# A CLINICAL AND PATHOLOGICAL STUDY OF PERIARTERITIS NODOSA*

## A Report of Five Cases, One Histologically Healed

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### Introduction

Periarteritis nodosa was first described by Kussmaul and Maier sixty years ago as a disease characterized by the formation of multiple circumscribed nodular thickenings of the smaller arteries of various organs of the body. Since their classic description in 1866 about 150 cases have appeared in the literature. Several investigators have attempted to discover the etiology of this very interesting disease, and to determine the site of origin in the arterial wall. A specific microörganism has not yet been found, but we shall see that the evidence today is in favor of the specific infectious nature of the disease. A very acute case with death in a few days, published by Fishberg, has shown that the primary changes are usually in the inner media and not in the adventitia. The confusion which exists in the literature regarding the site of origin in the arterial wall is due to the fact that changes of different age occur in arteries of the same patient, and often in the same organ. Each acute exacerbation of the illness is accompanied by fresh changes somewhere in the body, and by new symptoms which vary with the localization of the arterial changes.

We shall attempt to summarize our present knowledge of periarteritis nodosa, and to divide the disease into four stages with a discussion of the pathology and clinical symptoms of each stage. This division is based upon a clinical and pathological study of five cases at the First Medical Clinic (Professor K. F. Wenckebach) and the Pathological Institute (Professor R. Maresch) of the University of Vienna. In addition, we had the opportunity of studying three more cases postmortem. One of our cases reveals the histologically healed end-stage involving every organ of the body except the central

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nervous system. The study of this case has made it possible to complete the pathological picture of the disease, and to describe a new clinical syndrome caused by histologically healed periarteritis nodosa.

Periarteritis nodosa is an inflammatory disease of the arterial system, probably caused by a filterable virus, and characterized by necrosis of the media with fibrinous exudation. This is soon followed by a marked cellular infiltration and granulation tissue formation in and about the arterial wall, together with varying degrees of intima proliferation. The chief secondary changes in the arteries are aneurysm formation, thrombosis and hemorrhage. Death is usually due to hemorrhage from rupture of an aneurysm, or to necrosis or insufficiency of vital organs resulting from thrombosis of the arteries. The veins are free from changes in almost all the cases studied.

At present we know of no predisposing causes of this disease. There seems to be no relation to occupation. However, the disease is four times as frequent in males as in females. It may occur at any age: the youngest patient reported was an infant of three months, the oldest 78 years. About 50 per cent of the cases are found between the ages of 20 and 40 years. The duration of the illness is usually a few weeks to six months, rarely longer than a year. Fishberg's case was ill only six days. Our case of histologically healed periarteritis nodosa lived four years after his one and only attack of acute illness.

Our knowledge of the early changes in the disease is now quite complete except for the question of involvement of the endothelium of the affected arteries. The endothelial changes are difficult to demonstrate, but we believe that they do occur. We know that the most marked changes develop in the media, and this fact has led to the question whether periarteritis nodosa is not related to the changes found in the arteries by Wiesel, von Wiesner, and others in various infectious diseases. They have found degenerative changes in the media which they believe are related to the development of arteriosclerosis in some arteries, such as the coronary. Recently Pappenheimer and VonGlahn have found similar changes in the arteries in rheumatic fever. Spiro has attempted to bring these changes in close relation to those found in periarteritis nodosa, and considers the latter no disease *sui generis*, but only a form of postinfectious mesarteritis. Gruber is also of the opinion that peri-

arteritis nodosa is a disease of toxi-infectious origin without a specific cause. We cannot share this view, and we believe from our study of five cases of this disease that we are dealing here with a specific infectious disease, the virus of which has an elective affinity for the arterial system and enters the arterial walls directly from the lumen and through the vasa vasorum in the larger arteries.

The view that syphilis is the cause can now be dropped entirely. To be sure, a luetic patient may also contract periarteritis nodosa, but even the cases with a positive Wassermann have shown changes characteristic of periarteritis nodosa and not of luetic arterial disease. Most cases have a negative Wassermann, spirochetes have never been found in the lesions, gummas are not found, giant cells very rarely occur, and the localization is different from that of syphilis. Also the occurrence of periarteritis nodosa in lower animals speaks against syphilis as a cause. The view of several early writers that it attacks individuals with a hereditary or acquired weakness of the arterial walls need no longer be considered.

The most promising work on the etiology of the disease is that of Harris and Friedrichs, and of von Haun, who have succeeded in producing quite similar changes in experimental animals. Furthermore, the finding of a similar disease in lower animals (calf, swine, dog, deer), where it at times occurs in epidemic form, also speaks for the specific infectious nature of the disease.

The organs most frequently attacked are the kidneys (80 per cent), heart (70 per cent), liver (65 per cent), gastro-intestinal tract( 50 per cent), pancreas (25 per cent), mesenteric artery (30 per cent), muscles (30 per cent), and peripheral nerves (20 per cent). *The central nervous system is involved* in only 8 per cent of the cases. The disease may also remain confined to a single organ for some time.

We shall divide the disease into four stages according to the changes present in the arteries, and discuss the clinical and pathological findings in each. These are: (1) alterative-degenerative or beginning stage; (2) acute inflammatory stage; (3) granulation tissue stage, and (4) healed end-stage, or scar tissue stage.

### First or Degenerative Stage

*Pathology:* The beginning stage is characterized by alterative-degenerative changes in the media, with edema and the appearance of a thready fibrinous exudate about the elastica interna. There is

a swelling of the muscle cells with separation by the exudate. *In the smaller arterioles*, those without vasa vasorum, the changes are chiefly in the innermost media, in the subendothelium. No doubt the causative agent enters from the lumen producing endothelial changes as well. A part or the entire circumference of the vessel wall undergoes a coagulation necrosis with a hyaline-like appearance of the inner media. The endothelium may also be affected so that the cells become desquamated or disappear over the affected area. The subintimal changes, the edema and fibrinous exudation may elevate the endothelium causing it to bulge into the lumen or even reducing it to a narrow slit. The fibrin network may extend through the endothelium into the vessel wall. *In the larger arteries*, those with vasa vasorum, the changes appear more often in the outer media, lying near the elastica externa. Here the hyaline areas of necrosis appear and seem to go out from the vasa vasorum or from smaller branches of the vessel. Of course, when the necrotic changes become more extensive they may also reach the endothelium in these vessels. Usually a portion of the vessel circumference presents in the media an area of necrosis with edema and fibrinous exudation. Serial sections often show this region to extend longitudinally in the vessel wall. The areas form an ellipse with the long diameter axially arranged, less often transversely. The entire thickness of the media may become hyalinized. Leukocytes begin to wander into the necrotic area. They are chiefly polymorphonuclear neutrophiles, though eosinophiles may also be present in considerable numbers. In this stage the adventitia is often unaffected.

In the early stage changes may also be present in the large arteries and even in the aorta. We have found in one case fragmentation of the elastica interna, with vacuolization and round cell infiltration about the elastica interna in large arteries. That endothelial changes occur in periarteritis nodosa is shown by findings in the brain in one of my cases. Here we observed circumscribed hemorrhages forming a ring about a number of small arterioles, without any demonstrable change in the vessel wall. We must assume, therefore, an increased permeability of the endothelium with hemorrhage by diapedesis into the surrounding lymph space.

*Clinical Symptoms:* In this beginning stage the disease is often latent, especially when the changes are limited to a small area, hence the difficulty of determining the exact age of changes seen post-

mortem. At this stage the diagnosis is not possible, the changes are still microscopic. There may be no symptoms whatever; or only a rise of temperature. We hardly need state that we cannot sharply separate these stages from one another. The earliest case in the literature, that of Fishberg, with clinical symptoms of only six days duration, died of renal insufficiency due to extensive infarction of both kidneys. Fever, hematuria, icterus, myocardial insufficiency or pains in the extremities often mark the onset of the disease.

### Second or Acute Inflammatory Stage

*Pathology:* This is the exudative inflammatory stage. A great infiltration of the media and adventitia with polymorphonuclear neutrophiles, sometimes also many eosinophiles, lymphocytes and plasma cells rapidly takes place. The fibrinous exudate extends to the intima and outward in the adventitia. There is destruction of the inner media and of the elastica interna which becomes stretched and fragmented. The process may also extend through the adventitia and spread by way of the perivascular lymphatics. The perivascular connective tissue becomes edematous and leukocytes appear in large numbers. There may be destruction of the entire vessel wall over a part or all of its circumference. The muscle cells of the media become separated from one another and then undergo complete necrosis, the elastica becomes fragmented, survives longer than the muscle cells, but soon also disappears. When the exudate reaches the intima the fibrin threads may penetrate into the lumen and leukocytes wander from the lumen into the subendothelial tissue. A marked subendothelial connective tissue proliferation takes place, a reactive intima proliferation. At the height of this stage secondary thrombosis of the lumen with infarction of the various organs is common. Toward the end of this stage aneurysm formation or rupture of the vessel wall with hemorrhage into the adventitia or surrounding tissue occurs. There is no suppuration, and pyogenic bacteria are not found. In cases without aneurysm or nodule formation the changes may be overlooked without microscopic examination.

*Clinical Symptoms:* This is the stage with high fever, chills, a polymorphonuclear leukocytosis (sometimes also an eosinophilia) and all the symptoms of a severe infection. The fever may be con-

tinuous or intermittent. After a time a secondary anemia develops. The symptoms vary with the location of the process and the nature of the secondary changes in the vessels. Renal, cardiac, peripheral nerve, and gastro-intestinal symptoms are the most common. Icterus may also develop due to involvement of the liver. The spleen is often, though not always, enlarged. There are frequently somewhat enlarged, hard lymph glands. The pulse is as a rule regular and accelerated even when the fever has disappeared.

Death is frequent in this stage, due to rupture of an aneurysm with fatal hemorrhage. This may occur in any of the affected organs. Or, renal insufficiency due to extensive infarction may cause death. Another common cause is cardiac failure due to extensive coronary involvement with thrombosis or intima proliferation.

The finding of subcutaneous nodules, which on histological examination show the characteristic arterial changes, offers a means of making a sure diagnosis *in vivo*.

### Third or Granulation Tissue Stage

*Pathology:* This is the reparative or granulation tissue stage. There is a marked proliferation of fibroblasts from the adventitia into the inflammatory zone, accompanied by a reduction in the polymorphonuclear leukocytes with an increase in the lymphocytes and plasma cells. Sometimes eosinophiles appear in considerable number. The fibrin network and hyalinized necrotic media are gradually replaced by the cellular granulation tissue rich in fibroblasts and newly formed blood capillaries. This granulation tissue not only replaces the destroyed media, but also extends outward through the adventitia, and longitudinally as well as circularly beyond the area of destruction. It may also penetrate the subendothelial tissue through the defects in the elastica interna. It may even pass through the entire wall and invade thrombi formed in the lumen.

In addition to the granulation tissue formation there is usually a very marked reactive intima proliferation with a partial or total occlusion of the lumen. This intimal thickening consisting of a loose fibroblastic connective tissue usually extends beyond the area of destruction of the media. It is often circular, but may also extend longitudinally on only one side of the vessel. The proliferation is

usually thickest at the site of the lesion with the result that the narrowed lumen often lies eccentrically on the less affected or unaffected side. The spread of the intima proliferation beyond the area of media destruction explains why we so often find in transverse sections a marked intimal thickening without changes in the vessel wall. We have convinced ourselves by a study of many serial sections from different organs that these areas lead to vessel wall changes usually at the place where the intimal proliferation is most marked. In other words, the intimal thickening in periarteritis nodosa is usually the consequence of vessel wall changes in the media.

In this stage of granulation tissue formation, aneurysms or rupture of the wall may occur or there may be only a thickening of the wall from intimal proliferation, or granulation tissue formation outside the adventitia. Cases without nodule formation on the vessels may be overlooked unless examined microscopically.

*Clinical Symptoms:* In this stage marked anemia, emaciation and marasmus usually develop if the involvement is widespread. If confined to a non-vital organ or tissue, healing may occur, clinical as well as histological. The fever and leukocytosis usually drop or may entirely disappear. However, acute exacerbations are the rule, with the development of fresh foci. The symptoms in this stage are due to vascular occlusion of the kidneys, heart, gastro-intestinal tract, peripheral nerves, muscles, and glands of internal secretion. They are hypertension, nephritis, renal insufficiency, cardiac failure, intense pains in the abdomen, icterus, ulcerations or gangrene of the bowel, peripheral neuritis, muscular atrophy, Addisonoid symptoms, etc. Or a sudden collapse due to internal hemorrhage may occur (kidneys, liver, gall bladder, gastro-intestinal tract, pancreas, lungs, brain, etc.). The diagnosis of rupture of an artery can then be made. Such hemorrhage is more common in the second stage of the disease.

### Fourth or Healed Granulation Tissue Stage

*Pathology:* This is the histologically healed end-stage or scar tissue stage, as illustrated by the case of periarteritis obsoleta nodosa of four years duration, which we shall describe. The destroyed arterial wall, often only the inner media including the elastica interna, is replaced by an indifferent fibrous scar tissue poor in nuclei. The lumen is greatly reduced in size or totally obliterated. Often only

narrow channels run axially through the greatly thickened vessels. Nodular thickenings of the outer wall occur when the process involves the outer media and adventitia. Then a marked periarterial fibrosis takes place as a result of the histological healing of the granulation tissue in the adventitia and surrounding connective tissue.

Three processes here are active, separately or very often combined: (1) a marked subendothelial connective tissue proliferation which may be accompanied by the new formation of elastic fibrils and often extends beyond the area of media destruction; (2) thrombosis of the injured vessels with complete organization with or without recanalization, and (3) healed granulation tissue scar formation in and about the injured vessel wall. These three processes can often, but not always, be distinguished from one another.

Only cases of severe periarteritis nodosa with a tendency toward thrombosis and intimal proliferation will reach this advanced stage. The cases with aneurysm formation usually lead to fatal hemorrhage. Also, early complete occlusion of the blood supply to vital organs, whether by thrombosis or intimal proliferation or both, will result in early death. It is, therefore, possible for a generalized periarteritis nodosa to become histologically healed only when the blood supply is not reduced below the minimum necessary for the maintenance of function of the vital organs. Case 5 will demonstrate this fact very well. No disease better illustrates the great factor of safety in the blood supply to vital organs than does periarteritis nodosa.

The intimal proliferation is a reactive local proliferation in response to the injury of the inner media. It is characterized by the absence of blood capillaries and hemosiderin deposits such as are seen in organized granulation tissue or thrombosis. The fibers are arranged more or less concentrically in cross-sections of the artery. The elastica interna presents all stages of degeneration and necrosis. A new formation of elastic fibrils with marked thickening of the intima occurs in arteries where the changes in the media are less severe and hence the elastica has not been destroyed.

The healed granulation tissue which grows into the adventitia and media is characterized by a richness in fibroblasts, the presence of numerous newly formed blood capillaries, and fine deposits of hemosiderin. As this tissue grows older it becomes more and more hyaline and fibrous, the capillaries are compressed and obliterated,

and the hemosiderin slowly disappears. The healed scar tissue remains as evidence of the severity and extent of the earlier acute inflammatory process. The perivascular mantles of scar tissue, which we have found surrounding the arteries with extensive destruction, we consider to be characteristic for this healed end-stage. These arteries lie embedded in thick sheaths of scar tissue radiating through the affected organ, producing the appearance of an interstitial scar tissue formation. Where the arterial destruction is greatest there the periarterial healed granulation tissue is the thickest.

The final organ changes in this stage are contracted kidney, contracted scarred liver (hepar lobatum), myomalacia scars, adrenal atrophy, necrosis or ulceration in the gastro-intestinal tract, encephalomalacia, muscle atrophy, and peripheral nerve degeneration. In other words, we may have healed infarcts or atrophy in any of the organs with characteristic arterial changes. The vessel changes may be microscopic or macroscopic. With severe changes there are often nodules on the arteries produced by healed aneurysms or periarterial scar tissue formation. Elastic tissue stains of the arteries, and serial sections should be made in all suspected cases.

*Clinical Symptoms:* There is an absence of fever in this end-stage when, as in my case, all the lesions in the body are histologically healed. The pulse remains accelerated, but is usually regular. The leukocyte count is normal. The symptoms are due to a progressive reduction of the blood supply in the various organs, and may be as variable as in the earlier stages, depending upon the localization of the vascular process. We can expect as most common: renal insufficiency, cardiac failure (without pulmonary or other demonstrable cause) which is resistant to the action of digitalis, degenerative polyneuritis, marasmus, muscular atrophy, abdominal cramps, hepar lobatum, gastro-intestinal ulceration, encephalomalacia, adrenal insufficiency or even polyglandular insufficiency.

The difficulty in the diagnosis of the disease in the earlier stages seems to be even greater in this histologically healed end-stage. The history of a previous severe febrile attack, the symptoms of renal involvement, polyneuritis and polymyositis, and abdominal pains, that most common tetrad of symptoms in periarteritis nodosa, might enable one to diagnose the healed end-stage. The finding of nodules in the skin with the characteristic histological changes would render possible the diagnosis.

## Case Reports

Case 1. *Clinical History:* The patient, Franciska H., a dressmaker 46 years of age had the following history: Both parents died of old age. The patient has four sisters, one has heart disease, another gastric ulcer. The patient was always well until three years before her present illness when she had pneumonia. A year ago she had a "rheumatism" confined to the left shoulder joint.

The present illness began six weeks before entrance into the hospital with intense pain in the leg muscles so that the patient couldn't walk. Soon similar pains developed in the arms and hands. She stated that she had no fever at this time. About fourteen days ago the patient suddenly developed high fever to 40° C, with chills and slight sore throat. The angina disappeared after a few days, but not the fever.

Examination showed a medium-sized woman with poor musculature and very little subcutaneous fat. The cranial nerves were all free from disturbance. In the chest there was a slight dullness over both apices, but the lung borders were normal. The heart was not enlarged. There were no murmurs. The liver was slightly enlarged on percussion. The spleen was not palpable.

The pulse rate was 100–120 but regular.

There was marked tenderness on pressure over the sciatic nerve, also the peripheral nerves of the upper extremities. The patellar reflex was present, the Achilles' reduced. There was no Babinski, no clonus.

The white blood count was 12,400. The Wassermann was negative. Blood cultures taken at the height of the fever were negative. Repeated examination of the sputum failed to reveal tubercle bacilli. The patient's septic temperature continued unchanged in spite of the use of aspirin, electrocollargol, Pregl's solution, etc. The heart action remained good and no signs of endocarditis could be found.

Twelve days after entrance, on October 24, the pains in the arms increased. There were sensory disturbances in the radial nerve distribution of the right hand. The reflexes in the left arm were increased. On November 3, the condition of wrist-drop developed on both sides. The radialis no longer reacted to galvanization or faradization.

On November 5, the findings in the arms were as follows:

*Right Arm:* The patient could carry out all movements in the shoulder joint and elbow, but only slowly and with effort. The movement of the wrist and finger joints was practically impossible. The radialis showed no reaction to faradic or galvanic current. The ulnaris reacted slightly to faradization.

*Left Arm:* There was slight improvement, the radialis and ulnaris reacting to faradic with slow contraction of the muscles.

*Right Leg and Left Leg:* The peronealis reacted but the tibialis did n't.

On November 12, the reflexes were absent in the lower extremities. The reaction of the nerves of the arms varied, one day they reacted slightly, the next day not at all.

The patient became weaker every day and drugs were ineffective. On November 19, the patient collapsed and received camphor and caffeine. On November 28, the patient developed severe pain in the abdomen; the large intestine could be palpated and was strongly contracted. There was a slight diarrhea with bloody stool. On November 29, the patient became comatose, and developed a right-sided facial paralysis. Speaking was difficult, also swallowing. The patient died on November 30, in deep coma.

The clinical diagnosis was infiltration of the right upper lobe with abscess formation, polyneuritis, metastatic process in cerebro, enteritis.

The autopsy, performed by Dr. Feller, revealed an extensive periarteritis nodosa involving almost all the organs of the body, including the central nervous system as well as the peripheral nerves. Most marked are the changes in the gastro-intestinal tract. In the stomach there are infiltrations on the arteries up to the size of a pea along the greater and lesser curvatures. The nodules in large numbers produce protuberances of the mucosa so that the inner surface of the stomach appears nodular. Especially numerous are the nodules about the small arteries at the mesenteric attachment of the small and large intestine. Also in the intestines the nodules often cause protrusion of the mucosa into the lumen. In places the intestinal wall appears to be undergoing necrosis. In the large intestine (cecum, ascending and transverse colon) are a number of bleeding ulcers of the mucosa, some covered with a necrotic membrane. These vary in size up to 2 cm. In the ileum longer stretches of the wall are necrotic. There is a circumscribed fibrinous peritonitis over these areas.

Miliary to pea-sized nodules are found on the peripheral arteries. In the extremities along the muscle and nerve branches are numerous pinhead to millet-seed-sized nodules. Many nodules are seen in the liver along the branches of the hepatic artery, in the kidneys and in the pancreas. There are many nodules and areas of thickening on the coronary arteries.

A large fresh cerebral apoplexy exists in the region of the left basal ganglia and reaching almost to the cortex, with perforation into the left lateral ventricle. A confluent lobular pneumonia is present in the right lung, with fibrinous pleuritis.

Histological studies showed acute and chronic changes in the arteries of every organ in the body. I wish to call attention to the presence of multiple small periarteriolar hemorrhages in the brain, in some places without demonstrable arteriolar change other than a slight swelling or edema of the wall. The very extensive degeneration of the peripheral nerves, always accompanied by severe arterial changes with obliteration of the lumen in many places, is of special interest in this case. Also the marked involvement of the gastro-intestinal tract with numerous nodules in the submucosa commands our attention.

Summarizing our observations in this case we find:

A woman of 46 years developed a severe polyneuritis with pain, marked weakness, and atrophy of the muscles of the extremities, loss of reflexes and wrist-drop. This was accompanied by a persistent high septic temperature, a rapid regular pulse. Then came a severe collapse, followed by intense abdominal pain and bloody diarrhea. Death was due to cerebral apoplexy with rupture into the lateral ventricle. The autopsy revealed a generalized periarteritis nodosa. This variety of symptoms: weakness, septic temperature, polyneuritis, abdominal pain followed by melena, and cerebral hemorrhage, could not be "brought under one hat" by the clinician. We want to emphasize this very fact as characteristic of most cases of periarteritis nodosa. When we find such a variety of symptoms, referable to various organ systems, we should think of a common vascular cause such as periarteritis nodosa.

CASE 2. *Clinical History:* Joseph H., aged 55 years, had always been well. The family history revealed nothing of importance. Except for a severe burn sustained by the patient fifteen years ago he had always been well. The patient entered the hospital on October 20, 1925.

The present illness began three weeks ago with intense pain in the right calf of the leg. The pain then spread to the knee region and the toes. He had the feeling that the leg was swollen. The pain was more severe on walking than on lying in bed. There was a sensation of numbness in the leg, with paresthesia at times. A week later the same symptoms developed in the left leg, but not so severe as in the right. Still he could continue his work until October 16, four days before entrance into the hospital. On October 17, the pains became so intense that the patient was forced to bed. At this time similar symptoms developed in the left forearm and hand. The left extremity was weaker and anesthetic. The patient also had been vomiting two or three times a week in the morning for five weeks.

The patient drank five to six beers and about one quarter of a liter of wine daily. He had been a heavier drinker. Venereal disease was denied. The patient smoked, but not to excess.

We shall not give the complete physical findings, but only those facts of interest in connection with the disease.

The patient was a medium-sized well developed man in good nutritional condition. There was no edema, icterus or cyanosis. The head was entirely normal, the pupils reacted normally to light and accommodation. The thyroid was not enlarged, there were no abnormal glands palpable.

The heart and lungs were normal, except for a few râles at the base of the right lung posteriorly. The pulse was 100, regular. The temperature of the patient was remittent, rising afternoons to as high as 39° C. The liver and spleen were not enlarged. There was no abnormal resistance in the abdomen. The blood pressure was 145 to 160 mm. systolic. The Wassermann test of the blood was negative.

The movement of the left arm and both legs was considerably reduced, as also

the strength in these extremities. The patient dragged his foot somewhat on walking. The patellar and Achilles' reflexes were somewhat reduced.

The patient perspired considerably. He developed paresthesias in the right hand on October 24. On October 27, the pain in the calves disappeared, and the paresthesia was less marked. The patellar and Achilles' reflexes were gone. There was a slight edema over the internal and external malleoli. The muscle sense of the fingers and wrist was greatly disturbed. The right hand developed a wrist-drop with hyperesthesia in the radialis region. There was a marked atrophy of the interossei muscles.

On November 3, the edema about the ankles was still present. The temperature rose daily to 38 or 39° C. Both arms could be moved only with difficulty. The urine showed a trace of albumin, but no renal elements.

On November 10, the pain in the calves was still present. The heart dullness was enlarged, the pulse 104. On the 15th, the sensory disturbances of the ends of the lower extremities were somewhat reduced. The patient could lift his right foot a little better. On November 20, the movement of the wrists and finger joints was somewhat better.

On December 2, the patient developed severe dyspnea, with numerous bronchial râles over the entire lung. He had a tachycardia. The liver was enlarged, hard and painful to pressure. There was no ascites. On December 7, dullness was found over the right base posteriorly. The heart apex lay in the 6th interspace in the anterior axillary line. The edema of the lower extremities and sacral region was increased.

The patient died on December 15, after an illness of about ten weeks. The clinical diagnosis of Professor H. Schlesinger was: polyneuritis alcoholica, myodegeneratio cordis with marked decompensation, pneumonia.

The following laboratory findings are also of interest:

October 20: Urine negative, specific gravity 1020.
November 27: Urine: albumin positive, blood positive with numerous red corpuscles, few leukocytes and epithelial cells.
November 30: Urine: albumin positive, with few granular casts, leukocytes and epithelial cells, but no red corpuscles.
December 7: Albumin negative, no red corpuscles.
December 13: Albumin positive, urobilin and urobilinogen positive.
December 14: White blood count ..... 17,500
Polymorphonuclears ..... 81
Monocytes ..... 5
Lymphocytes ..... 14

The autopsy on December 15, 1925, performed by Dr. Matras in the Pathological Institute of Professor Maresch, revealed the following:

There is a universal edema of the skin. The dura of the brain is tense, the meninges are somewhat thickened.

The fluid in the subarachnoid space is increased, with a slight edema of the brain. The ventricles are slightly enlarged and contain a clear fluid. The cord presents no macroscopic changes.

Hydrothorax and hydroperitoneum are present. Hemorrhagic infarcts are visible in both lungs, with a lobular pneumonia and fibrinous pleuritis in the lower lobes. The heart is enlarged, with eccentric hypertrophy of both ventricles, and dilated auricles. The valves are all normal. The myocardium is pale grayish red to yellow, and its consistency is reduced. Everywhere are small scars of whitish color in addition to the general fatty degeneration. The coronaries are straight and delicate, but along their course are numerous pinhead-sized whitish spots or nodules.

The aorta is smooth and appears entirely normal, as also its large branches. The thyroid appears normal. The liver is large, of normal consistency. On the surface are many irregularly outlined bluish red depressions 1 to 3 cm. in diameter and easily visible through the delicate capsule.

These areas are mostly in the left lobe and left half of the right lobe. On the cut surface they are dark red and depressed. The liver parenchyma is destroyed leaving behind a vascular network filled with blood. Here and there are thickened vessels with narrow or obliterated lumen.

The gall bladder appears normal. The spleen is enlarged. The kidneys are large, the capsule adherent and thickened. The surface is very irregular with numerous dark red retractions of various sizes. There are other small yellowish necrotic areas. On the cut surface the thickened arteries are visible, some appearing as round grayish areas without any lumen. The adrenal and pancreas appear normal.

On the arteries along the lesser curvature of the stomach, on the arteries of the small intestine in the immediate vicinity of the mesenteric attachment to the bowel, and on the vessels from the mesocolon to the large intestine are everywhere numerous nodules, often arranged in chains like a string of pearls (*perlschnurartig*). The nodules are mostly of the size of a hempseed. Some vessels present thickenings in the wall which hardly protrude beyond the surface. The mesenteric lymph nodes are somewhat enlarged. The prostate, testicles and epididymes appear normal. There are fresh thrombi in the veins of the prostatic plexus, in the posterior tibials and the muscle branches of the lower extremities.

In this case of acute periarteritis nodosa we find as the predominating symptom the polyneuritis, with paresthesias, muscle pains and weakness, anesthesia, loss of reflexes and wrist-drop. The

second most important symptom is the remittent temperature. Vomiting was the only gastric symptom. Then came signs of cardiac decompensation. The renal symptoms were the transient hematuria and albuminuria. Death resulted from cardiac failure with pneumonia and hemorrhagic infarction of the lungs.

The histological changes were typical of acute and subacute periarteritis nodosa of the heart, kidneys, arteries of the peripheral nerves, liver, and mesenteric branches.

CASE 3. *Clinical History:* Hugo H., 50 years old, entered the Wenckebach Clinic on August 19, 1925. The patient had measles, whooping cough, scarlet fever and diphtheria in childhood. At the age of 21 years he had a soft chancre. The patient denied the use of alcohol and was a moderate smoker.

The present illness began in June, about two months before his entrance into the hospital. He had an attack of angina with fever lasting ten days. He remained in bed three weeks and then returned to his work. After a four-day afebrile period he developed a second attack of fever lasting five days. Fourteen days later a third attack occurred. This began about the second of August and lasted until his admittance on August 19. His temperature during the attacks reached 39 to 39.5° C. During the third attack *pain and swelling of the legs appeared.* A week's rest in bed brought relief. *The pain was chiefly in the calves and in the peroneal muscles, making walking impossible.*

The examination on August 20, revealed the following:

A well developed man, with somewhat atrophic musculature. The temperature 37.7° C, respiration 20, pulse 90 and regular. The pupils were equal, reacted normally to light and accommodation. The tonsils were enlarged. The lungs presented nothing pathological, except for a dullness over the left apex. The heart was slightly enlarged to the left. The blood pressure was 150 systolic. A soft systolic murmur at the apex was heard on August 29, ten days after admission. The liver was slightly enlarged. The spleen was not palpable.

On both legs there were *areas of paresthesia involving chiefly the peroneal distribution.* In the center of these areas there was complete anesthesia. Here the pain was most intense a few weeks earlier.

Examination of the fundus oculi was negative. X-ray examination of the chest showed a darkening of the left apex, with calcified spots in the left hilum region. The heart showed an enlargement of the left ventricle. I found a hitherto undescribed anomaly of the aorta, a right-sided retro-esophageal aorta which was confirmed at autopsy. The blood and spinal fluid Wassermann were negative. Agglutination reactions for typhoid and paratyphoid were negative. The blood examination showed 12,000 leukocytes with 82 per cent polynuclear neutrophiles and 3 per cent eosinophiles. The red count was 3,600,000 and the hemoglobin 60 per cent, an index of 0.9. The spinal fluid was normal.

The examination of the patient failed to reveal the cause of his intermittent temperature which in the mornings reached as high as 39.3° C. The patient gradually developed an edema of both legs. The pulse was always rapid, averaging 110.

Several examinations of the urine revealed about 1/4 per 1000 albumin and numerous red blood cells and some leukocytes in the sediment. The residual nitrogen in the blood was normal.

Six days ante mortem the patient had a collapse, the pulse being 140, the temperature only 36.8° C. The next day râles were heard at the base of both lungs. Then dullness developed on both sides. The dyspnea became more severe and bronchial breathing was audible over the entire lung. The patient died on September 17, after a six-day fever-free period. The clinical diagnosis was sepsis of unknown cause with terminal afebrile pneumonia.

The postmortem examination performed by Dr. Feller in the Pathological Institute of Professor Maresch revealed the following:

A recent confluent lobular pneumonia of all the lobes, with a high grade pulmonary edema; eccentric hypertrophy of both ventricles, especially the left. The coronary arteries are normal except for slight atherosclerosis. There is a fatty degeneration of the myocardium. A right-sided aorta, which runs over the right bronchus and behind the esophagus, is found.

The liver displays on its surface numerous irregularly outlined dark red depressions which vary in size up to 2 cm. in diameter. Similar areas can be seen on the cut surface. The branches of the hepatic artery show marked periarteritis nodosa with occlusion of the small branches. The reddish depressed areas represent infarcts.

The kidneys are irregularly coarsely granular. The reddish gray depressions represent multiple healed infarcts. There are also many fresh anemic infarcts present. The branches of the renal artery show extensive changes with wall destruction, aneurysm formation, thickening of intima and thrombosis. Many are in the acute inflammatory stage. Those in the granulation tissue stage are often surrounded by a mantle of periarterial connective tissue. Some of the glomeruli present the typical picture of a glomerulonephritis. The pancreas and adrenal are macroscopically normal. The arteries of the arms and legs show miliary aneurysms on their smaller muscular branches. The arteries of the peripheral nerves show no typical changes macroscopically, but microscopic examination reveals marked changes.

The stomach and intestines appear normal. There are also no changes in the central nervous system.

When we briefly summarize this case we find: A man of 50 years suffered from an angina followed by three attacks of fever. The last attack was accompanied by edema of the legs with intense pain in the muscles, chiefly the peroneal group. He had a polymorphonuclear leukocytosis and intermittent temperature to 39.3° C, a nephritis with hematuria but no increased blood pressure. Death

was due to confluent lobular pneumonia and cardiac weakness. The postmortem examination revealed an acute and chronic periarteritis nodosa affecting chiefly the kidneys, liver, muscles of the extremities, and peripheral nerves. The presence of multiple infarcts in the kidneys in the absence of an endocarditis should always call to mind the possibility of periarteritis nodosa. We have diagnosed two cases postmortem by this finding, together with thickenings and nodule formations on the arteries.

CASE 4. *Clinical History:* Jacob S., aged 34 years had no children's diseases, and was never seriously ill until his present illness. The family history revealed nothing of importance. The patient's present illness began in June, 1924, five months before he came to the clinic. He had at the onset *generalized rheumatic symptoms* with temperature to 39° C. *There was no swelling of the joints*, but slight edema of the legs in the afternoon when the patient was up and about. He was under a physician's care and at home for seven weeks. He then went to a clinic where he remained four weeks on account of an acute nephritis and left feeling quite well. The rheumatic pains in the extremities disappeared. A few days after returning home the patient again developed the pains in the extremities with edema of the legs. Then severe headaches set in for about fourteen days. About two weeks after the onset of this attack an orchitis appeared. It lasted about four weeks. Since the development of the headaches the patient's vision has suffered. There were no mental disturbances. On account of the severe headaches the patient came to the clinic on November 17, 1924. The patient stated that he drank about one liter of wine daily, and smoked 30 to 40 cigarettes. He denied venereal infection.

The patient was a medium-sized well nourished man. He was somewhat stuporous. The skin was pale but not edematous. The pulse was 88, regular. The pupils were equal and reacted normally to light and accommodation. The thyroid was not enlarged, nor were any enlarged glands present in the neck region. The thorax was symmetrical, the lung borders normal. The heart dullness was slightly increased to the left. The aortic second sound was accentuated. The liver and spleen were not palpable. There was no ascites. The external genitals appeared normal.

Examination of the eyes on November 18, revealed the following: In the right eye there were no certain changes in the fundus. In the left there were variations in the caliber of the small arteries in the region of the papilla. There was a slight edema of the retina about the papilla. The residual nitrogen in the blood on November 20, was 34 mg. Examination of the urine showed albumin 2 per 1000 (Esbach) with erythrocytes, leukocytes and many granular casts in the sediment.

On November 27, the patient's headaches became more intense, with vomiting, sleeplessness and still greater reduction of vision. On December 3, the fundus showed: In the right eye the border of the papilla was indistinct, with marked edema of the retina, and small hemorrhages. No foci of retinitis were visible. There was an ablatio retinae in the nasal peripheral zone. The left eye showed more marked unsharpness of the papilla and edema around it. Many radiary hemorrhages were seen about the papilla. Ablatio retinae in the lower periphery. The residual nitrogen on December 5, was 50 mg.

Lumbar puncture yielded a pressure of 300 mm., the spinal fluid clear with 15 cells per cmm. The intense headache persisted. The patient had signs of cardiac failure with edema of the extremities and also râles at the base of both lungs. On December 10, the patient developed a deviation of both eyes to the left, unconsciousness and tracheal râles, and died.

The blood pressure of the patient varied between 170 and 190 systolic, and 110 and 120 diastolic. The concentrating power of the kidneys was reduced, the urine specific gravity never above 1017. The sediment contained red cells, leukocytes and casts, also renal epithelium. Once the stool gave a positive reaction for blood. The blood Wassermann test was negative. The temperature was subnormal mornings and reached 37.5° C afternoons. It was never above 37.5° C during the stay in the hospital.

The autopsy performed on December 10, revealed a chronic periarteritis nodosa affecting chiefly the kidneys, liver, heart, peripheral nerve vessels, and mesenteric arteries. There are numerous nodular thickening of the arteries. The most marked changes are seen in the coronaries, hepatic artery branches, renal arteries and mesenteric arteries.

The myocardium is macroscopically unchanged. There is a marked hypertrophy of the heart, especially the left ventricle. The liver presents numerous smaller and larger depressed and irregularly outlined gray-red areas, which consist almost entirely of blood capillaries and in which the liver parenchyma is destroyed.

The kidneys show the most marked changes. The surface presents relatively small light gray and grayish yellow, flat prominent smooth areas with irregular outline. These represent the rests of the cortex. Between these areas are numerous dark red depressions representing the healed infarcts due to arterial occlusion. The larger branches of the renal artery in the hilum region are greatly thickened. The testicles contain a number of smaller and larger fibrous scars. The vessels of the peripheral nerves *show no macroscopic changes.* The cerebral vessels appear macroscopically unchanged, yet in the region of the left caudate nucleus there are several grayish red unsharply outlined and slightly depressed areas. Also in the cerebellar cortex there are multiple foci of hemorrhage of various size up to 2 cm. Bilateral pleural effusion and uremic pericarditis are also present.

Histologically we find the vascular thickenings to be due to a thickening of all the layers of the wall, especially the intima and adventitia with rich perivascular connective tissue formation. In some places acute inflammatory changes are still present, with

leukocytes and a few eosinophiles. Many arteries are occluded by thrombi undergoing organization. Most of the nodules are in the granulation tissue stage.

The pathological diagnosis is: Periarteritis chronica nodosa; atrophia renis ex periarteriitide. Uremia.

In this case also the pains in the extremities, without any joint involvement dominated the clinical picture. An attack diagnosed acute nephritis followed two months after the onset of the disease. Then came an attack of orchitis, severe headaches and marked visual disturbance. The changes in the fundus are of great importance because their occurrence enables the ophthalmologist acquainted with periarteritis nodosa to make the diagnosis.

The hematuria and terminal uremia are quite characteristic of this disease. The hemorrhages in the central nervous system are unusual and have been seen in only nine cases to date. As in this case the diagnosis of acute nephritis is often made in the early stage because of hematuria.

[1] CASE 5. *Clinical History:* The patient, Joseph S., entered the hospital on August 11, 1922. There was nothing of importance in the family history. The patient was never sick until 1918, when he became suddenly ill with *a high fever, severe icterus and "acute nephritis."* He was then in a hospital for six weeks and gradually recovered and returned to his work.

The present illness began in May, 1922 (four years later) with cramp-like pains in the epigastrium. These pains were so intense that the patient was forced to bed. He had a feeling of pressure in the stomach region, which was intensified by the taking of food. It was relieved by hot applications. There was no vomiting. Appetite was poor. The patient was constipated. Several weeks' treatment by a family physician was without effect and the patient entered the clinic on August 11, 1922.

The patient was much emaciated, the musculature atrophic. The skin was brown and pigmented. The mouth mucosa was not pigmented. The pupils reacted normally to light and accommodation. The veins of the neck were somewhat dilated.

A slight asymmetry of the thorax was present. The lungs were normal. The heart was slightly enlarged to the right; the heart sounds were normal. The pulse was regular, 90 to 100 per minute. The blood pressure was 150.

The abdomen was retracted. The spleen was not palpable. The liver could be palpated below the costal margin and seemed to have an irregular border. The patient complained of intense pain in the epigastrium.

On August 15, the patient revealed a dullness at the base of both lungs with signs of bronchitis. The apex beat was two finger-breadths outside the midclavicular line. On August 24, a marked edema of the legs had developed, as well as a generalized anasarca. There was dyspnea, the pulse was 120. The bilateral hydrothorax was increased. There was a systolic murmur at the apex of the heart. *In spite of digitalis therapy* the patient's edema increased and the quan-

tity of urine decreased. The edema of the legs was relieved by puncture but soon recurred. On October 5, the patient became very dyspneic with marked congestion of the veins of the neck. The dullness over both lungs reached to the fourth rib. The patient died on October 11, 1922.

At no time during the patient's stay in the hospital was there any fever, the highest temperature being 36.8° C. At the same time the pulse was always 100 or more.

The following laboratory findings are of interest:

The stomach contents was anacid. The stool was positive for blood. The urine contained 1/4 per 1000 albumin, but no erythrocytes or leukocytes. The specific gravity was low, the chlorides reduced. The Wassermann was negative. The fundus oculi was examined October 7, and reported normal.

The autopsy was performed by Dr. Feller on October 11, 1922. The lungs are free from tuberculosis. There is a marked compression atelectasis of both lower lobes, with slight emphysema of the upper lobes. The lungs are congested. The heart is hypertrophic, especially the left ventricle. The subepicardial fat is absent. The coronary arteries are thickened. Numerous nodular thickenings are seen in the wall of both coronary arteries. On cross-section the wall appears greatly thickened, the lumen reduced to a narrow slit in places.

The aorta is practically free from atherosclerosis. A thrombus is present in the left auricle.

The liver is relatively small, and resembles a hepar lobatum syphiliticum. Its surface is coarsely granular, and in a number of places there are deeply penetrating depressed scars. The capsule of the liver is wrinkled in the sunken areas. The left lobe is small and more markedly affected than the right. On the cut surface are found septa of connective tissue containing obliterated thickened branches of the hepatic artery. Nodular thickenings occur on some of the branches. There are also areas of normal liver tissue with normal acinous structure; and immediately adjacent are areas of marked congestion in which the parenchyma has disappeared. The spleen is slightly enlarged. The pancreas is atrophic, but its lobular structure is well preserved.

The kidneys are about normal in size. The arteries are thick-walled and gaping. The surface is very irregular with numerous depressions of various size. These are reddish in color. On the cut surface are partly wedge-shaped and partly more rounded elevations which correspond to the nodules of parenchyma seen on the surface. In the retracted areas the cortex is absent. Everywhere

the branches of the renal artery are thickened, some have nodules. Many are totally obliterated. Some of the nodules are spindle-shaped and surround the entire circumference, others are smaller and involve only part of the circumference. In places linear thickenings appear in the wall.

The mesenteric arteries are rigid and gaping with scattered small nodules in the wall. In the testis are several large infarcts. The gastric arteries are thickened and rigid, some show no visible lumen.

The histological examination of over fifty blocks of tissue from various organs revealed the fact that we are dealing here with the *histologically healed end-stage* or *scar tissue stage* of a *generalized periarteritis nodosa*, a *periarteritis obsoleta nodosa*. Nowhere is there evidence of acute inflammation. In practically all the cases hitherto described various stages of the inflammatory disease have been found, due to the acute exacerbations so common in this disease.

The characteristic changes found in this case are:

(1) Intima proliferation with new formation of elastic fibrils, leading to stenosis or even complete occlusion.

(2) Extensive destruction of the media including the elastica interna, or of the entire vessel wall, with aneurysm formation and thrombosis. The thrombosis is followed by complete organization, with here and there deposition of hemosiderin.

(3) A periarterial healed granulation tissue mantle consisting of dense fibrous connective tissue containing capillaries and hemosiderin deposits.

(4) Extensive destruction with even aneurysm formation in arteries with high grade intima proliferation.

(5) Healed infarct scars in most organs.

(6) High grade stenosis of both coronary arteries.

The consequence of the periarteritis obsoleta nodosa in our case was the development of: contracted kidneys, hepar lobatum, high grade coronary stenosis, infarction of the testicle, myomalacia scars, etc.

Death resulted from myocardial and renal insufficiency. Of great interest is the fact that the patient had no symptoms of angina pectoris, although both coronary arteries were reduced to one-fourth or less of their normal caliber. This finding shows us that a reduction of the blood supply to the myocardium need not cause angina pectoris. Perhaps the rigidity of the arteries due to their

great thickness, which made spasm of the vessels impossible, explains the absence of angina pectoris in this case.

We have here a new clinical syndrome due to histologically healed periarteritis nodosa: renal insufficiency, cardiac insufficiency and hepar lobatum. The finding of hepar lobatum in this disease makes it necessary to examine the vascular changes in such livers more carefully, instead of assuming the syphilitic nature of this condition. Also extensive fibrosis or atrophy of other organs may be due to periarteritis nodosa.

## The Important Symptoms Observed in the Five Cases Herein Reported

| | |
|---|---|
| Accelerated regular pulse | 5 |
| Edema of the legs | 5 |
| Septic type of temperature | 4 |
| Pain in the extremities, polyneuritis (wrist-drop in two cases) | 4 |
| Hematuria | 4 |
| Cardiac insufficiency | 3 |
| Melena | 3 |
| Cerebral symptoms | 2 |
| Onset with acute angina | 2 |
| Abdominal pain | 2 |
| Changes in the fundus oculi | 1 |

## Summary

1. Periarteritis nodosa is a specific infectious disease probably caused by a filterable virus, with an elective affinity for the arteries of the body. The organs most commonly involved are the kidneys, heart, liver, muscles, peripheral nerves and gastro-intestinal tract. Any organ, or all may be affected.

2. The chief symptoms are a septic temperature, polyneuritis and polymyositis, hematuria or nephritis, abdominal cramp-like pains, progressive emaciation. The great variability of the symptoms, pointing to involvement of various organs, and the tendency toward acute exacerbations are suggestive of periarteritis nodosa.

3. The pathological changes in the arteries may be divided into four stages: (1) alterative-degenerative, (2) acute inflammatory, (3) granulation tissue, (4) histologically healed end-stage or scar tissue stage.

4. We have described the histologically healed end-stage of periarteritis nodosa. A patient with a single severe illness consisting of

icterus, high fever and acute nephritis died four years later of renal and cardiac insufficiency. The postmortem findings revealed a histologically healed end-stage of periarteritis nodosa affecting all the organs of the body except the central nervous system. The contracted kidneys, hepar lobatum, myomalacia scars, pancreatic and adrenal atrophy, and coronary stenosis were all due to this disease.

5. A new clinical syndrome characterized by cardiac insufficiency which failed to react to digitalis, renal insufficiency with low specific gravity of the urine and reduced chlorides, progressive emaciation, abdominal pain and hepar lobatum is described. Especially important is the fact that the patient lived four years after his single acute attack, and that the patient was entirely free from temperature during his fatal illness. The absence of temperature indicates histological healing of the disease.

6. Periarteritis nodosa is of interest to the surgeon because it can produce the symptoms of an acute cholecystitis with severe changes in the gall bladder, internal hemorrhage due to rupture of an aneurysm (kidney, liver, pancreas, brain, gastro-intestinal tract, lungs), or gangrene of the intestine with peritonitis. The great frequency of polyneuritis as the first and predominating symptom should interest the neurologist. In four of our five cases this was a prominent symptom. And the ophthalmologist who becomes acquainted with the disease may enable us to make the correct diagnosis *in vivo* by finding nodules or localized thickenings on the retinal arteries.

7. The diagnosis of periarteritis nodosa is very difficult, and it is only by keeping in mind the cardinal symptoms which we have described that the internist will be able to recognize the disease, after having ruled out other possibilities. In a few cases the diagnosis has been made by finding nodules in the skin with the characteristic histological changes in the blood vessels.

8. I wish to call attention to the fact that there is a microscopic form of periarteritis nodosa which can be recognized only by a careful study of tissues, especially with elastica stains of the blood vessels. Pathologists should examine carefully the arteries in atrophic organs or those with extensive fibrosis not to overlook changes such as we have described for the end-stage of periarteritis nodosa. It is possible that some cases of insufficiency of one or more glands of internal secretion may be due to atrophy caused by this disease. We

have seen changes in the thyroid, adrenal, pancreas, ovary, and testis due to periarteritis nodosa.

9. How often periarteritis nodosa of a single organ or of numerous organs, comes to a complete standstill is difficult to say. We are inclined to consider complete histological healing, as in one of our cases, a rare occurrence. For in practically all the cases till now described acute as well as chronic changes have been present.

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## DESCRIPTION OF PLATES

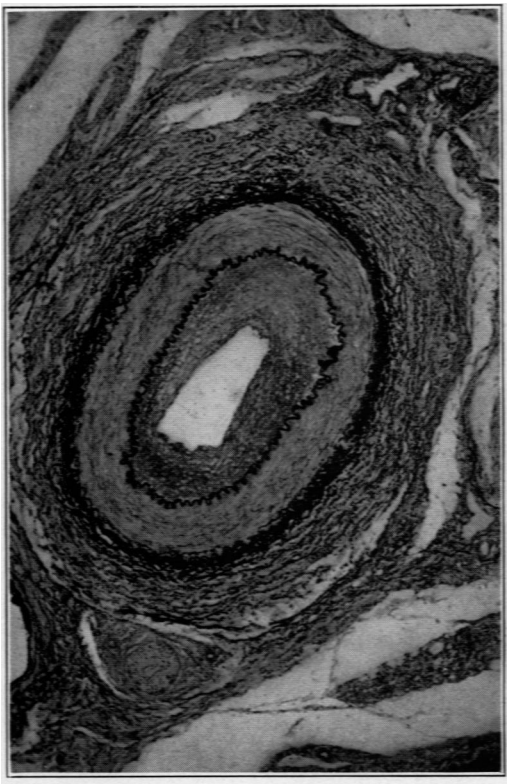
### PLATE 89

FIG. 1. (Case 5.) Healed periarteritis nodosa. A branch of the mesenteric artery with marked intimal proliferation with new formation of elastic fibrils. At this level the internal elastic layer is intact. Serial sections showed areas of wall destruction from which the intimal proliferation progressed. × 150.

FIG. 2. (Case 5.) Left coronary artery. This vessel presents an extensive destruction of about two-thirds of the circumference of the artery. The lumen has been greatly reduced in size by organized thrombi and intimal proliferation. There is also the characteristic periarterial healed granulation tissue mantle. Elastic tissue stain. × 100.

FIG. 3. (Case 5.) Pancreatic artery. Here the high-grade intimal proliferation predominates. At the other levels characteristic wall changes were found. Other arteries with complete obstruction by organized thrombi or intimal proliferation were found. × 150.

FIG. 4. (Case 5.) A bronchial artery at the lung hilum. This vessel presents remarkable changes due to wall destruction with aneurysm formations, high-grade intimal proliferation and final central thrombosis with organization and recanalization. Elastic tissue stain. × 200.



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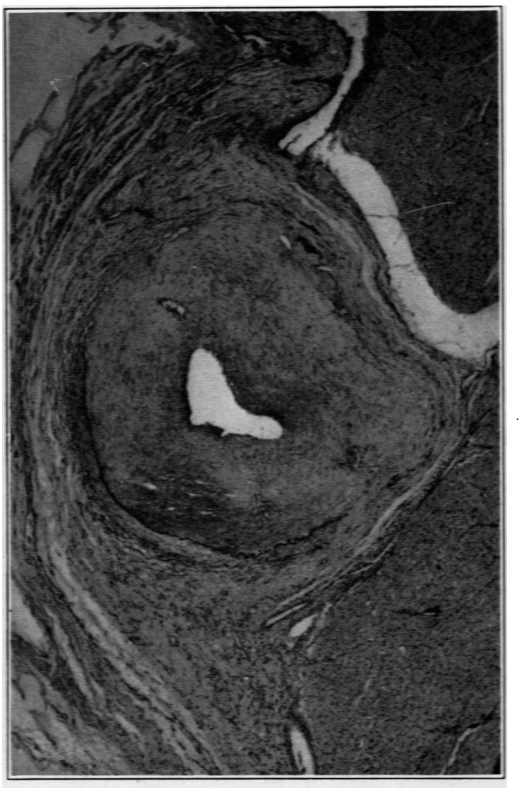

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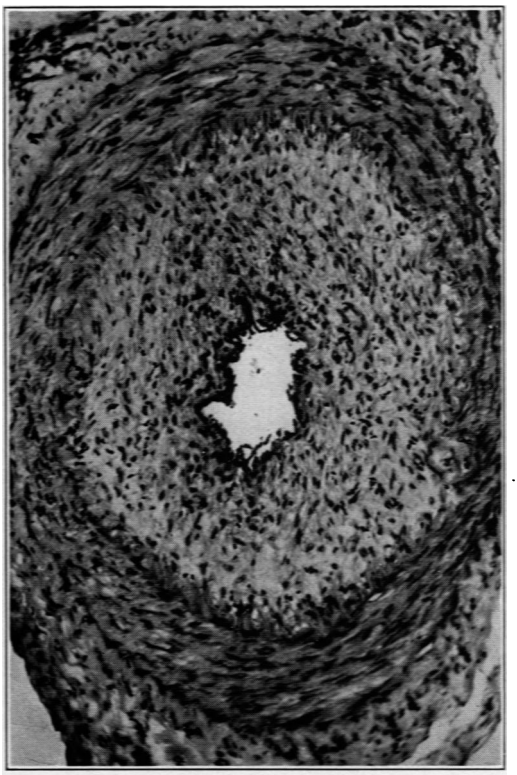

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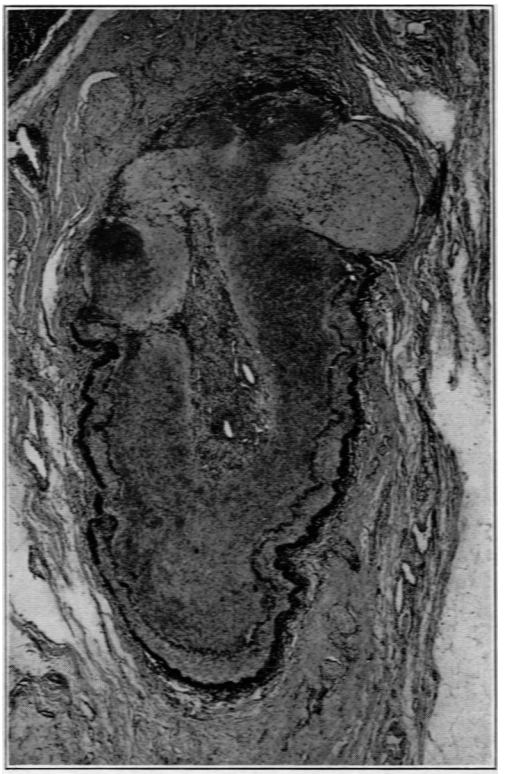

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Arkin

Periarteritis Nodosa

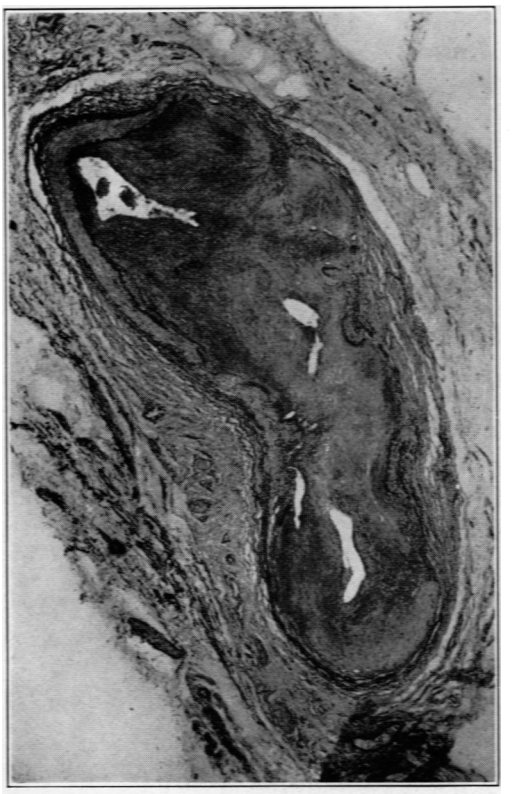
PLATE 90

FIG. 5. (Case 5.) Para-esophageal artery, showing extensive destruction of the wall with aneurysm formation and complete organization. There is also stenosis of the lumen due to thrombosis with organization, and intimal proliferation. Elastic tissue stain. × 150.

FIG. 6. (Case 5.) Hepatic artery in healed periarteritis nodosa. Note the almost complete destruction of the artery, with organized thrombosis of the lumen, and a very thick periarterial vascularized healed granulation tissue. The acute changes must have been very extensive. × 100.

FIG. 7. (Case 5.) Liver in healed periarteritis nodosa. Note the large area of liver cell destruction, with beginning regeneration from some of the bile ducts. The branches of the hepatic artery show very marked changes, with total occlusion of many. The resulting infarction with organization produced deep scars with wrinkling of the liver capsule. The gross appearance resembled that seen in hepar lobatum syphiliticum. Hematoxylin and eosin. × 75.

FIG. 8. (Case 5.) Older infarcts of adrenal due to periarteritis nodosa. Only a small zone of cells at the periphery appears normal. × 150.



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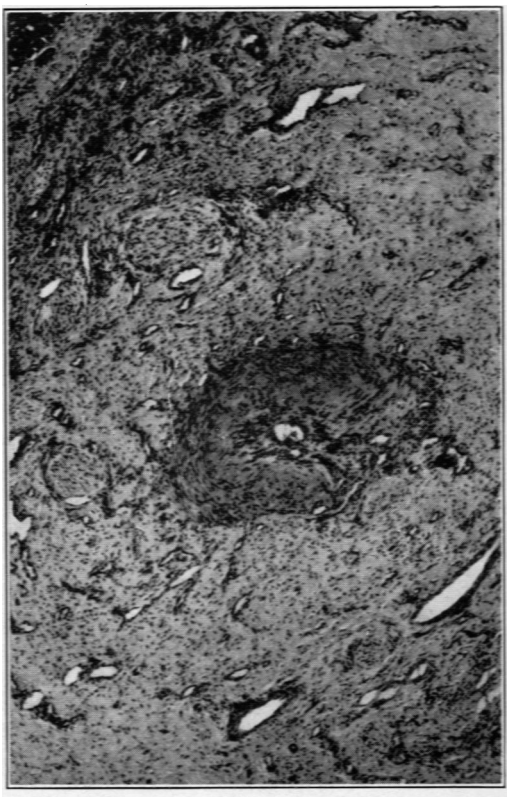

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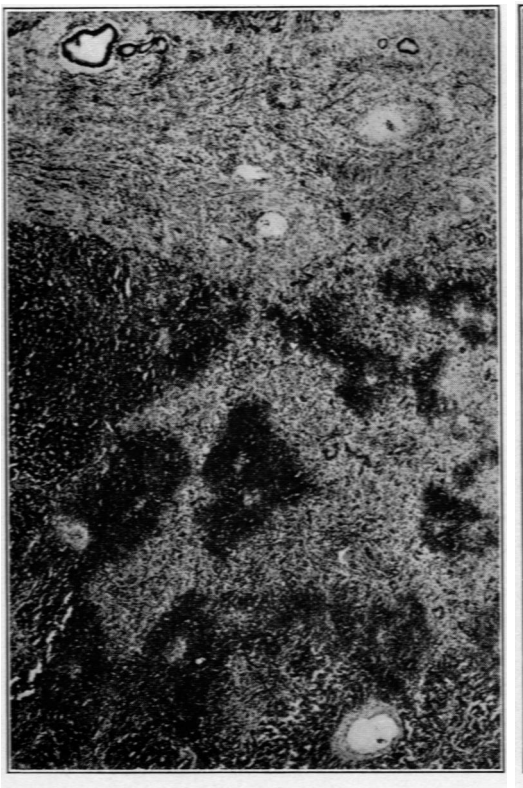

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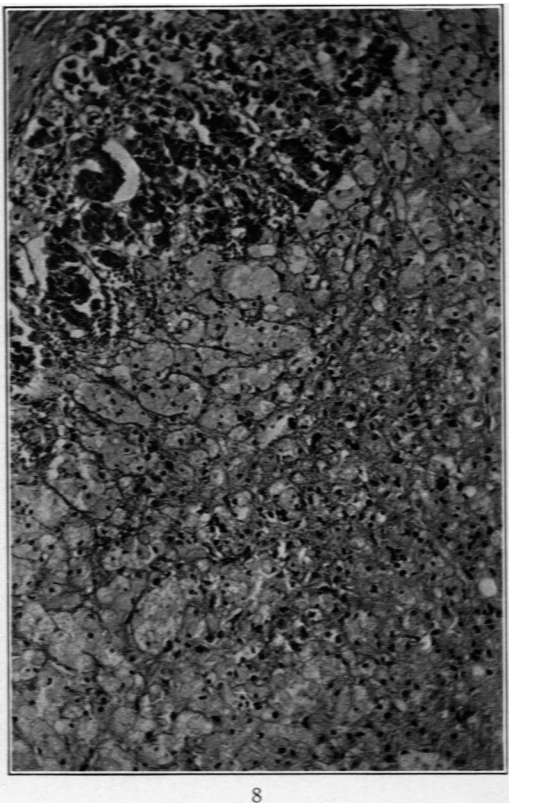

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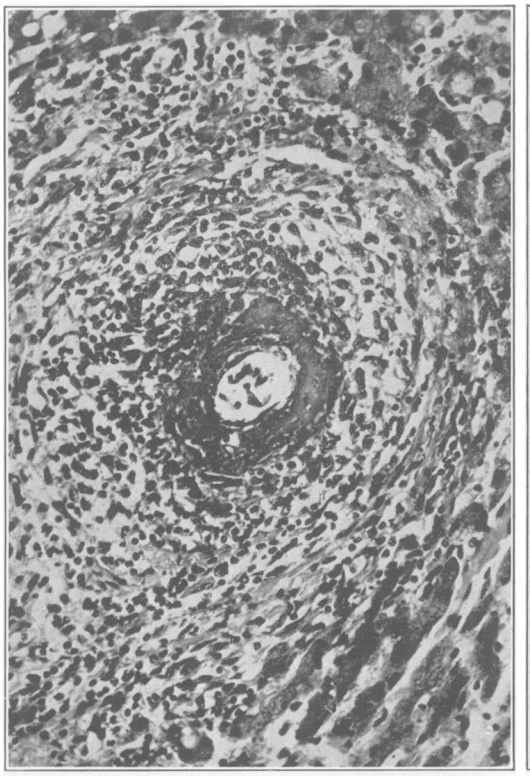
## PLATE 91

FIG. 9. (Case 1.) Acute periarteritis nodosa of the liver. This is the very early acute stage with hyaline necrosis and fibrinous exudation. There is some edema and cellular infiltration. × 200.

FIG. 10. (Case 1.) Acute periarteritis nodosa of the brain. This small arteriole reveals only a periarteriolar hemorrhage without any cellular infiltration. In other sections similar hemorrhages with wall changes were found. × 300.

FIG. 11. (Case 1.) Acute periarteritis nodosa of the sciatic nerve. This small artery reveals a very early acute stage, with fibrinous exudation and slight cellular infiltration. The process is in the media and subintimal connective tissue. The lumen has become V-shaped as a result of the exudation with elevation of the endothelium. This finding explains the eccentric lumen so often found in the arteries of the healed case. × 200.

FIG. 12. (Case 1.) Acute periarteritis nodosa of the kidney. This section shows an aneurysm formation, with thrombosis and early organization. The acute inflammation has subsided. Hematoxylin and eosin. × 50.



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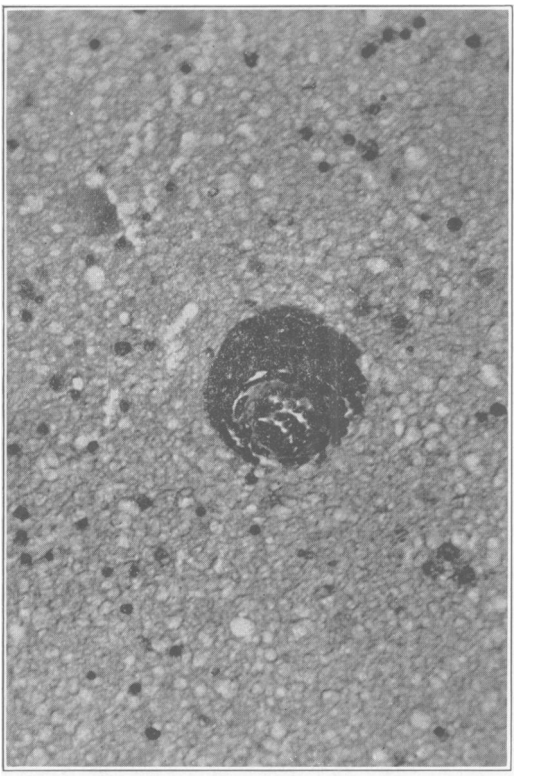

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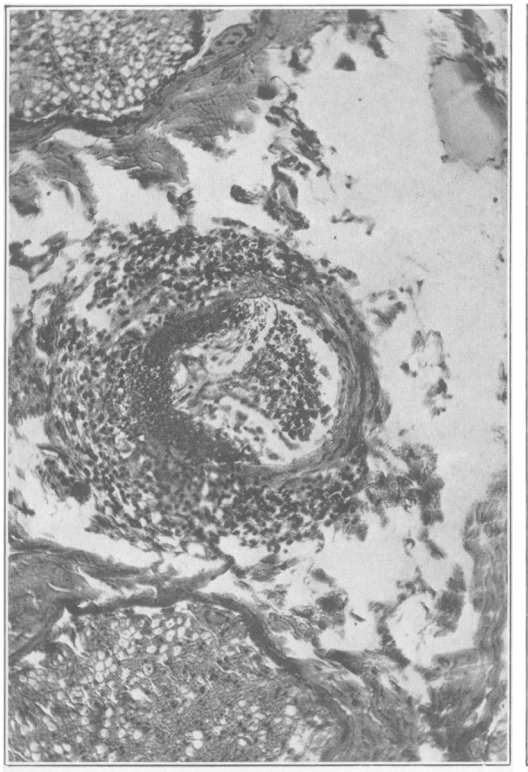

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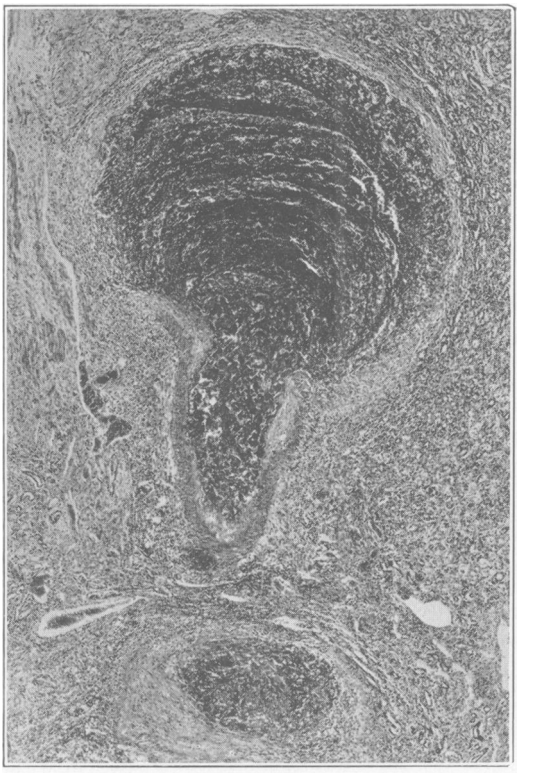

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Arkin

Periarteritis Nodosa