CELLULAR MECHANISMS OF ANTIBACTERIAL DEFENSE IN LYMPH NODES

I. Pathogenesis of Acute Bacterial Lymphadenitis*

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Plates 37 and 38

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Although many aspects of the pathological changes occurring in the lymphatic system during acute bacterial infection have been described in detail (1–15), the cellular reactions noted in lymph nodes during inflammation, and their relationship to the initial bacterial lesion have never been systematically investigated. The most extensive study of bacterial lymphadenitis is that of Benzançon and Labbé (16, 17), who noted granulocytic infiltration in the nodal sinuses of animals infected with *Bacillus anthracis*, *Staphylococcus aureus*, and *Corynebacterium diphtheriae* and described diapedesis of leucocytes from capillaries within the regional nodes. However, the presence of many polymorphonuclear leucocytes in the subcapsular sinuses and in the afferent lymphatics led these investigators to conclude that most of the cells arrived at the nodes from the primary sites of inflammation in the extranodal tissues. Menkin and Freund (18) also concluded that the primary inflammatory focus is the main source of polymorphonuclear leucocytes found in regional lymph nodes during acute lymphadenitis.

Numerous investigators have described acute lymphadenitis during the course of experimental or spontaneous bacterial infections in animals, but none have dealt with the problem directly. Thus the presence of polymorphonuclear leucocytes in mediastinal lymph nodes has been demonstrated during experimental pneumococcal pneumonia and in experimental pleuritis (19–21). Likewise granulocytes have been noted in the sinuses of regional lymph nodes of rabbits injected into the foot-pad with typhoid vaccine (22).

Epizootic lymphadenitis of guinea pigs due to group C streptococcus has been studied only during the late stages of necrosis and abscess formation (23–25). Changes in the lymph nodes of rabbits infected with *Listerella monocytogenes* have been described (26), but lesions produced by this non-pyogenic organism can hardly be considered comparable to those produced by the pyo-

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genic bacteria that commonly cause acute infection in man. That polymorphonuclear leucocytes gain access to nodal sinuses during the course of human bacterial infections, particularly those complicated by bacteremia, has been clearly established (27).

It is the purpose of the present paper to describe the pathogenesis of acute bacterial lymphadenitis, with particular reference to the evolution of the inflammatory response within the infected node. Subsequent reports will deal with the mechanisms of cellular defense that operate in lymph nodes during the course of acute pyogenic infections.

Methods

Animals.—White rats (Sherman strain) weighing 175 to 250 gm. were obtained from a single breeder, and care was taken to eliminate all animals with foot lesions of any kind.

Bacterial Cultures.—A Type I pneumococcus (A_5 strain) which was shown to be highly pathogenic for rats (28) was used in all but two experiments. Maximum virulence of the organisms was maintained by passage through mice every 3 weeks, and the stock culture was stored in the ice box in defibrinated rabbit blood under vaseline (28). Cultures for inoculation were prepared by transferring 0.1 ml. of stock culture to broth.[1] After 18 hours' incubation, 0.5 ml. of culture was placed in 4.5 ml. of broth and incubated 4 hours.

Two other organisms, (*Streptococcus hemolyticus* strain 100 and *Staphylococcus aureus* strain 235), used in analogous experiments, were handled in the same manner except that the final incubation of the streptococcus was limited to 2 hours to insure maximum encapsulation.

Preparation of Inocula.—After 4 hours' growth the pneumococci were centrifuged, washed in Locke's solution, and recentrifuged. The centrifugate was finally brought to the original volume with Locke's solution. Plate counts of the suspension repeatedly revealed $1.3\text{–}1.6 \times 10^9$ organisms per cc. Inocula were so diluted that 0.05 ml. contained approximately 7×10^5, 7×10^4, and 7×10^3, pneumococci. Several pilot experiments were performed with larger inocula.

Method of Inoculation.—Direct visualization of rat lymphatics in preliminary experiments demonstrated that all lymph capillaries of the foot-pad drain into the inferior pole of the popliteal node by two main tributaries. It is also known that intradermal injection of particulate matter constitutes in part an intralymphatic injection (29), although some of the injected material remains in the tissues at the site of inoculation. Accordingly the following procedure was adopted. The skin of the hind foot-pad was cleaned with alcohol and a site 0.5 cm. from the heel was selected for inoculation. Through a No. 27 gauge needle 0.05 ml. of inoculum was injected intradermally from a tuberculin syringe. Care was taken to avoid injecting the bacteria subcutaneously rather than directly into the skin.

Blood Cultures.—Blood cultures were taken from the tail vein, streaked on blood agar plates, and incubated for 24 hours. All organisms recovered were identified by the Neufeld Quellung reaction.

Methods of Pathologic Study.—Animals were killed with ether at intervals of from 5 minutes to 72 hours after inoculation. The skin and subcutaneous tissue of the foot-pad, the popliteal node, and the nguinal node of each rat were removed and fixed in Helly's solution. The tissues from all three sites were imbedded in a single block of paraffin and cut sections were stained with eosin-methylene blue, hematoxylin-eosin, and 0.02 per cent toluidine blue.

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[1] Beef infusion broth adjusted to pH 7.8, with 0.2 per cent dextrose and 10 per cent normal rabbit serum.

RESULTS

All the infected animals died 30 to 72 hours after inoculation. Death was slightly more rapid with larger inocula. Some animals had a transient bacteremia within an hour after inoculation, and all animals had bacteremia by 24 to 30 hours. A representative experiment is summarized in Table I.

(*a*) *Pathology of the Dermal Pneumococcic Infection.*—In general the inflammatory process in the foot-pad was similar to that reported in other animals (30–33). Two important differences were noted. First, many of the injected pneumococci were found to be phagocyted promptly in the interstitial

TABLE I

Survival Time and Incidence of Bacteremia in Rats Inoculated Intradermally in the Foot-Pad with Type I Pneumococci

Size of inoculum	Rat No.	Time after inoculation of foot-pad, *hrs.*								
		¼	1	3	6	18	24	30	48	72
7×10^5	1	+	0	0	0	0	+	+	Dead	
	2	+	+	0	0	+	+	Dead		
	3	0	+	0	+	+	+	+	Dead	
7×10^4	4	+	0	0	+	+	+	+	Dead	
	5	+	0	0	0	0	0	0	+	Dead
	6	+	0	0	0	+	+	+	Dead	
7×10^3	7	0	0	0	0	0	0	+	+	Dead
	8	0	0	0	0	0	+	0	+	Dead
	9	0	0	0	+	0	+	+	+	Dead

+ = blood culture positive for Type I pneumococcus.
0 = blood culture sterile.

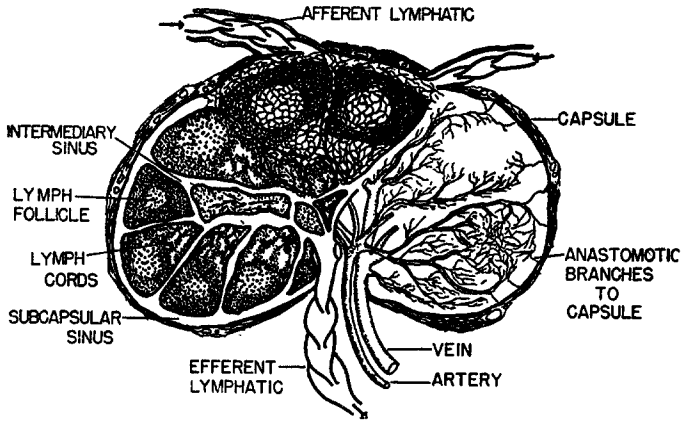
tissues, and secondly significant numbers of leucocytes were seen only in those lymphatic channels that had been previously thrombosed by the inflammatory process.

Within 15 to 30 minutes after inoculation, vascular dilatation, edema of the interstitial tissues, and "pavementing" of the capillaries with polymorphonuclear leucocytes (34) were evident. By 30 minutes to 1 hour polymorphonuclear leucocytes had entered the tissues and had begun to phagocyte pneumococci (Fig. 1). The rapidity of this process could be judged by the fact that leucocytes containing intracellular pneumococci were found within a few cell diameters of the capillary from which they had presumably emigrated (Fig.2). Five hours after infection large numbers of polymorphonuclear leucocytes had infiltrated the tissues and by 24 hours all pneumococci appeared to have been phagocyted (Fig. 3).

Within 2 hours after a large inoculation occasional lymphatics contained a fine meshwork of needle-like strands of fibrin (Fig. 4). By 3 to 5 hours fibrin formation was more dense, and although leucocytes could be seen infiltrating thrombosed lymphatics (Figs. 5 and 6) they were rarely seen in normal vessels. Fibrin formation never appeared to involve more than a few lymph channels.

(*b*) *The Normal Popliteal Lymph Node of the Rat.*—

In the rat, two main afferent lymphatics from the leg enter the capsule of the popliteal lymph node at the inferior pole, and promptly empty into the subcapsular sinus (Text-fig. 1). The lymph is carried through the node by both subcapsular and intermediary sinuses. The latter sinuses pass between the lymph follicles and medullary cords and all sinuses finally drain into the efferent vessel at the hilus. The sinuses in their course through the node are



TEXT-FIG. 1. Schematic diagram of a normal popliteal lymph node.

divided into myriads of tiny compartments by a dense network of trabeculae and reticulum cells (35). The sinuses are also separated from the parenchyma of the node (follicles, lymph cords, and trabeculae) by a lining of endothelial cells which is continuous with the afferent and efferent lymphatics (5).

The lymph node possesses an extensive blood supply which penetrates the node at the hilus, traverses the parenchyma to the periphery through the lymph cords and trabeculae, anastomoses freely within the lymph follicles, and returns along the course of the intermediary sinuses to empty again at the hilus. A few small capillaries anastomose across the subcapsular sinus with capillaries of the capsule (36).

Under normal circumstances lymphocytes, monocytes, macrophages, reticulum cells, and mast cells are found inhabiting the sinuses. Polymorphonuclear leucocytes are not found except under abnormal conditions.

(*c*) *Pathology of Pneumococcic Lymphadenitis.*—Throughout this series of experiments the pathologic picture in the popliteal node was affected by the size of the inoculum and by the number of pneumococci from each intradermal injection that entered the afferent vessels. This latter factor varied from one

animal to another, but after 5 hours sections taken at the same time interval were comparable. Pilot experiments revealed that inoculation of 7×10^5 pneumococci regularly resulted in a progressive but not rapidly overwhelming lymphadenitis.

Within 5 minutes following such an inoculum most of the injected organisms reaching the node were found deep in the intermediary sinuses. Fifteen to 30 minutes later the acute vascular reaction of inflammation was obvious, and polymorphonuclear leucocytes rapidly invaded the intermediary sinuses from adjacent capillaries. Phagocytosis of pneumococci was prompt, and after 5 to 7 hours, when an extensive granulocytic exudate had formed, pneumococci were difficult to find. Fifteen hours after inoculation macrophage cells were increased, no pneumococci were to be seen, and by 24 hours the node presented the picture of a subsiding acute inflammation.

1. Macroscopic Examination.—Within 3 hours after inoculation the popliteal node appeared only slightly reddened and enlarged. By 24 hours the node was moderately increased in size and exhibited definite erythema, apparently due to dilated capsular blood vessels.

2. Microscopic Study.—Five minutes after inoculation the sinuses of the popliteal node were moderately dilated, and as a consequence the number of macrophages in the sinuses appeared reduced. Pneumococci that had reached the node were found deep in the intermediary sinuses and scattered in the subcapsular sinus. Organisms were occasionally seen in the efferent lymphatic, suggesting a possible explanation (21) for the early transient bacteremia recorded in Table I.

After *15 to 30 minutes* the sinuses were further dilated, and the blood vessels about the hilar region and intermediary sinuses were more prominent. In the intermediary sinuses, where pneumococci were most numerous, the capillaries were "pavemented" by polymorphonuclear leucocytes many of which were in the process of diapedesis (Fig. 7). Macrophages and polymorphonuclear leucocytes that had infiltrated the sinuses, contained intracellular pneumococci (Figs. 7 and 8). Rarely even eosinophiles were found containing pneumococci (Fig. 9).

By *1 to 3 hours* there were many more polymorphonuclear leucocytes in the intermediary sinuses than in the subcapsular sinus. The few leucocytes present in the latter site appeared to have come from capsular vessels (Fig. 10). Extracellular pneumococci were reduced in number, and polymorphonuclear leucocytes were more actively phagocytic than the macrophages as judged from the number containing intracellular pneumococci.

Five to 7 hours after inoculation many polymorphonuclear leucocytes had entered the intermediary sinuses, but in the subcapsular sinus they were infrequent except at the juxtahilar area where they seemed to congregate (Fig. 11). The rim of lymphocytes about the secondary follicles was narrowed, and dis-

continuity of the sinus endothelium caused additional capillaries of the follicle to be exposed to the inflammatory process. As a result of this process granulocytes were now found in the subcapsular portion of the follicle and in diapedesis from follicular capillaries (Figs. 12–15). Pneumococci were rarely seen, even intracellularly, most of them apparently having been digested. In occasional sections some intermediary sinuses contained a few strands of fibrin. Afferent lymphatics appeared relatively free of polymorphonuclear leucocytes.

Nine to 15 hours after inoculation the inflammatory reaction had advanced still further, and no pneumococci were visible. Macrophages were increased in number and some had phagocyted leucocytes. The secondary follicles contained active germinal centers and a few primary centers were evident. Even at this time only few polymorphonuclear leucocytes were found in the afferent lymph vessels.

Eighteen to 24 hours after inoculation numerous macrophages were actively phagocyting cellular debris, and follicle regeneration was prominent. The pathologic picture differed strikingly from that of earlier sections in that the inflammatory process appeared to be subsiding.

The inguinal node, as late as 7 hours after inoculation, remained relatively normal except for slightly dilated sinuses. Subsequent sections, however, revealed an increased number of macrophages, more pneumococci, and infiltration of a few leucocytes. By 18 to 24 hours, when the edema zone in the tissues had reached the midthigh region, polymorphonuclear leucocytic infiltration was more pronounced, but never as striking as that seen in the popliteal node. This difference in degree of leucocytic infiltration probably resulted from fewer pneumococci entering the inguinal node.

Striking changes in the mast cells, which were found to be normal inhabitants of the sinuses of popliteal lymph nodes (Fig. 16), were noted during the course of the inflammatory process. Within 5 minutes after inoculation of the foot-pad, mast cells in the sinuses of the node appeared vacuolated and almost devoid of granules (Fig. 17). In some cells the cytoplasmic membrane appeared ruptured. Mast cell granules were scattered throughout the sinuses of the node, and 15 to 30 minutes after inoculation the free granules were not only decreased in number but many were several times normal size and stained poorly. Later there appeared to be a regeneration of granules, and occasional mast cells contained a homogeneous metachromatically stained cytoplasm. Some of the liberated granules were apparently phagocyted by macrophages. It was noted that fibrin formation usually occurred in sinuses free of mast cells or in which the mast cells appeared depleted (Fig. 18).

(*d*) *Infection of the popliteal node with streptococci and staphylococci* resulted in a pathologic picture almost identical with that described for the pneumococcus. Cellular infiltration, phagocytosis, and architectural changes in the follicles and sinuses occurred at approximately the same time intervals. The staphylo-

coccic infection produced somewhat more fibrin in the foot-pad tissues and sinuses of the node, but at no time was this "lymphatic blockade" (15, 16) complete.

DISCUSSION

Although the pathology of acute lymphadenitis caused by pneumococcus, streptococcus, or staphylococcus is generally similar to that of acute inflammation in other body tissues, it is apparent from the present study that the pathogenesis of the lesion is characterized by certain singular features. These distinguishing characteristics appear to be due to the anatomic arrangement of the sinuses, the presence of many histiocytes and mast cells in the normal sinuses, the continuous flow of lymph through the node, and the possible dual source of inflammatory cells.

The first change that occurs in the popliteal node 5 minutes after inoculation of the foot-pad is dilatation of the sinuses. It is well known that the flow of lymph is normally slowed during its passage through a node (3). Dilatation of the nodal sinuses slows the flow of lymph still further and thus acts to retain more organisms within the node. Although dilatation may also effect a relative dilution of the number of histiocytic cells in the nodal sinuses and thereby lower the phagocytic activity of these cells (37, 38), some of the macrophages of the sinuses can be seen phagocyting bacteria within 15 minutes after inoculation of the foot-pad (Fig. 8). Meanwhile, in the area of maximum stasis, deep in the intermediary sinuses, where the pneumococci are most numerous, the vascular reaction of acute inflammation is initiated by the persistence of extracellular organisms. Here the polymorphonuclear leucocytes migrating from the affected blood vessels can be seen to phagocyte the pneumococci almost immediately upon entering the sinuses (Fig. 7). As the inflammatory reaction progresses the relative stasis of lymph in the presence of this increased concentration of cells appears to promote a phagocytic reaction that finally brings about the destruction of the invading bacteria.

When the inflammatory reaction in the lymph node is well advanced (5 to 7 hours), the greatest concentrations of polymorphonuclear leucocytes are seen in the hilar portions of both the intermediary and subcapsular sinuses (Fig. 11). In this connection it has been observed that dyes reaching the node by the afferent lymphatics stain the whole node blue, but in a short time clear lymph flowing into the node carries the dye toward the hilus until only this area remains stained (39). In addition, due to occasional trauma of capillaries in the foot-pad during inoculation, red blood cells enter the lymphatics and are found mainly in the subcapsular sinus about the hilar region. Therefore, it may be concluded that cells carried by the lymph through the sinuses tend to congregate at the single outlet of the node, simulating a log-jam at the narrow outlet of a mill-pond. It seems likely that this congregation of leucocytes at the exit

of the node not only enhances the normal filtration power of the node, but also provides ideal conditions for "intercellular phagocytosis" (38).

One of the most striking features of the histopathology of acute pneumococcal lymphadenitis is the promptness with which invading organisms are phagocyted by the cells in the nodal sinuses. It will be recalled that the test organism used in the majority of these experiments, namely the pneumococcus, possesses a capsule which renders it resistant to phagocytosis in the test tube, except in the presence of specific opsonin. Although antibody is probably formed in lymph nodes (40–42), it seems most unlikely that a sufficient quantity could be manufactured within 15 minutes to account for the early phagocytosis of pneumococci in the sinuses of the node. Therefore, because of the promptness with which the phagocytic reaction takes place and because of the large surface area afforded the motile leucocytes by the trabecular network of the intermediary and subcapsular sinuses, it is assumed that the same non-antibody mechanism of "surface phagocytosis" is involved in pneumococcal lymphadenitis as that previously demonstrated in experimental pneumonia (37, 38).

Only indirect evidence exists concerning the origin of the polymorphonuclear leucocytes in the nodal sinuses during acute lymphadenitis (16–18). In the present study polymorphonuclear leucocytes have been demonstrated migrating from the capillaries of the intermediary sinuses (Fig. 7), capsule (Fig. 10), and subcapsular aspect of the follicles (Figs. 14 and 15). A lesser number of leucocytes, accompanied by occasional red blood cells, appear to come from the exudate in the foot-pad by way of the afferent lymphatics. Leucocytes from the primary inflammatory process, as evidenced by the location of the accompanying red cells, remain for the most part in the subcapsular sinus. Other investigators (16, 17) have described lymphatic channels in the primary focus of infection and about the regional lymph node congested with granulocytes and have concluded, therefore, that most of the cells in the nodal exudate come from the original inflammatory site in the tissues. The histologic findings of the present study do not confirm this concept, for only the relatively few lymphatic vessels which have become occluded with fibrin contain appreciable numbers of leucocytes (Figs. 4–6).

The concept that acute inflammation of lymph nodes is manifest initially and primarily by the outpouring of inflammatory cells from nodal blood vessels into the adjacent irritated tissue (the sinuses of the node), similar to inflammation elsewhere, has not previously been emphasized. Other investigators (16, 17, 21) have been more impressed with the rôle of lymph-borne leucocytes as participants in the cellular reaction during lymphadenitis. The present study indicates that infected regional lymph nodes respond as autonomous units by the formation of a granulocytic exudate which rapidly disposes of the invading parasites by the mechanism of phagocytosis. Direct experimental proof for this assumption will be presented in the following paper (43).

It has been suggested by Robertson and coworkers that one of the primary factors in the recovery phase of pneumococcic pneumonia is the macrophage reaction (44, 45). In experimental pneumonia (28), however, and also in experimental lymphadenitis, macrophages appear to increase in number only after phagocytosis of invading bacteria by the granulocytes is well under way or even complete. In unreported experiments the infected foot of the rat was amputated 1 hour after inoculation to eliminate the source of bacteria invading the regional lymph node, and an immediate change-over from a leucocytic to a macrophage reaction was repeatedly demonstrated (46). These findings suggest that the macrophage reaction does not effect recovery in acute bacterial infections, but, on the contrary, develops only after the polymorphonulcear leucocytes have phagocyted most of the invading bacteria and have thus removed the primary stimulus of inflammation.

Although fibrin formation is not uncommon in the lymphatics of the infected foot-pad, it is noteworthy that lymph rarely seems to clot in the sinuses of the regional lymph node. Were extensive clotting to occur in the nodal sinuses, the function of the node would obviously be impaired. It is tempting to assume that the mast cells, by discharging their heparin-containing granules (47–50) into the sinuses, as described, prevent clotting within the node. This attractive hypothesis remains to be proven, but the above observations suggest that mast cells may well be involved in the complex cellular mechanisms of antibacterial immunity.

SUMMARY

Acute pneumococcic lymphadenitis produced in rats by intradermal inoculation of the foot-pad is characterized by rapid infiltration of polymorphonuclear leucocytes into the intermediary sinuses of the node, and prompt phagocytosis of pneumococci by both the macrophages of the sinuses and the recently arrived leucocytes. After 5 to 7 hours the polymorphonuclear leucocytes are found densely congregated about the hilar region, and 9 hours after inoculation most of the phagocyted organisms have been digested. At the end of the 24 hour period the popliteal node presents the picture of a subsiding inflammation with a marked macrophage reaction and regenerating lymph follicles.

Phagocytosis of encapsulated pneumococci in the foot-pad and popliteal node occurs in less than 30 minutes after inoculation. It is assumed that this prompt phagocytosis is effected by the non-antibody mechanism of "surface phagocytosis."

The majority of polymorphonuclear leucocytes that enter the sinuses of the inflamed node appear to come from capillaries within the node itself rather than from the primary site of inflammation in the foot-pad. The prompt inflammatory response of the nodal tissues serves as an active defense against lymph-borne infection.

Macrophages invade nodal sinuses only after most of the pneumococci have been destroyed by polymorphonuclear leucocytes. It is suggested that the macrophage reaction follows removal of the primary inflammatory stimulus by the granulocytes, and thus constitutes only a late phase of recovery.

Fibrin formation in the sinuses of the lymph node is rare during acute lymphadenitis. This finding may be related to the observation that within 5 minutes after entrance of bacteria into the node, heparin-containing granules from mast cells are strewn throughout the sinuses.

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EXPLANATION OF PLATES

Sections were stained with eosin-methylene blue with the exception of those in Figs. 16, 17, and 18 which were stained with 0.02 per cent toluidine blue for 1 minute. The tissues were cut and stained by Mrs. Alice Hamlin and photographed by Mr. Cramer Lewis.

PLATE 37

FIG. 1. Phagocytosis of pneumococci by polymorphonuclear leucocytes in the foot-pad of the rat 1 hour after inoculation. Cells with large dark nuclei are fibroblasts of the subcutaneous connective tissue. × 1440.

FIG. 2. Phagocytosis of pneumococci by polymorphonuclear leucocytes in the foot-pad 30 minutes after inoculation. The cells indicated by the arrows are seen to lie within three cell diameters of the lumen of the capillary from which they appear to have migrated. × 1890.

FIG. 3. Marked accumulation of leucocytes in the tissue of the foot-pad at 12 hours. Practically all the pneumococci have been phagocyted. × 1440.

FIG. 4. Early fibrin formation in a lymphatic of the foot-pad 2 hours after inoculation. × 495.

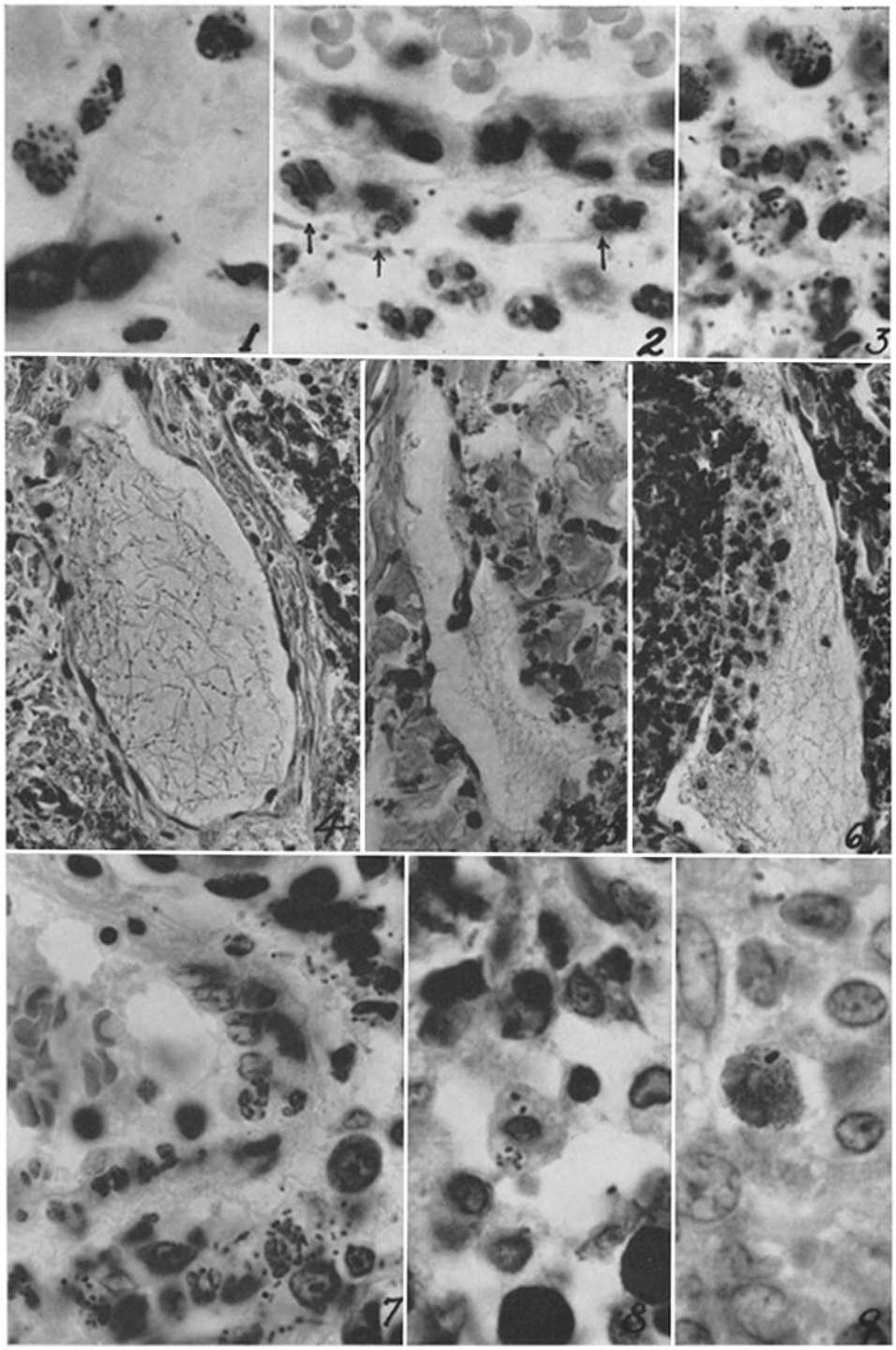
FIG. 5. Fibrin formation in a foot-pad lymphatic 3 hours after inoculation. The lumen above the valve is uninvolved, and where the fibrin attaches to the lymphatic endothelium a few leucocytes are invading the vessel. × 600.

FIG. 6. By 5 hours leucocytes are invading the fibrin plug along the line of attachment. The remainder of the endothelial wall remains intact. × 540.

FIG. 7. Section of the popliteal node at 30 minutes. A venule lined with leucocytes, and with many in the process of diapedesis, is seen to the left. Leucocytes and macrophages in the intermediary sinus contain many intracellular pneumococci. × 1440.

FIG. 8. Phagocytosis of pneumococci by a macrophage in an intermediary sinus of the popliteal node 30 minutes after inoculation of the foot-pad. × 1440.

FIG. 9. Phagocytosis of a pneumococcus by an eosinophile in the popliteal node 30 minutes after inoculation. × 1890.



(Smith and Wood: Antibacterial defense in lymph nodes. I)

PLATE 38

FIG. 10. A polymorphonuclear leucocyte (arrow) in the process of passing through the wall of a capsular venule to enter the subcapsular sinus of the popliteal node. Animal sacrificed 1 hour after inoculation of foot-pad. × 990.

FIG. 11. Congregation of leucocytes at the hilar portion of the subcapsular sinus of the popliteal node (arrow) 5 hours after inoculation of the foot-pad. At extreme upper right sinus is seen to contain fewer leucocytes than in hilar region × 100.

FIG. 12. Relatively normal secondary follicle of the popliteal node 1 hour after inoculation. The subcapsular sinus is dilated and contains relatively few cells. Entrance to the intermediary sinus (arrow) is narrow and is filled with reticular cells and macrophages. × 510.

FIG. 13. High-power view of the area marked in Fig 12, showing intact endothelium (arrows) lining follicular side of subcapsular sinus. The rim of lymphocytes about the follicle extends all the way to the endothelium. × 510.

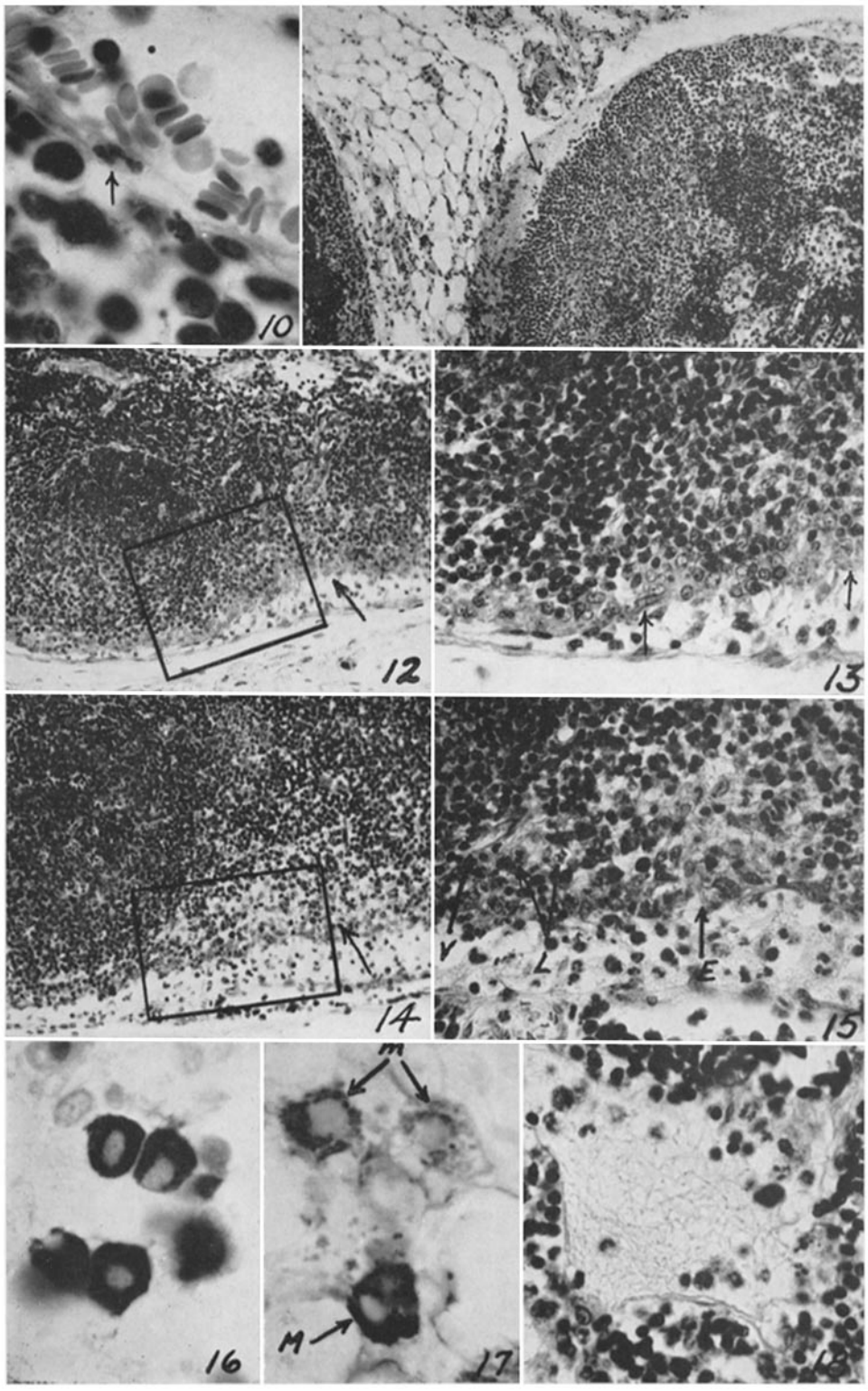
FIG. 14. Section of the popliteal node at 7 hours showing narrowing of the rim of lymphocytes about the follicle and apparent widening of the entrance to the intermediary sinus (arrow). × 510.

FIG. 15. High-power view of the area marked in Fig 14. Note: (1) the disrupted endothelium lining the follicle (E), (2) the leucocytes (L) in the area previously occupied by the rim of lymphocytes, and a small dilated vessel (V) previously within the follicle but now involved in the inflammatory reaction. × 480.

FIG. 16. Metachromatically stained mast cells in the intermediary sinus of a normal popliteal node. × 1440.

FIG. 17. Mast cells in an intermediary sinus of the popliteal node 5 minutes after inoculation of the foot-pad. The mast cell (M) is vacuolated but still contains a moderate number of metachromatic granules. The other two cells (m) have discharged most of their granules into the surrounding area. × 1440.

FIG. 18. Intermediary sinus of the popliteal node containing a few strands of fibrin. No mast cells were demonstrable in this sinus. × 1440.



(Smith and Wood: Antibacterial defense in lymph nodes. I)