electrolytes and liver functions) were normal. Stool had 4 + guaiac reaction; ASO 166 Todd units.

Hospital Course: There was no specific therapy. There was no evidence of a venous congestion at any time. During the first few days, her abdominal symptoms subsided and her rash began to resolve. She continued to have microscopic hematuria for the first 4 days and her BUN rose to 30 mg% (creatinine 1.5 mg%). At the time of discharge (8 days), she was symptom-free without azotemia. Urinalysis disclosed a trace of albumin as the only abnormality.

Skin biopsy disclosed an arteritis; disintegrated nuclear fragments were present.

Renal biopsy revealed a focal glomerulonephritis with mesangial and endothelial proliferation with some neutrophilic infiltration. Of great interest, was the finding of one afferent arteriole with a distinct exudate vasculitis. Here, there was a marked neutrophilic, and slight lymphocytic and eosinophilic infiltration with nuclear fragments.

Case No. 2 - [redacted]

The patient was a 59-year-old [redacted] woman who was admitted because of a skin rash, hypertension, and azotemia. Three months prior to this admission, she presented to the EOR with a history of personality changes with headached of about 2 months duration, and a left-sided weakness of about 24 hours duration. In the EOR, she had a grand mal seizure. Ultimately, a history of

hypertension of about 10 months duration was obtained. Examination at that time revealed a blood pressure of 180/112; fundi disclosed arterial narrowing and there was weakness, particularly in the left upper extremity. The weakness quickly subsided and she was considered to have no neurological findings by the second day. Despite this, an EEG demonstrated signs of a possible right-sided mass. An angiotensin infusion test disclosed increased reactivity. She was discharged improved on guanethedine and dilantin.

Her course was not remarkable until some 2 months after admission, when in the clinic, she was noted to have a pruritic skin rash. Her family thought her "mind had failed". Some 20 days after this, she had a chill and was returned to the EOR. At this time, a papular erythematous rash was noted and a BP of 80/56 were noted. Guanethedine was discontinued. She was seen in clinic 4 days later where the rash was said to exhibit vesicles. Dilantin was stopped and epinephrine and benadryl were given. Two days later, because of abdominal pain and dysphagia she was admitted.

Important findings included numerous erythematous non-tender macules over the upper and lower extremities and upper trunk. The blood pressure was 107/70. The patient was disoriented. The mouth was bloody and the tongue beefy red. Tenderness prevented adequate examination. The heart and chest were not remarkable. There was a mild generalized tenderness of the abdomen; no organs were felt. Aside from some periorbital edema, there was no peripheral edema.

Initial blood chemistries revealed a BUN of over 200 mg% accompanied by an acidosis and hyperkalemia. Peritoneal dialysis was instituted. Prednisone, 60 mg daily, was started the next day. Severe oliguria developed which was not corrected by volume expansion. However, her mental status and rash did appear to respond, presumably, to dialysis and steroid therapy. Urine volume ultimately reached 800 cc/day. However, after stopping dialysis, azotemia returned and on the 10th admission day peritoneal dialysis was reinstituted. On the 14th day she had fever (102°R) and became jaundiced and hypotensive. Despite measures directed at a septacemia, she had a downhill course and expired on the 18th day after repeated generalized seizures.

Skin biopsy at the site of the rash on the second hospital day included muscle and showed a vasculitis of the dermis with fibrinoid necrosis and an arteritis without fibrinoid of an arteriole in the muscle.

Autopsy revealed splenic infarct without evidence of vasculitis and the kidneys were compatible with changes of malignant hypertension with the more unusual finding of perivascular inflammatory reaction around arterioles and interlobular arteries. These lesions were thought, in review, to be compatible with nearly healed periarteritis. No gross lesions of periarteritis nodosa were found. No vascular lesions of the gastrointestinal tract were seen.

Case No. 3 - [redacted]

About two weeks prior to admission, this 22-year-old [redacted] man received penicillin for a sore throat and fever. His throat quickly improved, but about a week later he developed flank pain with some dysuria and noted dark urine. Because these symptoms persisted, he visited another M.D. who gave penicillin both orally and parenterally. Because of albuminuria, the M.D. referred the patient to [redacted] for admission two days later. There was no history of dyspnea or orthopnea.

Examination disclosed a BP 174/110, temperature 101°F. Fundi showed segmental arterial narrowing. The chest was clear. The heart was at the upper limits of normal size. Abdomen was not remarkable except for mild tenderness in the right upper quadrant. There was bilateral CVA tenderness. No pitting edema of extremities or sacrum was present.

Laboratory Results: There was a mild venous congestive state as evidenced by VP 19 cm and CT 15 seconds. Hgb 12.2 gm%, WBC 25,000 (76 segs., 3 bands, 8 lymphs, 3 eosin). Sed. rate 55 mm. Urinalysis: Specific gravity 1.012, proteinuria 3 +, sediment with many RBC and WBC with hyaline, granular and red blood cell casts. BUN was 74 mg%; creatinine 4.7 mg%. Bilirubin

1.7 mg%; BSP 31% with other liver function studies normal. Creatinine clearance 8 ml/min.

Hospital Course: About 5 days after admission, a pruritic, urticarial skin rash developed which later became hemorrhagic. Skin biopsy disclosed a vasculitis involving the arterioles of the superficial dermis.

Oliguria was present and worsened, and peritoneal dialysis was required. Prednisone, 100 mg/day, was begun after receiving the results of the skin biopsy and continued at this dose for 20 days. It was then slowly reduced in dosage over the next two weeks. Hypertension was controlled with Aldomet and reserpine. A slow diuresis began shortly after Prednisone was started.

ASO titers were 250 Todd units. An anti-hyaluronidase titer of 1024 was obtained, however. At discharge, the patient had modest hypertension and a creatinine of 2.2 mg%. Urinalysis disclosed a trace of protein with the sediment containing few WBC, many of which were eosinophils, and few RBC. Creatinine clearance was 50 ml/min.

Renal Biopsy: Two biopsies were done. Unfortunately, only one glomerulus was obtained, but this was studied by both light and electron microscopy. In this glomerulus there was marked mesangial and endothelial cell proliferation. The basement membrane was slightly thickened. There was also a modest proliferation of the epithelial cells lining Bowman's capsule. In addition, on the electron microscope preparations, one small vessel, probably an arteriole, was seen to have subendothelial deposits probably representing fibrinoid.

In the medullary portion of the biopsy obtained just after steroids were started, there was a polynuclear and lymphocytic interstitial infiltrate that included some eosinophils which appeared to be primarily around capillaries. The lumens of the vessels were, for the most part, closed, presumably, because of endothelial swelling. Other larger vessels were not involved in the inflammatory processes.

The second biopsy was obtained near the end of steroid therapy. The basic change was almost complete clearance of the inflammatory process as described above. No glomeruli were obtained on this biopsy.

Classifications of Angiitis

Table I

From Zeek: References 5,6, and 7.

Five Types of Necrotizing Angiitis

1. Periarteritis Nodosa - A recurrent, progressive, necrotizing, inflammatory disease of muscular type arteries. Frequently, a complication of severe hypertension. Polyneuritis, fever, and "multiple system disease" are common.

2. Hypersensitivity Angiitis - An acute necrotizing inflammation of the smallest branches of blood vessels, arteries and veins. Affects viscera, connective tissue and skin. Renal death common.

3. Rheumatic Arteritis.

4. Allergic Granulomatous.

5. Temporal Arteritis.

Table 2

From Rose: References 17 and 18.

1. Polyarteritis with lung involvement - Usually begins as a respiratory disorder. Eosinophila common. Hypertension uncommon. No family history of asthma or hay fever.

2. Polyarteritis without lung involvement - Severe renal involvement common. Hypertension common. Not caused by hypertension.

Table 3

From Allen: Reference 21

1. Periarteritis Nodosa - Renal failure common. Produces hypertension.

2. Allergic Angiitis - Characteristics: a) history of asthma, b) normal or only moderately elevated blood pressure, c) myocardial involvement, d) drug history.

Table 4

From Goldberger: Reference 22.

1. Lesions of muscular arteries - Seen at hila of viscera, in striated muscle and at bifurcations and branchings of vessels. No lesions in pulmonary arteries or spleen.

2. Microscopic arteriolar lesions - Heart, kidneys, and pulmonary vessels involved. All lesions appear the same age.

3. Extravascular lesions - Found in all organs, lung included. Frequent alterations in collagen with eosinophils and sometimes granulomas.

Renal Involvement

Table 5

Pathology: References 23-30.

1. Arteritis lesions:

   a) May involve all sizes of vessels from renal artery to capillaries.
   b) Large aneurysmal lesions have resulted in kidney rupture.
   c) May not be present even in most severe forms of disease.
   d) Healed lesions show fibrotic changes with minimal or no inflammation. Renal infarcts may be present.

2. Glomerular lesions:

   a) Present often without arteritis.
   b) Involvement tends to be both focal and lobular.
   c) Histology reveals mesangial and endothelial proliferation frequently with an acute exudate and necrosis. May have crescents as well as sclerosed glomeruli.
   d) Less commonly, periglomerular granulomas present.

Table 6

Clinical Manifestations of Renal Involvement

References 36-40

1. Early - Only evidence may be mild proteinuria.

2. Urine sediment ultimately has a nephritic picture (red cells with red cell casts). May have "telescoped" sediment. In stained sediments, eosinophils may be identified. Severe gross hematuria has been reported.

3. In arteritis form with gross lesions, hypertension usually severe.

4. Glomerular lesions - Mild hypertension; modest azotemia; edema and venous congestive state follow.

5. Oliguric renal failure with uremia common.

6. Healing of arteritic lesions may be accompanied by severe hypertension.

7. Manifestations other than renal:

a) Fever
b) Leukocytosis
c) Rapid ESR
d) Arthralgia and arthritis
e) Abdominal pain and tenderness
f) Muscle pain
g) Palpable nodules
h) Neuritis
i) Skin rash
j) Asthma
k) Eosinophilia
l) Weight loss

Table 7

List of Drugs that have Caused Arteritis

References 46-53

Penicillin
Chloramphemicol
Streptomycin
Sulphonamide
Organic Arsenics
Barbiturates
Uracil Compounds
Chlorpromazine
Hydantoin derivative
Iodides
Bismuth, Mercury, Gold
Hydralazine
Quinidine
Guanethidine

Probably not a complete list.

Table 8

	No. of Patients	Dead	Alive	Follow-up Years
Johnsson and Leonhardt Reference 62	41	21*	20†	2 to 3
Shick Reference 63	30	9	21‡	1 to 5
British Medical Council Reference 65	21	11**	7	3

* 10 patients died in acute stage.
† 3 patients survived with improvement.
‡ Some of these patients only "adequately suppressed".
** 9 deaths in acute stage.

REFERENCES

1. Smith, C.C., Zeek, P.M., and McGuire, J. Periarteritis nodosa in experimental hypertensive rats and dogs. Am. J. Path. 20:721, 1944.

2. Smith, C.C., and Zeek, P.M. Studies on periarteritis nodosa. II. Role of various factors in etiology of periarteritis nodosa in experimental animals. Am. J. Path. 23:147, 1947.

3. Zeek, P.M., Smith, C.C., and Weeter, J.C. Studies on periarteritis nodosa. III. Differentiation between vascular lesions of hypersensitivity. Am. J. Path. 24:889, 1948.

These three papers describe experimental studies in rats, rabbits and dogs, and form the basis of Zeek's primary thesis that hypertension may lead to periarteritis nodosa.

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4. Thompson, R.T., and Zeek, P.M. Acute necrotizing angiitis due to hypersensitivity following sulfonamide therapy. Ohio Med. J. 41:824, 1945.

A description of a case with severe renal involvement. Authors conclude that hypersensitivity angiitis can occur in response to sulfa therapy as Rich described.

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5. Zeek, P.M. Periarteritis nodosa. A critical review. Amer. J. Clin. Path. 22:777, 1952.

6. Knowles, H.C., Zeek, P.M., and Blankenhorn, M.D. Studies on necrotizing angiitis. IV. Periarteritis nodosa and hypersensitivity angiitis. Arch. Int. Med. 92:789, 1953.

7. Zeek, P.M. Periarteritis nodosa and other forms of necrotizing angiitis. New Eng. J. Med. 248:764, 1953.

Reference No.7 is now probably the most quoted paper on periarteritis nodosa. (See Table 1). Unfortunately, although these papers are intended as more clinical than pathological, there is very little clinical information given. The evidence does not seem sufficiently strong to prove that hypertension leads to periarteritis nodosa.

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8. Rich, A.R. Role of hypersensitivity in periarteritis nodosa as indicated by seven cases developing during serum sickness and sulfonamide therapy. Bull. Johns Hopkins Hosp. 71:123, 1942.

In 1925 Gruber was the first to suggest that periarteritis nodosa might be an allergic disease. The seven patients described here would appear to be clear-cut examples of allergic arteritis. Zeek always denied they had true lesions of periarteritis nodosa.

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9. Rich, A.R., and Gregory, J.E. Experimental demonstration that periarteritis nodosa is a manifestation of hypersensitivity. Bull. Johns Hopkins Hosp. 72:65, 1943.

Experimental evidence for the production of arteritis. Zeek maintained she could not reproduce these experiments. Since then, however, many people have. (See Ref. 12).

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10. Rich, A.R. Hypersensitivity in disease with especial reference to periarteritis nodosa, rheumatic fever, disseminated lupus erythematous and rheumatoid arthritis. Harvey Lectures 42:106, 1946-1947.

11. Rich, A.R. The pathology and pathogenesis of experimental anaphylactic glomerulonephritis in relation to human acute glomerulonephritis. Bull. Johns Hopkins Hosp. 98:120, 1956.

Reference 11 has beautiful photographs of the experimental lesions. Vascular lesions resemble periarteritis closely.

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12. Van Zandt, C.H., and Janeway, C.A. Histological and serological sequences in experimental hypersensitivity. J. Exp. Med. 85:571, 1947.

13. Stefanini, M., and Mednicoff, I.B. Demonstration of antivessel agents in serum of patients with anaphylactoid purpura and periarteritis nodosa. J. Clin. Invest. 33:967, 1954. (Abstract)

14. Lockhmann, P.J., Muller-Eberhard, H.J., Kunkel, H.G., and Paronetto, F. Localization of in vivo bound complement in tissue sections. J. Exp. Med. 115:63, 1962.

15. Paronetto, F., and Strauss, L. Immunocytochemical observations in periarteritis nodosa. Ann. Int. Med. 56:289, 1962.

These papers lend strong support to the thesis that periarteritis nodosa is an allergic disease.

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16. De La Pava, S., Nigogosyan, G., and Pickren, J.W. Fatal glomerulonephritis after receiving horse anti-human-cancer serum. Arch. Int. Med. 109:67, 1962.

This paper actually gives details of Rich's rabbit experiments performed in human. The results were entirely similar.

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17. Rose, G.A., and Spencer, H. Polyarteritis nodosa. Quart. J. Med. 26:43, 1957.

18. Rose, G.A. The natural history of polyarteritis. Brit. Med. J. 2:1148, 1957.

Rose makes a classification of periarteritis nodosa based on the presence or absence of lung involvement. Hypertension the result, not the cause of periarteritis nodosa.

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19. Rackemann, F.M., and Greene, J.E. Periarteritis nodosa and asthma. Trans. Assn. Amer. Phys. 54:112, 1939.

20. Wilson, K.S., and Alexander, H.L. The relation of periarteritis nodosa to bronchial asthma and other forms of human hypersensitiveness. J. Lab. & Clin. Med. 30: 195, 1945.

The idea of dividing these patients on the basis of pulmonary involvement was not new. Wilson and Alexander made the point that the patients with asthma are the ones with eosinophilia. In 151 cases without asthma, only 6 had any degree of eosinophilia.

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21. Allen, A.C. The Kidney: Medical and Surgical Diseases. Grune and Stratton, New York, 2nd Ed., 1962.

Allen divides patients as Zeek, but only for convenience. States that Zeek's segregation of periarteritis nodosa, hypersensitivity angiitis, etc., is "not fully warranted".

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22. Goldberger, E. Etiology and pathogenesis of syndromes associated with periarteritis nodosa lesions. A unified theory. Am. J. Cardiol. 3:656, 1959.

If a classification must be made, this seems most reasonable (See Table 4). Goldgerger's other thoughts on the disease are rather at odds with current concepts, however.

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23. Arkin, A. A clinical and pathological report of 5 cases, one histologically healed. Am. J. Path. 6:401, 1930.

First adequate description of the pathology of periarteritis nodosa. Clearly described the spontaneously healed lesions of this disease.

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24. Davson, J., Ball, J., and Platt, R. Kidney in periarteritis nodosa. Quart. J. Med. 17:175, 1948.

A classic paper. Clearly distinguishes the lesions of malignant hypertension from periarteritis nodosa.

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25. Churg, J., and Strauss, L. Allergic granulomatosis, allergic angiitis, and periarteritis nodosa. Am. J. Path. 27:277, 1951.

First descriptions of granulomas in arteritis.

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26. Dawson, D. Acute periarteritis nodosa with chronic glomerulonephritis. Arch. Path. 68:651, 1959.

Suggest a possible causal relationship - more likely pathology of chronic nephritis results from arteritis. (See Ref. 17).

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27. Harrison, C.V., Loughridge, L.W., and Milne, M.D. Acute oliguric renal failure in acute glomerulonephritis and periarteritis nodosa. Quart. J. Med. 33:39, 1964.

Report of microscopic polyarteritis. States that crescents and fibrosis of glomeruli seen as early as 6-8 days after onset of illness.

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28. Moskowitz, R.W., Baggenstoss, A.H., and Slocumb, C.H. Histopathologic classification of periarteritis nodosa: A study of 56 cases confirmed at necropsy. Proc. Staff Meetings Mayo Clinic 38:345, 1963.

A good study of 56 patients collected from 1926 to 1957 at Mayo Clinic. Did obtain histologic evidence of healing of lesions after steroid therapy.

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29. McGrae, J.D. Perirenal hematoma secondary to polyarteritis nodosa. Arch. Int. Med. 104:427, 1959.

30. Joachim, G.R., and Becher, E.L. Spontaneous rupture of the kidney. Arch. Int. Med. 115:176, 1965.

Rupture of the kidney is a rare complication of periarteritis nodosa. Ref. 30 is a good review.

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31. Powell, R.E., and Pritchard, J.E. Periarteritis nodosa: With report of a case involving one kidney. Brit. J. Urol. 4:317, 1932.

32. Howard, J.E., and Connor, T.B. Hypertension produced by unilateral renal disease. Arch. Int. Med. 109:62, 1962.

Two instances where arteritis appears to be confined to a single kidney and cured by nephrectomy.

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33. Lecutier, M.A. A case of the Schönlein-Henoch syndrome with myocardial necrosis. J. Clin. Path. 5:336, 1952.

34. Dodge, W.F., Travis, L.B., and Daeschner, C.W. Anaphylactoid purpura, polyarteritis nodosa, and purpura fulminans. Ped. Clin. N. Amer. 10:879, 1963.

Two papers that strongly suggest that anaphylactoid purpura is really a form of polyarteritis.

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35. Patalano, V.J., and Sommers, S.C. Biopsy diagnosis of periarteritis nodosa. Arch. Path. 72:1, 1961.

These authors suggest that early renal biopsy might be the best route to diagnosis in polyarteritis; certainly superior to skin and muscle biopsy.

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36. Spiegel, R. Clinical aspects of periarteritis nodosa. Arch. Int. Med. 58:993, 1936.

37. Harris, A.W., Lynch, G.W., and O'Hare, J.P. Periarteritis nodosa. Arch. Int. Med. 63:1163, 1939.

Two early review papers. Despite its age, Ref. 37 is still an excellent clinical presentation of the disease.

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38. Ralston, D.E., and Kvale, W.F. Renal lesions of periarteritis nodosa. Proc. Staff Meetings Mayo Clinic 24:18, 1949.

A review of the renal aspects of the disease in 30 patients. Authors stress that early, a urinalysis is more of a clue to the disease than are G-U symptoms or azotemia. All patients with abnormal urines had histologic changes in their kidneys. Glomerular lesions most common.

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39. McCombs, R.P. Periarteritis nodosa and related disorders of blood vessels. Dis. of the Month, August, 1960.

40. Black, R.L. The characterization of polyarteritis nodosa, dermatomyositis and progressive systemic sclerosis. Med. Clin. N. Amer. 45:1295, 1961.

Two more modern clinical reviews.

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41. Kipkie, G.F., and Johnson, D.S. Possible pathogenic mechanisms responsible for human periarteritis nodosa: As suggested by occurrence of 2 instances of this disease in association with glomerulonephritis. Arch. Path. 51:387, 1951.

42. Fordham, C.C., Epstein, F.H., Huffines, W.D., and Harrington, J.T. Polyarteritis and acute post-streptococcal glomerulonephritis. Ann. Int. Med. 61:89, 1964.

Reference 41 makes the suggestion that periarteritis may complicate post-infectious acute glomerulonephritis. However, both of their patients received sulfa drugs for treatment of URI's prior to onset. In Reference 42, a clearer relationship is presented between streptococcal infection and polyarteritis. Certainly, the disease might be expected on the basis of the experimental work of Rich, Dixon, and others.

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43. McCombs, R.P., Patterson, J.F., and MacMahon, H.E. Syndromes associated with allergic vasculitis. New Eng. J. Med. 255:251, 1956.

44. Winkelmann, R.K., and Ditto, W.B. Cutaneous and visceral syndromes of necrotizing or "allergic" angiitis. A study of 38 cases. Med. 43:59, 1964.

Two papers discussing, primarily, the cutaneous manifestations of arteritis. When lesions are limited to the skin, the course is usually benign, particularly, with steroid therapy.

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45. Krupp, M.A. Urinary sediment in visceral angiitis. (Periarteritis Nodosa, Lupus Erythematosus, Libman-Sachs "Disease"). Quantitative Studies. Arch. Int. Med. 71:54, 1943.

A much quoted paper that probably overrates the diagnostic specificity of a telescoped urine.

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46. Rich, A.R. Hypersensitivity to iodine as a cause of periarteritis nodosa. Bull. Johns Hopkins Hosp. 77:43, 1945.

47. Miller, H.G., and Nelson, M.G. Periarteritis nodosa developing during antisyphilitic treatment. Lancet 2:200, 1945.

48. Van Wyks, J.J., and Hoffman, C.R. Periarteritis nodosa. A case of fatal exfoliative dermatitis resulting from "dilantin sodium" sensitization. Arch. Int. Med. 81:605, 1948.

49. Frankel, A.L., and Rothermich, N.W. Polyarteritis nodosa: Review together with report of case due to hydantoin sensitization treated with cortisone. Ohio State Med. J. 47:1013, 1951.

50. Gibson, P.C., and Quinlan, J.T. Periarteritis nodosa in thiourea therapy. Lancet 2:108, 1945.

51. McCormick, R.V. Periarteritis occurring during Propylthiouracil therapy. J. Amer. Med. Assn. 144:1453, 1950.

52. Spring, M. Purpura and nephritis after administration of procaine penicillin. J. Amer. Med. Assn. 147:1139, 1951.

53. Dewar, H.A., and Peaston, M.J.T. Three cases resembling polyarteritis with guanethidine. Brit. Med. J. 5409:609, 1964.

A partial list of papers citing various drugs with causal roles in angiitis.

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54. Bennett, I.L., Jr., Berthrong, M., and Rich, A.R. Further study of effect of adrenocorticotropic hormone (ACTH) upon experimental cardiovascular lesions produced by anaphylactic hypersensitivity. Bull. Johns Hopkins Hosp. 88:197, 1951.

Presents evidence that ACTH can block the formation of lesions in experimental arteritis.

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55. Shick, R.M., Baggenstoss, A.H., and Polley, H.F. The effects of cortisone and ACTH on periarteritis nodosa and cranial arteritis: Preliminary report. Proc. Staff Meeting Mayo Clin. 25:135, 1950.

56. Rose, B., Pare, J.A.P., Pump, K., and Stanford, R.L. Preliminary report on ACTH in asthma. Canad. Med. Assn. J. 62:6, 1950.

57. Beck, J.C., Browne, J.S.L., Johnson, L.G., Kennedy, B.J., and MacKenzie, D.W. Occurrence of peritonitis during ACTH administration. Canad. Med. Assn. J. 62:423, 1950.

58. Stefanini, M., Roy, C.Z., Zannos, L., and Dameshek, W. Therapeutic effect of pituitary adrenocorticotropic hormone (ACTH) in a case of Henoch-Schönlein vascular (anaphylactoid) purpura. J. Am. Med. Assn. 144:1372, 1950.

Early reports suggesting that both ACTH and cortisone might be effective in periarteritis, and anaphylactoid purpura. In the latter, skin lesions quickly corrected without effect on nephritis.

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59. Baggenstoss, A.J., Shick, R.M., and Polley, H.F. Effect of cortisone on lesions of periarteritis nodosa. Am. J. Path. 27:537, 1951.

60. Ehrenreich, T., and Olmstead, E.V. Malignant hypertension following administration of cortisone in periarteritis nodosa. Arch. Path. 52:145, 1951.

Two reports suggesting that hypertension might increase with therapy. Suggested that this might be related to healing arteritic lesions in kidney.

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61. Malkinson, F.D., and Wells, G.C. Adrenal steroids in periarteritis nodosa. Arch. Derm. 71:492, 1955.

Report of a mild case of perhaps temporal arteritis treated with cortisone for 5 months with complete remission - A one year follow-up.

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62. Johnsson, S., and Leonhardt, T. Polyarteritis nodosa and its treatment with ACTH and cortisone. Acta Med. Scand. 157:479, 1957.

63. Shick, R.M. Periarteritis nodosa and temporal arteritis: Treatment with adrenal corticosteroids. Med. Clin. North Amer. 42:959, 1958.

64. Report to the Medical Research Council by the Collagen Diseases and Hypersensitivity Panel. Treatment of polyarteritis nodosa with cortisone. Results after one year. Brit. Med. J. 1:608, 1957.

65. Report to the Medical Research Council by the Collagen Diseases and Hypersensitivity Panel. Treatment of polyarteritis nodosa with cortisone. Results after three years. Brit. Med. J. 1:1399, 1960.

The available reports on series of patients. References 64 and 65 interesting in that they contained retrospective controls. From these studies it appears quite clear that steroids will lead to healing of arteritis, but hypertension and renal failure still a major cause of death.

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66. Barzel, U.S. Polyarteritis nodosa and hypertension; treatment with corticoids with complete remission. New York State J. Med. 63:2263, 1963.

Although a simple case report, contains an excellent discussion of the problems of therapy.