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A STUDY OF THE ENDOCARDIAL LESIONS DEVELOPING DURING PNEUMOCOCCUS INFECTION IN HORSES.

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The development of the lesions of vegetative endocarditis during the process of immunizing horses for the production of therapeutic serum is of interest, not only on account of its significance in interpreting some of the fundamental conditions underlying pneumococcus infection, but also in its relation to the pathology of endocarditis in general. Recognition of the infectious nature of endocarditis has come about very gradually in recent years. The first step was that of distinguishing malignant vegetative endocarditis which was found to be invariably associated with bacterial infection. Malignant endocarditis was considered to be invariably fatal. The next step was the recognition of the less severe and serious processes which were found also to be associated with bacterial infection. The term infectious or bacterial endocarditis was introduced, and included a much larger number of conditions than the old term of malignant endocarditis. Gradually the infectious nature of many subacute and chronic or even healed lesions of the endocardium and valves of the heart were suspected to have been originally bacterial, and it then became difficult to distinguish the lesions which should

be attributed to rheumatism or chorea. The recognition of acute arthritic rheumatism as an infectious disease of bacterial incitement now breaks down all of these distinctions which have been drawn between bacterial infectious endocarditis, no matter now severe the form, and chronic endocarditis that is associated with or follows rheumatism.

In a former paper on "The Bacteria as Incitants of Malignant Endocarditis" it was suggested that the distinctions between infectious endocarditis and malignant endocarditis could not be sharply drawn, and it was practically impossible to distinguish infectious bacterial endocarditis from the forms of the disease associated with rheumatism and chorea. At this time older clinicians of long clinical experience questioned the possibility of recovery ever taking place from malignant endocarditis. In the discussion of my paper, E. J. Janeway cited one case of recovery from gonorrheal vegetative endocarditis, which was the only one in his experience.

So recent is the recognition of the infectious nature of endocarditis that statistics are lacking to show the relationship of the disease to other diseases; but apart from rheumatism and chorea the later statistics show that pneumonia and sepsis, especially the puerperal form, are the diseases which are most commonly associated with the old types of infectious or malignant endocarditis. In sepsis and in pneumonia the occurrence of generalized infection, bacteriemia, has been demonstrated with the improved technic of blood cultures Bacteriemia in general has been found to be much more prevalent in infectious disease than was formerly thought possible. The occurrence of bacteriemia even without marked febrile reaction has been recorded following pneumonia after the crisis, by Wolf,[1] and I have also found it in susceptible animals which have been immunized. Although it is extremely unlikely that bacteriemia occurs ordinarily without febrile reaction, yet the fact that it may occur in the animal that is highly immune is significant, and especially if any light is thrown upon the localization of the organisms of such a bacteriemia in susceptible tissues at points of least resistance; for example, such as the cardiac valves.

For some years in my experiments with pneumococcus infections in animals I have observed lesions such as have been described by Rosenow[2] and thus I am able to confirm some of his observations. But interesting as is his theoretical explanation of these lesions, this can hardly as yet be considered to have been demonstrated. The hemorrhagic lesions in my experience were due to the toxic effects of the inoculation. In the rabbit it was difficult to ascertain just how the lesions developed in the heart. In some instances the inoculation was given through the ear vein and the hemorrhagic lesions were entirely limited to the right heart, suggesting a direct action of the poison carried in the blood stream to the tissues of the heart. Rabbits die promptly after the inoculation, so that no valvular vegatations developed in this animal. In two old rabbits which had been immunized a long time I recall chronic lesions of the arteries, with atheroma and calcareous deposits throughout the aorta extending into the iliac arteries.

These phenomena of pneumococcus infection are to be considered manifestations of the action of the pneumococcus poison and thus illustrative of the action of this poison on certain tissues of the body. The pneumococcus, like all other pathogenic bacteria, varies in its production of toxin, and doubtless certain conditions, as yet unknown, are essential not only for its production by the pneumococcus but for its action on the tissue elements as well. This is true of all pathogenic bacteria and of all the known bacterial toxins. Although interesting it is indeed misleading to follow Rosenow to the point of assuming an exclusive or peculiar quality, faculty or adaptative capacity in the inciting agent as the dominant factor. In pneumococcus infection adaptation, broadly considered and not specifically limited to certain tissues, is one of the most important factors determining the development of infection; but localization in different tissues or organs after the development of infection elsewhere may also be determined by many conditions, such as the temperature of an organ or the character of the tissues in satisfying nutritive requirements of the pneumococcus, and like conditions. The fact that the blood vessels are especially susceptible to the action of the poisons of the pneumococci and streptococci; the fact that the blood often, better than any other tissues, satisfies the nutritive requirements of the pneumococcus and streptococcus, as evidenced by the uncomplicated bacteriemia; the fact that these nutritive conditions of the blood are often quickly exhausted by pneumococcus and to a much lesser extent by the streptococci, as evidenced by the prompt, early and often complete, or nearly complete, disappearance of the pneumococci from hemorrhagic exudative lesions — all of these observations

suggest that localization in pneumococcus and streptococcus infection follows the general laws of infection, adaptation of the agent and susceptibility of the host. If it were necessary to theorize concerning the localization of pneumococcus infection, it would be helpful to have an explanation of why it is that the blood vessels of some tissues are often injured by the bacterial poison and rupture while others may escape. But still more profitable would be the results of careful investigation to determine the conditions in the tissues affecting the action of bacterial poison on the tissue elements or the nutritive conditions affecting bacterial growth, temperature, available oxygen, food elements and so on. Progress in our knowledge of infection and in the clarity of our conceptions of infectious processes is now marked by and largely limited to the results of study along these lines.

In the light of this previous experience the occurrence of lesions of the endocardium in horses attracted my attention and led to the study at autopsy of seven animals immunized against Types I., II. and III. of the pneumococcus.

Antipneumococcus serum is produced by the immunization of horses with living virulent cultures of the pneumococcus. Dead cultures are used at first for a short time in order to protect the animal against the development of infection, but even after the animals have attained a high degree of immunity, yielding serum of therapeutic value, signs of joint involvement or other infectious processes appear which incapacitate them for a longer or shorter period. Some of these horses recover, but others lose weight and strength and die. If the joints are not badly affected by the repeated inoculations with living cultures, these can be continued for some time before the periodic bleedings show a diminution in the therapeutic potency of the serum.

Six years ago, before the importance of the differentiation of the pneumococcus types was fully demonstrated to be essential in the serum therapy of the disease, I undertook experiments to produce a potent serum in horses. The first animals which I immunized were inoculated with a single strain of the pneumococcus — it so happened a Type I. organism. The organism was passed through rabbits to maintain its virulence, but in the light of recent investigations[7] showing the importance of rapid transfer whether in animals or culture, it is doubtful if the organism was always maintained

at the maximum virulence. The first two horses were not examined at autopsy. The third died in less than two years, after failing for some months to produce as satisfactory serum as it had previously. At autopsy no significant lesions were found in the lungs, kidney, spleen, liver or viscera, but petechial foci were discovered in the endocardium and the heart valves were also involved. Recalling marked hemorrhagic lesions in the hearts of rabbits inoculated through the ear vein with large doses of virulent cultures of the pneumococcus in previous experimental studies, the lesions in the heart of this horse attracted my attention, and suggested the study of six others dying during pneumococcus immunization, in all of which were found far more marked and extensive lesions of vegetative endocarditis. Thus, in all, eight horses were autopsied, and lesions of endocarditis were found in all but one of them. Five of the horses were immunized against pneumococcus Type I., one against Type II. and one against Type III. The character of the lesions did not differ in these horses. Some of them were much more marked than others, but marked vegetative lesions were found in the horses immunized with all three types of the pneumococcus, showing clearly that there is no essential quality or character of the strains which would in any way predetermine the development of lesions in the heart. On the contrary, it appears that conditions locally in the tissues were the dominant factors in determining the development of the lesions.

Protocols of the experiments have been abstracted and are published to record the significant facts regarding the immunization of each horse. A description and discussion of the lesion follows these protocols.

Horse " G," Type I., was immunized from the fall of 1913, at Bellevue Hospital, with living cultures of pneumococcus, probably of moderate and variable virulence, in doses ranging up to 1,000 to 1,500 cubic centimeters until the spring. In September the horse was transferred to Albany and received 18 intravenous inoculations of the standard virulent cultures varying from 5 up to 1,250 cubic centimeters. The last dose of 1,500 cubic centimeters was given on March 18. April 1 the animal was bled, and April 16 it was killed. During the immunization at Bellevue the animal did not suffer from any of the inoculations; in fact, it was

continually driven on the ambulance, but during the course of immunization in Albany the animal suffered greatly from the inoculations. The febrile reaction was marked with severe chills and sweating. It developed lameness toward the last, and the hind legs were very painful.

Horse 28, Type I., was immunized from August, 1915, until August, 1916, receiving first 10 intravenous inoculations of cultures killed at 56° C., and then 65 doses of living cultures varying from 25 to 200 cubic centimeters, when the animal was allowed to rest. The immunization was resumed in December by 7 inoculations of heated cultures followed by 25 inoculations of living cultures varying from 5 to 175 cubic centimeters. The animal became lame early in the immunization, — the latter part of January, 1916. Lameness developed during the second immunization in February, 1917, after about two months' immunization, and continued until the animal failed to such an extent that it was shot July 15, 1917. A sinus of an abscess of the right hind foot was found to extend up along the bones of the leg about halfway to the knee. No significant lesions were found in the lungs or viscera. On opening the heart an extensive vegetative endocarditis was found.

Horse 38, Type I. — The immunization was begun the last of January, 1916, with 11 intravenous inoculations of heated culture varying from 10 to 400 cubic centimeters, and then followed by 27 inoculations with living cultures varying from 5 to 250 cubic centimeters. Lameness developed in the hind leg after four months' immunization, and reappeared at times during a period of rest and before the second course of immunization, beginning the first of February, 1917, and comprising 7 inoculations of heated cultures followed by 20 inoculations of living cultures varying from 5 to 225 cubic centimeters of living virulent organisms. The lameness and emaciation continued. September 15 the animal was shot. Apart from a general anemia, no significant lesions were found in the lungs or other viscera. The pleura of the left lung was adherent over an area a foot long and the width of two ribs. The pericardium was normal but several edematous areas had developed in the heart. On opening the heart the extensive lesions of vegetative endocarditis in all stages were found in the heart valves.

Horse 37, Type I. — Immunization was begun February 27, 1917, with an attenuated Type I. culture. First, 3 inoculations with heated cultures were given, and then 21 inoculations of living cultures until July 20, when the horse became ill. During the immunization the dosage was increased from 100 cubic centimeters up to 700 and 800 cubic centimeters and the inoculations were given on two successive days, repeating the dose unless the temperature reaction indicated a reduction and then the horse rested six days before the next two doses. August 11 the horse died after having been very weak, with starring coat, stiff gait, anorexia, weak, rapid pulse and a high temperature. The lungs were congested in areas, and hemorrhagic petechiæ were noted. The spleen was congested and also hemorrhagic petechiæ were noted. No significant lesions were found in the other organs. The pericardium was adherent to the apex of the heart. On opening the heart, a marked vegetative endocarditis of the valves was found, and this was preserved in Kaiserling's fluid.

Horse 39, Type I. — The immunization was begun at the same time as horse 37, with an attenuated Type I. pneumococcus; in fact, the immunization corresponded, the dosage having reached 900 cubic centimeters July 9, and was continued until September 7. On the 24th the animal was shot.

Horse 16, Type II. — This horse had received preliminary injections of a streptococcus, but later Type II. organisms were substituted. This animal was rested from September, 1916, until January, 1917, when the immunization was resumed with heated cultures followed by inoculations with the living cultures.

Horse 20 was immunized against an attenuated Type III. culture from May 25 to June 19, 1917, receiving in that period 3 doses of heated cultures of 10, 100 and 250 cubic centimeters followed by inoculations with the living attenuated culture in doses of 100 to 250 cubic centimeters. July 15 the animal was found dead in the stable. The day preceding, the animal was recorded as thin, very dyspneic, and had scabs of dried blood in both nostrils. Examination of his lungs revealed extensive areas of pleural inflammation. He was found dead the following morning, and by the time of the post-mortem there was considerable putrefaction. Areas of consolidation and extensive fibrinous pleurisy were found in the lungs. There was considerable fibrinous pericarditis, and the heart was of a deep blood-red color. Opening the heart showed the endocardium to be deeply stained with hemoglobin. The blood clot was tarry in consistency. This appearance of the heart and the blood clot may have been due to putrefaction. An extensive vegetative endocarditis was found on the valves. Other organs were practically normal. No other local foci of infection were found anywhere in this animal.

Horse 44. — Recently this pneumococcus horse died and was autopsied. The endocardium and heart valves were apparently free from lesions, but in both ventricles and auricles large thrombi had formed and had undoubtedly persisted for a long time, accounting for the progressive emaciation and death of the animal. The thrombus in the right heart was about twice as large as that in the left. It was located in the right auricle, filling the appendages, leaving only a channel for the venous blood, and extended by strands of fibrin through the tricuspid into the ventricle and out through the pulmonary valves into the pulmonary arteries. The thrombus in the left auricle enmeshed the mitral valve. The thrombi were held firmly in place but at no point were they adherent to the endocardium, which was smooth and normal everywhere after removal of the thrombi. No pneumococci were obtained in cultures.

Seven days before death Major Alexander Lambert examined the heart with me. On auscultation it was thought murmurs were heard at the apex of the heart, but these could not be made out very definitely — the sounds were so muffled.

The character of the lesions which were found in these different horses varied only in the degree or stage of development which had been reached. Photographs and drawings

are to be found reproduced at the end of this paper, showing different phases of the lesions. Practically all of the lesions were attributable to the action of the bacteria and their poisons carried through the circulation of the tissues affected. No signs of embolism were detected in the different organs except possibly in the kidney, and in these lesions it was difficult to distinguish between embolus, thrombosis and the changes incident to the inflammatory reaction of a bacterial focus involving the blood vessels, extending into the walls and lumen, and infiltrating the tissues: areas of endarteritis, periarteritis and phlebitis of the small vessels were commonly present in the tissues of different organs. These lesions are of special interest on account of the fact that the anatomical changes of this inflammatory reaction in the arteries correspond so closely with those of some of the lesions of arteriosclerosis.

Parenchymatous degeneration of the liver and kidney, areas of exudation into the tissues of the kidney and into the alveoli of the lung, together with foci of inflammation, degeneration, thrombosis or hemorrhage were found in the organs. Many of the hemorrhages were petechial in nature, lying under the capsule of the liver, spleen and kidney. Apparently the heart was one of the most vulnerable organs. In the myocardium, areas of inflammatory reaction and edema were found with degeneration of the muscle fibers, together with thrombosis and organization of the infiltrating exudate which was attributed partly to the thrombosis and partly to the inflammatory reaction which doubtless preceded it. All of these lesions which have been described, however, were variable in extent and not always marked.

More interesting and constant were the changes of the endocardium. The endocardial lesion in the earliest stage did not differ from those found in other organisms, and, so far as it was possible to ascertain, consisted primarily of a hemorrhagic extravasation extending under the endocardium in much the same way as the petechiæ were distributed in the capsules of the different organs. Although these hemorrhagic foci in the endocardium were to be found in the auricles and in the ventricles and in the papillary muscles, they were most

frequently located in the blood vessels of the valves. A partial or complete resolution or organization or an inflammatory process developed, the amount of organization and scar tissue depending upon the amount of necrosis following the inflammatory reaction. In places, evidence of complete healing and restitution of the tissues, but with considerable thickening and some contraction, causing roughening or sclerotic condition of the endocardium, was found. In others elsewhere the inflammatory reaction extended, infiltrating the tissues of the valve; and breaking down in places, evidently vegetations developed from the ulcerating surfaces, or the vegetations became grafted on to the valvular lesions as the clot accumulated. Near the surfaces of these vegetations a few foci of pneumococci were found developing in them.

Few pneumococci were found in the sections of the lesions, and pneumococci were not obtained in cultures of the serum of the bleedings. The interval between the inoculation and these bleedings was eight days. In the thickened tissues, in the areas of organization in the inflammatory areas and even in many of the areas of necrosis, pneumococci were not present in sufficient numbers to be definitely recognized. It was possible to be reasonably certain of their absence in the processes which were not necrotic, but where the cells had broken down the chromatin elements and the granules of fibrin were present in considerable numbers; these could not be distinguished defintely from cocci. On the fresh surfaces of the vegetations a few foci of the pneumococcus were readily demonstrated in one animal, and the organisms were present in considerable numbers — in clumps and masses. These foci, superficial in the vegetations, did not suggest that the bacterial invasion of the valves took place from the main blood stream because they were considered chance colonies surviving for a brief time. They did not penetrate the deeper layers of the clot or vegetations and they were not surrounded by any zone of inflammatory reaction. They were few in number. In no instance was there any evidence that lesions developed from superficial ulceration — on the contrary, it appeared from careful study of the different stages that the development

took place from the injury of the blood vessels of the endocardial tissues induced by bacterial invasion through the coronary circulation. The importance of predisposing injury in the development of the lesions is well shown by the fact that in some of them confluent zones and areas in distinct stages of development, resolution or repair were recognized as successively active processes, the localization being determined by the previous injury. The early investigators, notably Prudden,[3] demonstrated experimentally the effect of injury in favoring localization of bacteria on the heart valves, but in these experiments the rupture of the blood vessels with hemorrhage, thrombosis or the infiltration of the walls of the vessels and occlusion was clearly due to the action of the bacterial poison and was followed by bacterial development. This was frequently evanescent, as so few of the lesions even in the earliest stages contained bacteria.

In some local lesions the pneumococci disappear early in the process. In pneumonia they are present in large numbers during the very first stages of the lesion, but unlike the streptococcus and Friedlander's bacillus they disappear early and are present in large numbers only in certain areas. It is thus evident that the pneumococcus poisons, like those of many other bacteria poisons, act on the blood vessels — injuring them so that larger or smaller hemorrhages may take place. These form foci from which the inflammatory process develops. The extent of the inflammatory process varies, but the organisms usually (especially in these lesions of the endocardium) disappear early, and resolution healing with scar tissue follows.

In the cardiac valves of these horses signs of old, healed, inflammatory foci were present everywhere. In fact, the fresh vegetations were grafted on to the old, healed lesions of previous inflammatory processes. The presence of numerous areas completely healed by the formation of fibrous tissue showed conclusively that the valves in these horses had been involved for a long time before the animal succumbed, and it was found on testing the serum derived from these horses that it still possessed a degree of potency which would make it serviceable for the treatment of pneumonia in man — that

is, .2 cubic centimeter of the serum protected against .1 cubic centimeter of the culture, .000001 of which killed the control mouse in less than forty-eight hours. The fact that the serum of these horses maintained such a high degree of potency deteriorating only very little, and the persistence of the pneumococci on the lesions, only serve to illustrate the necessity of distinguishing sharply the parasitic activities of the organisms from its ability to produce toxins.

In previous experimental studies of pneumococcus infection attention was directed to this distinction, that the reactions between the pneumococcus poisons and the immune serums which neutralized them may take place independently of the parasitic activities of the organism, and may only indirectly affect its vegetative capacity and ability to grow in the tissues. This apparently holds true for all the types of the pneumococcus, and it is more reasonable to assume that it is the parasitism and degree of toxin production which varies and which constitutes the basis of the present classification into types rather than any fundamental difference in the character of the organism or its poison, and especially since the present classification is determined by the degree of agglutinability and the degree of protection obtained with different serums.

In forming definite conceptions of disease processes as they develop in man from the results of an experimental study of infection in animals, there is always a break which it is difficult, sometimes impossible, to bridge, owing to the fact that conditions are not always comparable. But in man and in these horses, conditions as they relate to pneumococcus infection are not fundamentally different. Man is relatively insusceptible to pneumococcus infection. The extensive lesions of lobar pneumonia which pneumococcus infection develops give an indication of relative insusceptibility or partial immunity, as I have demonstrated in previous experimental studies.[4] The horse is also relatively insusceptible, and the horse, while undergoing active immunization with the pneumococcus and possessing a degree of immunity sufficient to yield a serum of therapeutic potency, may develop typical pneumococcus pneumonia as recorded by

White.[5] The channel by which the pneumococci are carried to the heart, namely the blood stream, does not conceivably differ in the experimental intravenous inoculation of horses during immunization and in the pneumonias of man. But in other respects conditions of the experiment in the horse may differ from those in man.

The bacterial activity in the lesions of the immunized horse is apparently more evanescent than in the infectious endocarditis of man, but in the horse undergoing immunization the tissues are repeatedly subjected to the action of the bacteria and their poisons by frequent inoculation. That these, however, are scarcely fundamental and entirely negligible for the purposes of this study is indicated by the fact that there are no fundamental differences in the anatomical changes — the lesions — which are practically identical in man and in the horse.

SUMMARY AND CONCLUSIONS.

Horses undergoing active immunization by the intravenous inoculation of living virulent pneumococcus cultures develop infectious processes locally in the joints and in the tissues of the organs, but especially in those of the heart including the heart valves. These lesions are intimately associated with injury of the blood vessels due to the action of the pneumococcus poisons, and are thus infectious processes in which the bacterial development may be evanescent and promptly followed by complete resolution or by reparative processes with scar tissue, or the bacterial development may persist, inciting varying degrees of inflammatory reaction and necrosis before the bacteria are destroyed and the reparative process heals the injury. All stages of these lesions were found in the heart valves: petechial and larger hemorrhages with and without inflammatory reaction and larger and smaller areas of necrosis in which pneumococci were present in large or small numbers or absent altogether, all in various stages of development, resolution and repair. These lesions correspond with those of acute and chronic endocarditis in man. The anatomical changes of the ulcerative or vegetative and the sclerosed lesions in man are all to be found in these lesions

of the horse. It is therefore not necessary to assume that the chronic lesions of endocarditis in man, however slight or marked, or however free from evidences of bacterial activity, have not been originally infectious processes.

In these studies, as in the experiments of Prudden and other early investigators, the importance of predisposing injury determining the localization of the bacteria is also demonstrated, but it is evident that the bacterial poisons produce this injury so that the bacterial localization may be practically coincident with it or follow it immediately. It also appears that in these experiments on the horse, and doubtless also in the disease as it occurs in man, the endocardial lesions arise from injury of the bacteria and their poisons carried to the endocardial tissues through the coronary circulation and not from the direct action on the endocardium of bacteria and their products passing in the main blood stream of the ventricles and auricles.

In order to clarify our conceptions of pneumococcus infection, and doubtless also streptococcus infection, it is necessary to recognize the parasitic and the toxic activities of the inciting agents as distinct phases of the infectious processes and yet not as entirely separate or independent activities because they are in point of fact closely linked and largely if not wholly dependent one upon the other.

REFERENCES.

1. Wolf, Journ. Infect. Dis., 1906, iii, 446.
2. Rosenow, Journ. Infect. Dis., 1909, vi, 245.
3. Prudden, Am. Journ. Med. Sc., 1887, xliii, 55.
4. Wadsworth, Journ. Exp. Med., 1912, xvi, 54, 78.
5. White, Journ. Exp. Med., 1899, iv, 425.
6. Libman, Proc. New York Path. Soc., 1911, xi, 118.
7. Wadsworth and Kirkbride, Journ. Exp. Med., 1918, xxviii, 791.

DESCRIPTION OF PLATES.

1. Photograph of the tricuspid valve, showing practically the normal condition, with the exception of a hemorrhagic lesion in one cusp.

2. Photograph of the tricuspid valve in another horse, showing the well-marked thickening of the cusps, due to successive acute and subacute inflammatory reactions, followed by permanent thickening.

3. Photograph of the aortic semilunar valves and one mitral cusp, showing more marked and acute lesions of vegetative endocarditis.

4. Drawing of a section through a hemorrhagic focus in one valve at its base. The hemorrhagic area lies in the subendocardial tissues, and is continuous with larger areas in the heart wall at the base of the valve near by. No bacteria were found in the sections of this lesion and no evidence of acute inflammatory reaction. The lesions thus suggest the earliest stages.

5. Photomicrograph of a valve, showing marked thickening without any evidence of acute inflammatory reaction.

6. Photomicrographs of sections through the lesions of the valves shown in the photograph (3) of the lesions in gross. The section is stained by the method of Gram and Weigert, to demonstrate bacteria and fresh fibrin. Bacteria are to be found in foci near the surface or in a few of the necrotic foci, as indicated in photomicrographs 8, 9 and 10. The dark areas of fibrin show the patchy character of the lesion, due to the successive inflammatory reaction or to the development of new vegetations or thrombi on the valves.

7. Photomicrograph of a section through a necrotic area located under the endocardium in a connective tissue septum of the heart wall separating the bundles of muscle fibers. The pneumococci were not in large numbers and were difficult to distinguish from the cellular necrotic and chromatin elements.

8. Photomicrograph of a bacterial focus situated near the surface of one of the vegetations.

9. Photomicrograph with higher magnification to show the pneumococci.

10. Photomicrograph of the heart muscle showing infiltration of the tissues and an acute inflammatory focus in the center of which there is varying degrees of necrosis, such as is shown in photomicrograph 8.

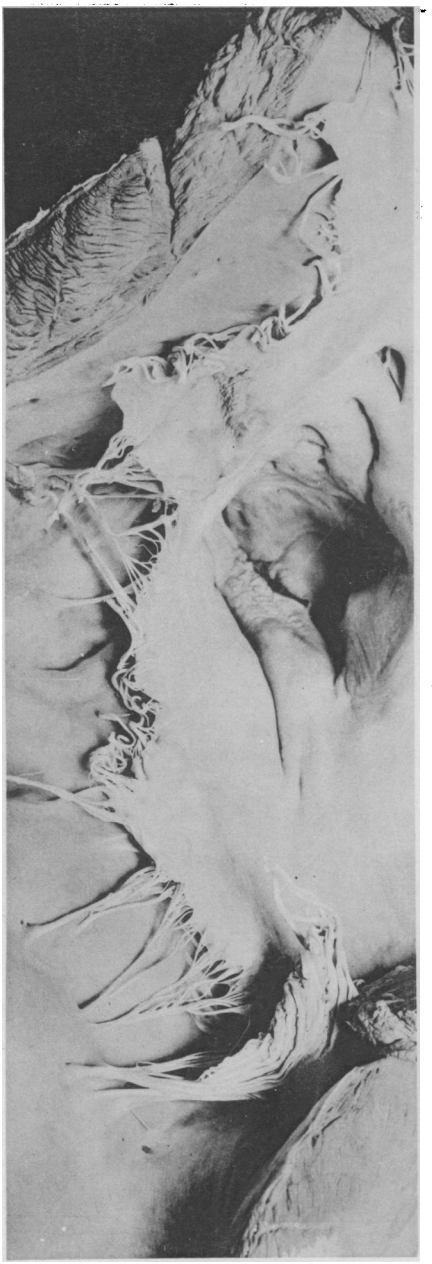
11. Photomicrograph of a section through the heart walls, showing infiltration of the tissues, but especially the chronic changes in the walls of the blood vessels.

12. Drawing under high power of the small artery shown in photomicrograph 13, which was cut longitudinally.

13. Photomicrograph of the small artery, which was cut at right angles, shown indistinctly on the edge of photomicrograph 13.

14. Photomicrograph of a section of the kidney showing the acute inflammatory reaction in this organ, described by some other observers as acute glomerulonephritis (Libman)[6]. Thickening of the blood vessels, hemorrhagic extravasation, extreme congestion and infiltration of the adjoining tissues, such as appear in the photomicrographs and drawings of the heart wall, were also found in sections of the kidney.

15. Drawing of the congested glomeruli, degenerated tubules and infiltrated tissues shown in the center of photomicrograph 17. The distended blood vessels near by, and also the hemorrhagic areas which were present, were not in the field which was drawn under the high power.



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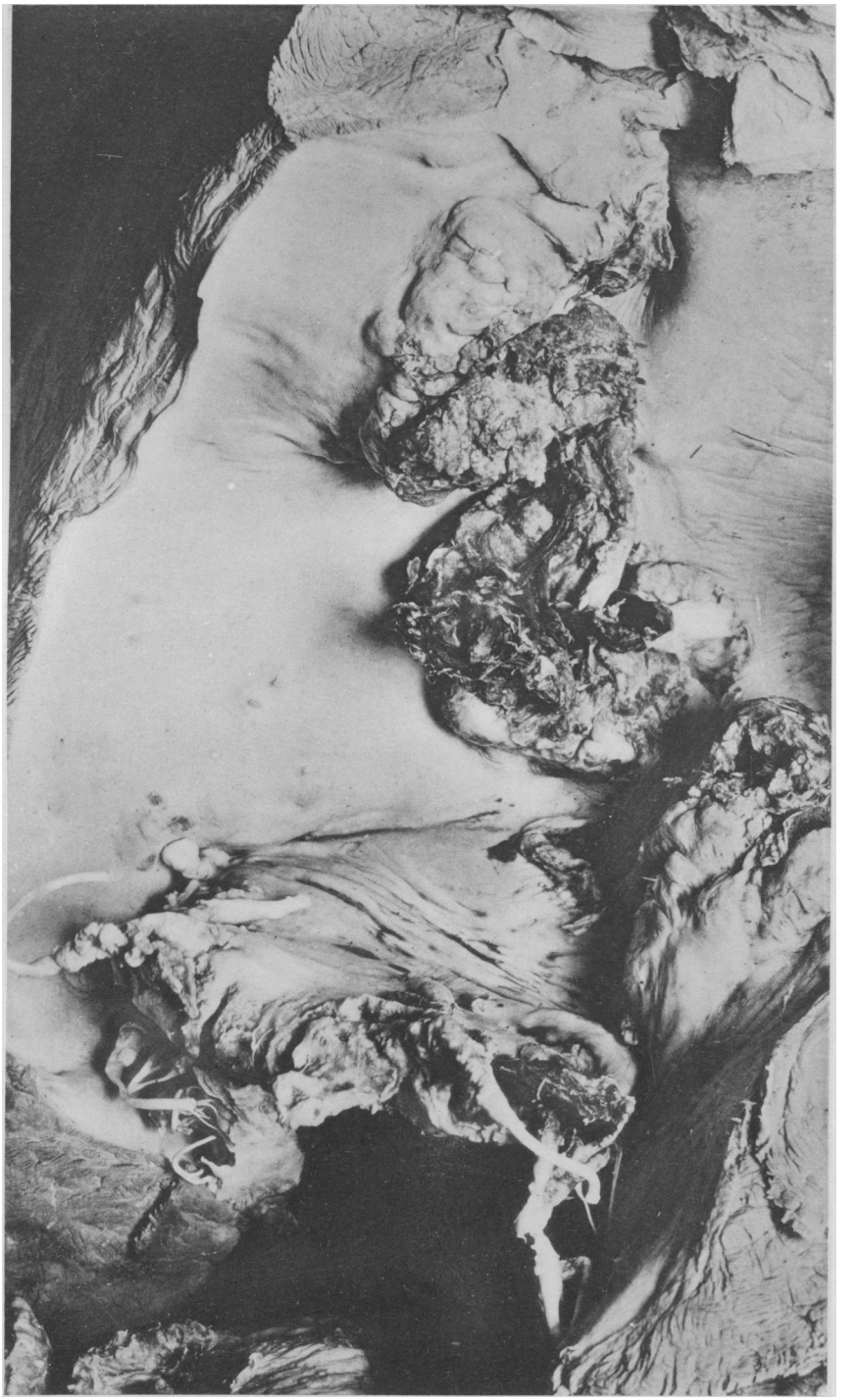
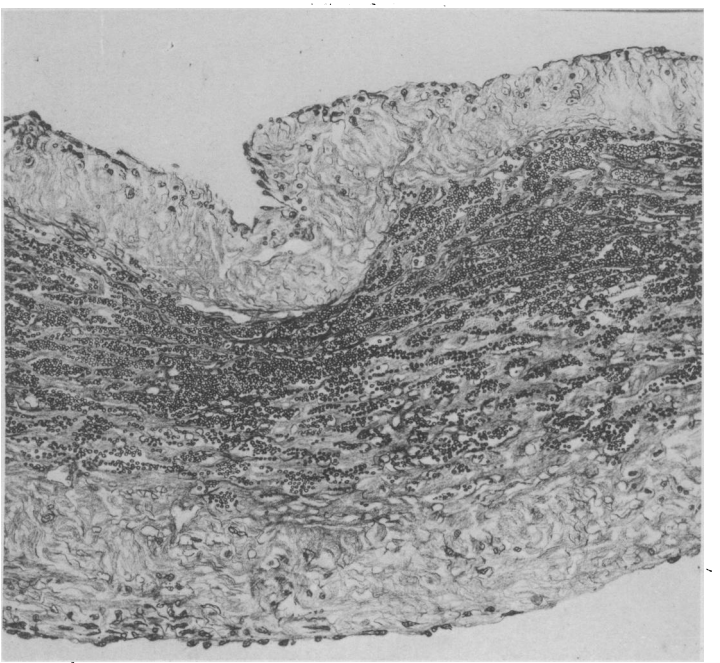
Wadsworth. Pneumonic Lesions.



Wadsworth. Pneumonic Lesions.



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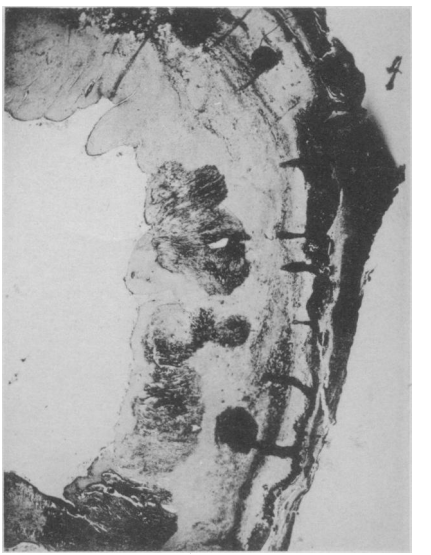

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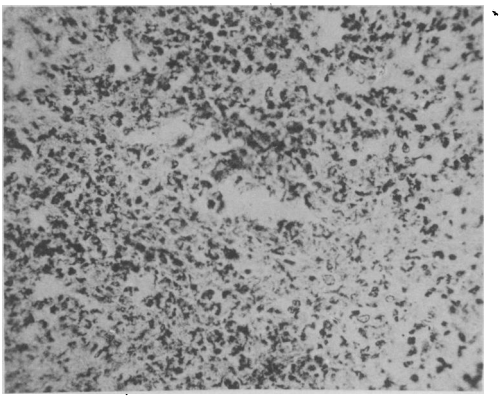

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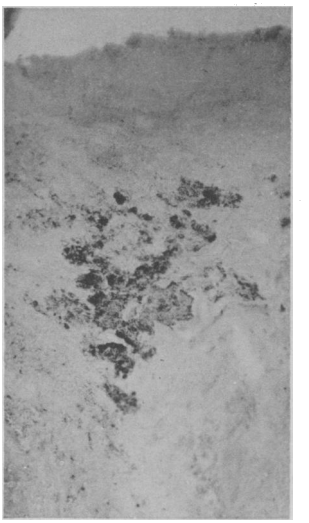

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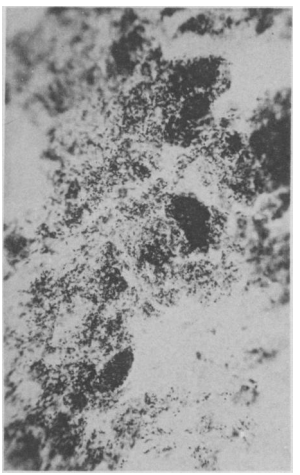

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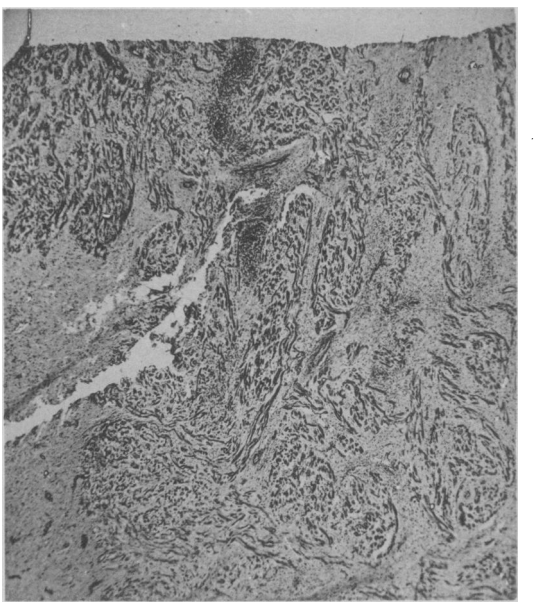

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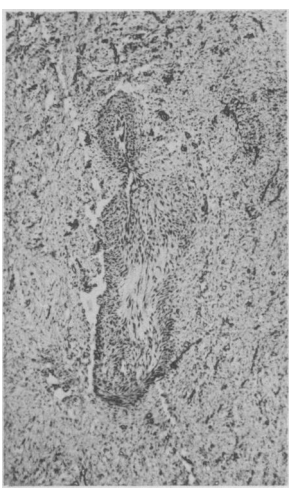

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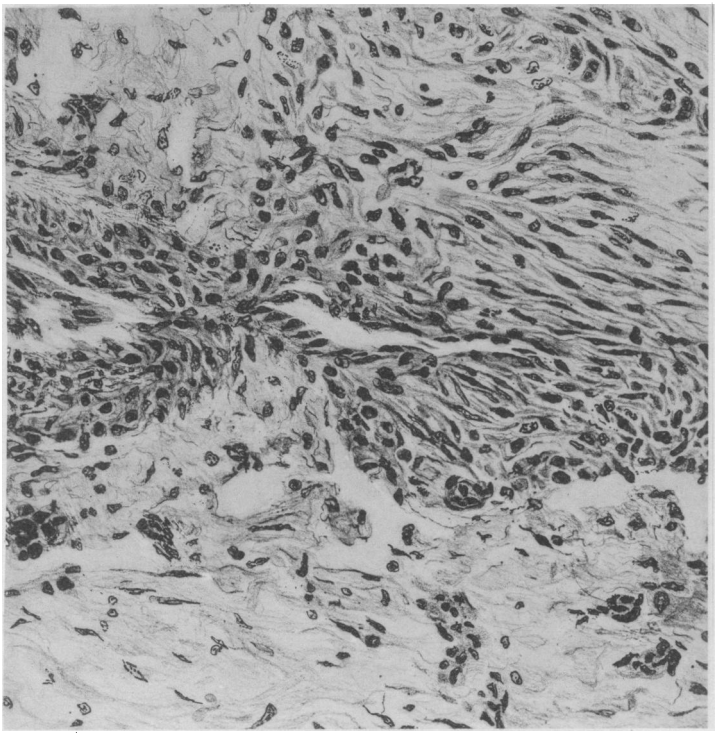

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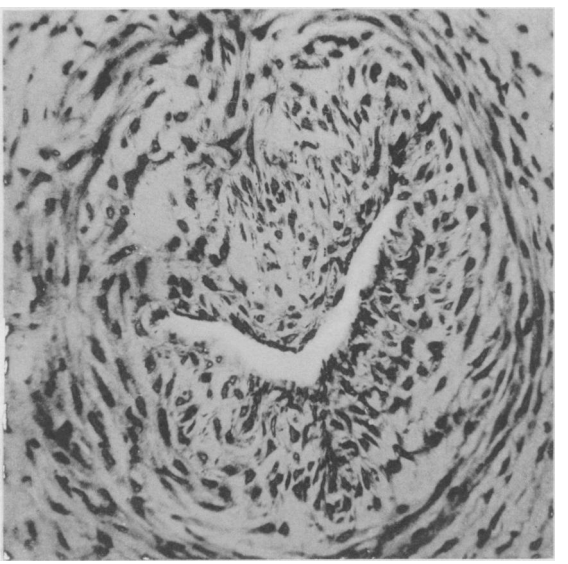

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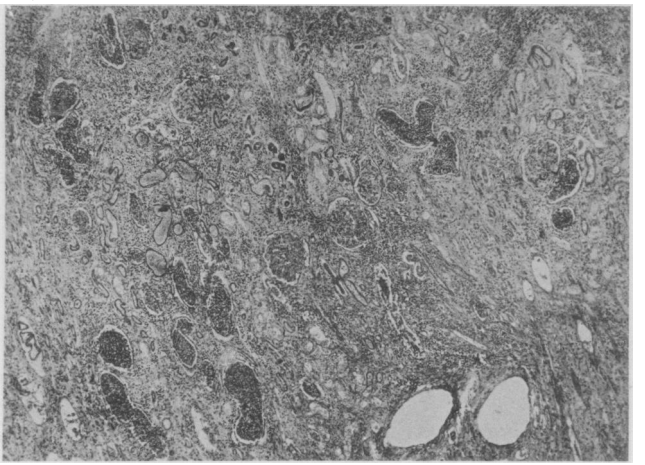

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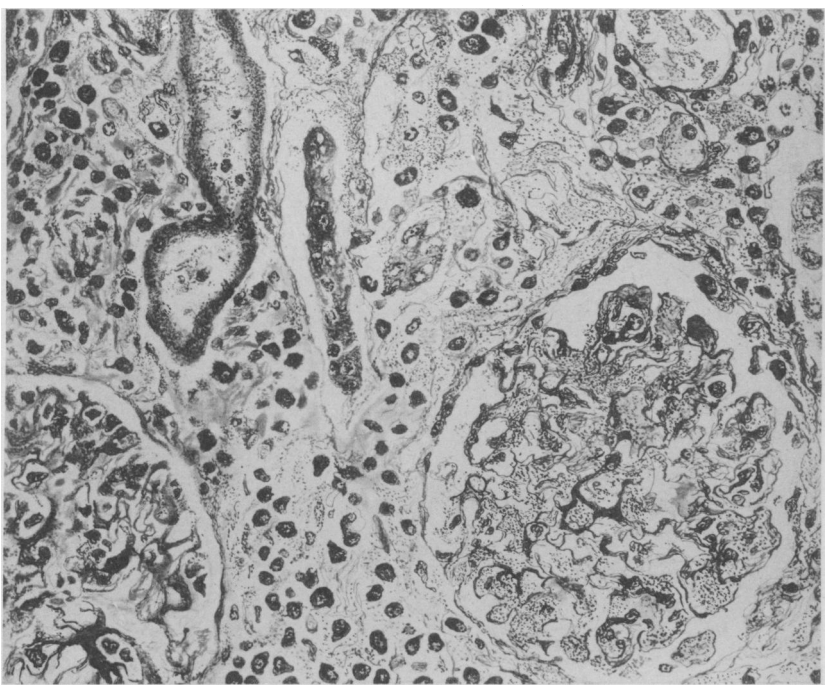

15