Electron-microscopic Study of the Mouse Leukemia Virus (Gross), and of Tissues from Mice with Virus-induced Leukemia*

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SUMMARY

Virus-like particles present in thymus, spleen, lymph node, bone marrow, lung, kidney, liver, salivary gland, and mammary gland of C3Hf mice with passage A virus-induced leukemia were examined with the electron microscope. The morphology, size, and location of budding particles, doughnut-type particles, cylindrical and multiple particles, and particles with nucleoids and with tail-like structures were studied. Budding of particles occurred from lymphoblasts, lymphocytes, monoblasts, monocytes, erythroblasts, developing eosinophils and neutrophils, plasma cells, reticular cells, megalakaryocytes, and the epithelium of apparently normal mammary and salivary glands. Also observed were smaller doughnut-type particles present within the endoplasmic reticulum.

In addition, the appearance of leukemic tissues was described, including the infiltration of leukemic cells into lung, liver, and kidney, the presence of particles in vacuoles and inclusion bodies of phagocytic reticular cells and macrophages, and typical morphologic changes within the cell.

MATERIALS AND METHODS

The tissues employed for our study were obtained from mice of strain C3Hf/Bi, which developed leukemia at the age of 2½-3½ months as a result of inoculation within the first week after birth with passage A virus filtrate (24). A total of ten leukemic mice served as donors of tissues for our studies. All these mice were obtained from Dr. L. Gross' laboratory.

After the mice were sacrificed by ether inhalation, the various organs—thymus, spleen, lymph node (peripheral and mesenteric), bone marrow, liver, kidney, lung, and salivary and mammary glands—were immediately removed and fixed in 1 per cent phosphate-buffered osmic acid on ice for 1–1½ hours. The specimens were rinsed in 50 per cent ethanol and dehydrated in successive changes of 70, 95, and 100 per cent ethanol. After being immersed in propylene oxide, followed by an equal mixture of propylene oxide and Epon for approximately 2 hr. in an oven at 60°C., the specimens were embedded in Epon and allowed to harden at 60°C. for at least 2 days. The specimens were cut with a diamond or glass knife on a Porter-Blum microtome converted into a thermal advance model. Sections were placed on uncoated 300-mesh copper grids, lightly coated with carbon, and stained with a saturated solution of uranyl acetate for about 15 min. and then with lead hydroxide (34) by a modified technic (19). The sections were examined in an RCA EMU-3F electron microscope at 50 kv. From 250 to 500 sections of each organ were examined.

RESULTS

Budding particles.—From the electron micrographs of tissues studied in this experiment, it appeared that the
principal manner in which particles originated was by budding from the cell membrane. Furthermore, the budding of particles seemed to occur not only from leukemic cells, but also from cells apparently uninvolved in the leukemic process. In addition, particles were observed budding from both mature and immature cells of the blood-forming organs.

In the budding process, one or more areas along the cell membrane increase in thickness and electron density. As these areas grow, they appear to round up and extend into the extracellular spaces. Eventually they form a complete sphere and are released from the cell. A more detailed description of budding, illustrated by electron micrographs, follows.

The first stage in budding consists of the formation of an electron-dense, crescent-shaped membrane concentric with the cell membrane and a concomitant thickening of the cell membrane (arrows, Figs. 1, 10c, and 13a). This is usually accompanied by an increase in density of the region between the two concentric membranes and a slight protrusion of the thickened cell membrane into the extracellular space. Occasionally, small vesicles or vacuoles (v) occur posterior or lateral to the budding particle (Figs. 2). The inner membrane proceeds to grow, increasing in convexity (arrows, Figs. 2, 3a, 10a [left], and 11) and eventually forms an almost complete shell (arrows, Figs. 10a [right], 10d, and 21a [upper left]) and then a complete shell (arrows, Figs. 5, 8, and 21a [upper right]). At the same time, the outer membrane assumes the shape of a hemisphere (arrows, Figs. 2, 3a, 10a [left], and 14). It continues to round up (arrows, Figs. 5, 9, and 21a) and finally breaks off from the cell with the inner membrane to form a spherical particle, which presents a doughnut-like image in thin sections.

Budding of particles has appeared in lymphocytes, lymphoblasts (Fig. 3), monoeytes (Fig. 13, M; enlargement in Fig. 13a), and monoblasts. It was also observed in megakaryocytes and occasionally in reticular cells (Fig. 4), erythroblasts (Fig. 5), mature (Fig. 11) and immature (Fig. 10) plasma cells, and eosinophilic (Fig. 8) and neutrophilic (Fig. 9) metamyelocytes. Budding was frequently noted in the mammary epithelium (Fig. 1) of pregnant mice (21).

In four out of five salivary glands examined, budding appeared from the salivary gland epithelium. Figure 21 is a low magnification electron micrograph of two acini of a salivary gland. On the basis of an electron-microscopic study of the salivary glands (31), it would appear that this gland is probably the submaxillary. Groups of particles are present in the lumen (L) of the acini proximal to the plasma membrane and in an intercellular space (arrow). A higher magnification of an intercellular space from a different area of the same section (Fig. 21a) demonstrates several particles, two of which (arrows) are budding from the cell membrane. Also evident are three secretory granules (S).

1 Arrow = →; crossed arrow = ↔; double crossed arrow = ↔→. The positive identification of cells and differentiation of developing from mature cells was not always possible because of the small area (approximately 1/300th) of the total cell observed in the electron microscope.

Except for megakaryocytes, budding was observed at the plasma membrane of all the above cells and rarely from vacuolar membranes or granules. In megakaryocytes, budding has been apparent so far only in granules (arrows, Figs. 6 and 7) and from vacuolar membranes.

**Doughnut-type particles.**—The doughnut-type particle formed as a result of budding usually consists of two concentric membranes (Fig. 12a, enlargement of outlined area in Fig. 12), but occasionally three or more membranes were resolved. The innermost membrane appears more electron-dense than the others (Fig. 12a). The measurement of at least 100 doughnut-type particles indicated that the diameter of the total particle ranges from 80 to 110 mμ, the average being 96 mμ. The thickness of the outer shell varies from 16 to 28 mμ, with an average of 22 mμ, and the diameter of the inner sphere ranges from 42 to 65 mμ, averaging 52 mμ. Particles were located in extracellular spaces (Fig. 12; crossed arrows in Figs. 21a and 35), and sometimes in cytoplasmic vacuoles (arrows, Figs. 4a [center] and 35) and in granules. They occur singly (crossed arrow, Fig. 13a), in small groups (Fig. 12), or scattered among particles containing nucleoids.

**Cylindrical and multiple particles.**—Cylindrical particles or filaments consisting of a membrane system similar to the doughnut-type particle were observed. Many of these particles appeared to be in the process of rounding up to form doughnut-type particles (Figs. 16, 18–20). In Figures 18 and 20 the structure of filaments suggests an early stage of segmentation, while in Figures 16 and 19, typical doughnut-type particles appear more evident.

Often two or more of the doughnut-type particles may be attached to one another, other than in filaments. Two and three particles sharing a common core are shown in Figure 17. Occasionally, during the budding process, particles appear connected to one another, situated either perpendicularly (Fig. 14) or parallel (Fig. 15) to the cell membrane.

**Particles with nucleoids.**—The morphology of particles with nucleoids varies considerably. The shape of the outer membrane or of the nucleoid may appear round (arrow, Fig. 24), elliptical (arrows, Fig. 22), or pleomorphic (arrows, Figs. 23 and 25). The nucleoid varies in density; it can appear opaque (arrows, Figs. 22 and 24), moderately dense (arrows, Figs. 23 and 25), or electron-lucent (crossed arrows, Fig. 25). The nucleoid is usually located toward the center of the particle (arrow, Fig. 24), but occasionally may be situated peripherally. Rarely, two nucleoids are present within one particle (double crossed arrow, Fig. 25). The region between the nucleoid and the outer shell also varies in density.

According to the measurement of at least 100 particles with nucleoids, the over-all diameter of these particles ranges from 75 to 170 mμ, averaging 105 mμ. The size of the nucleoid varies from 50 to 125 mμ in diameter, with an average of 68 mμ. Usually the smaller particles have a more regularly shaped outer membrane and nucleoid, and a denser nucleoid (arrow, Fig. 24), whereas the larger particles are more irregular in shape and have a less dense nucleoid (arrow, Fig. 23).

Particles with nucleoids were generally located in extracellular spaces (Fig. 22), cytoplasmic vacuoles (Fig. 25),...
and inclusion bodies (IB) (Figs. 25, 27, and 34) in moderate to abundant numbers.

**Particles with tail-like structures.**—It is of interest that we have observed in this study, as well as in our previous studies (21), particles with “tails.” In this study, particles with tail-like structures were occasionally observed in extracellular spaces and vacuoles of cells from leukemic animals. Figure 28 is a low magnification micrograph from a section of cervical lymph node. A group of particles with “tails” is present in a vacuole (outlined). A higher magnification of this area (Fig. 28a), and a particle with a “tail” as shown in Figure 23 (lower right), demonstrates their structure more clearly. The head of the particle is similar to particles containing nucleoids, especially those which are irregular in shape. On the basis of at least 50 particles measured, the average diameter of the head appears slightly larger (110 μm) than those particles containing nucleoids but no “tails” (105 μm). In thin sections, the “tail” of the particle often appears less dense than the head (Fig. 28a). This may be interpreted as follows: the average width of the “tail” is about 30 μm, slightly less than one-third the diameter of the head. The thickness of the sections cut are generally 20–30 μm. Thus, only part of the plane of section is likely to pass through the thickness of the “tail,” whereas the entire plane of section is apt to pass through the head of the particle. The length of the “tail” ranges from approximately 120 to 550 μm, with an average of 240 μm. Occasionally, within one plane of section several overlapping “tails” are visible (arrow, Fig. 28a).

**Smaller doughnut-type particles.**—Although there was a considerable variation in size among the large numbers of doughnut-type particles examined, there appeared to be a particular form of doughnut-type particle that could be differentiated from the others on the basis of certain features, such as size, morphology, and location (d, Figs. 9, 10b, 26b, 29–31). The measurement of at least 50 particles of this type indicated that its over-all diameter ranges from 65 to 85 μm, with an average of 75 μm. The thickness of the outer shell varies from 11 to 21 μm, averaging 15 μm, and the diameter of the inner sphere ranges from 37 to 57 μm, averaging 45 μm. The particle consists of two concentric membranes; intermediate membranes have not been observed. The two membranes appear equal in density. This particle was noted only in association with the endoplasmic reticulum, either rough or smooth, lying free within vesicles or cisternae (d, Figs. 9, 10b, 26b, 30, and 31) or budding from the surrounding membrane (Fig. 29 [compare with particle on right, arrow]). Occasionally multilobed particles (Fig. 31) appeared. So far, these particles were observed on one or more occasions in lymphocytes and lymphoblasts (Fig. 29), monocytes and monoblasts (Fig. 26b), mature and immature (Fig. 10) plasma cells, developing neutrophils (Fig. 9), reticular cells, and Kupffer cells of the liver of leukemic C3Hf mice; and in lymphocytes, lymphoblasts, reticular cells, mammary epithelium, platelets, Kupffer cells of the liver, and glomerular epithelium of embryo kidney of normal C3Hf mice. In the tissues of both the leukemic and normal mice, their distribution was sparse.

**Infiltration of leukemic cells in liver, lung, and kidney.**—Particles did not appear to bud off from liver, lung, and kidney cells and were not observed in areas of sections made up exclusively of these cells. However, when areas of these tissues containing infiltrated leukemic cells were encountered, particles budding from the leukemic cells, as well as doughnut-type and nucleoid-containing particles, frequently were noted; occasionally, particles with “tails” were also present.

An area of liver tissue containing infiltrated cells is shown in Figure 12. Typical liver cells are present on the left and bottom, while infiltrated cells (L), which may be lymphocytes or lymphoblasts, are shown at the top and right. Between two of these cells is situated two doughnut-type particles (outlined), shown at higher magnification in Figure 12a.

A low magnification micrograph of lung tissue appears in Figure 13. In an enlargement of the outlined area, as shown in Figure 13a, two particles are budding from a cell which may be a monocyte (M, Fig. 13). Also present is a doughnut-type particle (crossed arrow).

**Particles in vacuoles and granules.**—Groups of particles were often found within vacuoles and inclusion bodies of phagocytic reticular cells and macrophages. Generally, these particles contained nucleoids, although doughnut-type particles and particles with “tails” were also noted. Particles were rarely observed budding from vacuolar membranes of phagocytic reticular cells and macrophages.

The presence of particles in cytoplasmic vacuoles and inclusion bodies of phagocytic reticular cells and macrophages could be interpreted in a twofold manner. One explanation would imply that such particles were formed within the cells themselves; another, that particles entered these cells from the surrounding extracellular spaces by phagocytosis.

Figure 26 is a low magnification micrograph of a phagocytic reticular cell extending from upper left across to lower right. It contains inclusion bodies (IB) of varied size and appearance, several cellular extensions or projections (p), and pinocytotic vesicles (v). An enlarged area (Fig. 26a) of part of the cell demonstrates the presence of a few particles in an extracellular space partially surrounded by a cellular projection (p). Figures 4a, 32, and 33 show parts of three other phagocytic reticular cells. Inclusion bodies (IB), which are possibly lysosomes, containing hydrolytic enzymes, appear in Figures 4a and 32. Fingerlike projections or processes (p) surround groups of particles (Figs. 4a, 32, and 33). In some areas, these projections appear to join (arrows, Figs. 4a [center], 32, and 33), perhaps enclosing particles within the cell.

Figures 25, 27, 34, and 35 illustrate parts of cells, identified as macrophages. These cells contain inclusion bodies (IB) varying in size, density, and structure, which may be lysosomes. Groups of particles appear in cytoplasmic vacuoles (Fig. 25; arrow, Fig. 35) or within inclusion bodies (IB, Figs. 25, 27, and 34), often mixed with cellular debris.
In some areas, a vacuole containing particles is situated proximal to an inclusion body (arrow, Fig. 35). Particles within inclusion bodies sometimes appear swollen or devoid of their nucleoids (arrows, Fig. 27). When the inclusion body is dense, the particles within it often become difficult to identify (Fig. 25, lower center).

**Typical structural modifications.**—A low magnification micrograph (Fig. 36) of thymus from a normal C3Hf mouse contains apparently healthy lymphocytes (L) and a reticular cell (R, lower left). In comparison, a section of thymus from a leukemic mouse (Fig. 37) lacks the structural pattern of the normal thymus. The nuclear chromatin (N) appears clumped or pyknotic in several cells. In addition, the plasma membrane seems ruptured in some instances (arrows), and the mitochondria (m) necrotic. The extracellular spaces are filled with cellular debris. Similar cellular destruction is apparent in Figure 40. Cells which have acquired a bizarre configuration are shown in Figures 28 and 39 (arrows). Both these cells and their nuclei are unusually shaped. Besides an over-all increase in density, large opaque areas appear in the cytoplasm and nuclei.

In addition to these changes, small granules, varying in shape and size, often appeared in the nucleus (arrow, Fig. 41). Other granules, resembling ribosomes, were observed in profusion, either scattered freely within the cytoplasmic matrix (Fig. 41, lower left), lined up along the cisternae of the endoplasmic reticulum, adjacent to mitochondria (m, Figs. 41 and 42), or lying within inclusion bodies (Fig. 32, upper left; Fig. 42). In addition to these granules, inclusion bodies (IB) often contained finer granular material (Fig. 34, upper left; Fig. 35, lower left), membranous lamellar structures (Fig. 35, center), viruslike particles (Figs. 25, 27, and 34), or cellular debris, such as mitochondria (m, Fig. 42).

However, many areas of tissues from leukemic mice were composed of cells which appear morphologically healthy. One such area from a lymph node containing lymphocytes (L) is shown in Figure 38.

**DISCUSSION**

This study suggests that particles, which presumably represent the mouse leukemia virus, can bud off from a number of cells, such as lymphocytes, lymphoblasts, monocytes, monoblasts, early eosinophils and neutrophils, mature and immature plasma cells, erythroblasts, reticular cells, and megakaryocytes. In the animals studied in this experiment, production of particles by the above cells was not always accompanied by an abnormal increase of the number of these cells in the blood or tissues, as revealed by light microscopy. Previously we reported that particles were observed budding from epithelial cells of the mammary gland during pregnancy (21). In this study, we also found particles present in, and apparently being formed by, epithelial cells of the salivary gland, free from leukemic cell infiltration. It thus appears that the leukemia virus can replicate in certain cell types without, at the same time, inducing an abnormal multiplication of such cells, as has previously been noted for the megakaryocyte (11, 15, 18).

From the electron micrographs studied, it appears that particles may initially form by budding from the cell membrane (Figs. 1 and 2). The doughnut-type (Fig. 12a), cylindrical (Figs. 18 and 20), and multiple (Fig. 17) particles produced by budding seem to be released into extracellular spaces. The cylindrical and multiple particles may possibly segment to form doughnut-type particles (Figs. 16 and 19). Particles with nucleoids (Figs. 22–24), which occasionally possessed tail-like structures (Fig. 28a), were also observed in extracellular spaces. The presence of tail-like protruberances observed in electron-microscopic studies of different viruses is controversial. The question has been raised for a number of years whether these processes represent an artifact or a real part of an undamaged virus particle. Some have claimed that it represents a real structure (10); others are not of this opinion (3, 16, 32).

In the megakaryocytes, particles are usually formed along the walls of "platelet demarcation vesicles or tubules" (35) and are released into their interiors. When platelets are formed by the coalescence of these channels (35), particles are probably liberated into extracellular spaces.

Groups of particles, most of which contained nucleoids, appeared within cytoplasmic vacuoles (Fig. 25) and inclusion bodies (Figs. 27 and 34) of phagocytic reticular cells and macrophages. In many of these cells, particles observed within inclusion bodies often appeared swollen or degenerated (Fig. 27). Although macrophages are known to be rich in lysosomes, containing digestive enzymes (13, 14, 27), the relationship between lysosomes and particles in inclusion bodies remains speculative.

An abundance of ribosomes was often observed in association with necrotic cells and inclusion bodies (Figs. 41 and 42). The accumulation of ribosomes in the area of inclusion bodies has been previously reported, and their role in the production of hydrolytic enzymes for the digestion of phagocytized material was suggested (25).

Doughnut-type particles and particles with nucleoids, which we observed in this study in tissues of mice with passage A virus-induced leukemia, had been described previously in mice with spontaneous leukemia (5, 17), and also in mice and rats with passage A virus-induced leukemia (4, 17, 18, 28, 29); furthermore, similar particles were reported in mice which developed leukemia as a result of inoculation of either the Moloney (11) or Graffi (26) virus strains, as well as in mice with the Friend disease (15).

The smaller doughnut-type particles, described in this paper in association with the endoplasmic reticulum, were also observed in spontaneous leukemia in AK and SL(2) strain mice, as well as in virus-induced (11) leukemia. In addition, these particles were observed in a variety of other malignant mouse tumors (1, 6–9, 12, 22, 30, 33). Furthermore, similar particles were noted in normal epididymis in mice of strains DBA and C57BL (20).

We also carried out electron-microscopic studies of ultrathin sections of tissues from different organs of healthy C3Hf mice that had not been treated with injections. These particles may contain nucleoids, which are often observed in the same areas as the particles without nucleoids. The significance of this observation is not yet clear.

**REFERENCES**

2. K. S. Fields and H. M. Eisen, unpublished data.
3. J. E. Cavanagh, unpublished data.
4. More detailed data of these examinations will be presented in a subsequent publication.
We found, in these tissues, particles which were apparently identical with those observed in the leukemic mice; there was, however, a quite distinct quantitative difference. The budding and doughnut-type particles, numerous in various leukemic tissues, were found only in very small numbers in the thymus, and occasionally also in the bone marrow of normal mice. Particles with nucleoids, also regularly observed in leukemic mice, appeared in normal mice even less frequently than budding and doughnut-type particles. The smaller doughnut-type particles, however, were observed with about similar frequency in tissues of leukemic as well as normal mice.

REFERENCES


Fig. 1.—Part of mammary epithelial cell of pregnant mouse. Budding particle (arrow) consists of a thickened cell membrane and a dense crescent-shaped membrane posterior to it. \( \times 60,640 \).

Fig. 2.—A section through a hemispherically shaped budding particle (arrow), demonstrating the presence of several vesicles and a vacuole (v) posterior and lateral to the particle, respectively. \( \times 63,672 \).

Figs. 3 and 3a.—Section through a lymphoblast from spleen. A particle budding from the cell membrane (outlined area) is magnified in Figure 3a. Figure 3: \( \times 12,870 \). Figure 3a: \( \times 44,793 \).

Fig. 4.—Low power electron micrograph of a reticular cell of spleen. The outlined area demonstrates a particle budding from a cytoplasmic extension. \( \times 8,400 \).

Fig. 4a.—A higher magnification of part of the outlined area of Figure 4, illustrating more clearly the budding particle (right, arrow). Also shown is part of a phagocytic reticular cell containing inclusion bodies (IB), several donut-type particles in vacuoles (center, arrow), and a cytoplasmic process (p). \( \times 29,645 \).

Fig. 5.—Part of an erythroblast from bone marrow. A budding particle (arrow) appears to be breaking off from the cell. \( \times 37,327 \).

Figs. 6 and 7.—Section of megakaryocyte from bone marrow. Particles (arrows) are budding into several granules of the cell. Figure 6: \( \times 43,320 \). Figure 7: \( \times 33,880 \).

Fig. 8.—Part of an eosinophilic metamyelocyte from bone marrow. A particle (arrow) is apparently budding from the cell membrane. \( \times 40,527 \).

Fig. 9.—Part of a neutrophilic metamyelocyte from bone marrow, illustrating one budding particle (arrow) breaking off from the cell, and two small donut-type particles (d) within the endoplasmic reticulum. A centriole (c) is shown. \( \times 32,186 \).
Fig. 10.—Section through rather immature plasma cell from mesenteric lymph node, showing budding of particles along the cell membrane (outlined areas a, c, and d). (Golgi zone (G) appears on the left. × 14,820.

Fig. 10a, c, and d.—Enlargements of outlined areas a, c, and d of Figure 10, demonstrating more clearly the budding particles (arrows). × 33,880.

Fig. 10b.—Enlargement of outlined area b of Figure 10, illustrating the presence of a smaller doughnut-type particle (d). × 33,880.

Fig. 11.—Part of a mature plasma cell from mesenteric lymph node. A particle (arrow) is budding from the cell membrane. Golgi zone (G) is present. × 33,880.

Fig. 12.—Low power electron micrograph of liver infiltrated by leukemic cells. Liver tissue appears at the left and bottom, and infiltrated cells (L) at the right and top. × 9,120.

Fig. 12a.—Higher magnification of the outlined area in Figure 12, demonstrating the presence of two doughnut-type particles. × 43,320.
FIG. 13.—Low magnification electron micrograph of lung tissue. Several particles are budding from an infiltrated cell (M), apparently monocyte. X 10,920.

FIG. 13a.—A higher magnification of the outlined area of Figure 13, demonstrating more clearly the presence of both budding (arrow) and a doughnut-type particle (crossed arrow). X 43,320.

FIG. 14.—Section of mesenteric lymph node, demonstrating budding of both a single (arrow) and double particle. Only one part of the double particle appears attached to the cell membrane. X 82,280.

FIG. 15.—A double budding particle, in which both halves are connected to the cell membrane; from section of spleen. X 60,640.

FIGS. 16-20.—Cylindrical and multiple particles. Figures 18 (spleen) and 20 (peripheral lymph node) show filaments in an early stage of segmentation. In Figure 16 (cervical lymph node) and 19 (thymus), doughnut-type particles are more apparent. Double and triple particles sharing a common core are shown in Figure 17 (spleen). Figure 16: X 128,000. Figure 17: X 82,280. Figure 18: X 60,640. Figure 19: X 43,320. Figure 20: X 60,640.
Fig. 21.—Low power electron micrograph through two acini of a salivary gland (probably the submaxillary). Particles are found within the lumen (L) of the acini proximal to the cell membrane and in an intercellular space (arrow). \( \times 9,120 \).

Fig. 21a.—Higher power electron micrograph of intercellular space of salivary gland from same section as Figure 21, but different area. Several particles appear along the cell membrane, two of which (arrows) are budding. Also present are a few doughnut-type particles (crossed arrows) and three secretory granules (S). \( \times 32,186 \).

Fig. 22.—Section through spleen, demonstrating typical particles with nucleoids (arrow) in an extracellular space. \( \times 43,320 \).

Fig. 23.—Area of megakaryocyte from bone marrow, illustrating many particles with nucleoids and one particle with a tail (lower right), within cytoplasmic vacuoles. A typical pleomorphic particle is indicated (arrow). \( \times 33,880 \).
Fig. 24.—Section through spleen, demonstrating typical particles with nucleoids (arrow).  × 33,880.

Fig. 25.—Section of a macrophage from a peripheral lymph node. Inclusion bodies (IB) and cytoplasmic vacuoles contain particles with nucleoids. Arrow indicates particle with moderately dense nucleoid; crossed arrow, electron-lucent nucleoid; and double crossed arrow, two nucleoids.  × 23,520.

Fig. 26.—Low power electron micrograph of area from a cervical lymph node. A phagocytic reticular cell containing inclusion bodies (IB), cellular processes (p), and pinocytotic vesicles (v) extends from upper left across to lower right.  × 9,600.

Fig. 26a.—Enlargement of outlined area (a), showing a cytoplasmic extension (p) partially surrounding a group of particles.  × 43,320.

Fig. 26b.—Enlargement of outline area (b), illustrating a smaller doughnut-type particle (d) within a cisterna of the endoplasmic reticulum.  × 43,320.
FIG. 27.—Part of a macrophage from a cervical lymph node. Inclusion bodies (IB) contain particles with nucleoids, a few of which appear swollen (arrows). × 32,186.

FIG. 28.—Low power electron micrograph of a necrotic area from a cervical lymph node. Cellular debris and an abnormally dense cell (arrow) are present. × 6,800.

FIG. 28a.—An enlargement of the outlined area from Figure 28, demonstrating the presence of an abundance of particles with “tails.” The “tails” of several particles appear to overlap (arrow). × 40,527.
FIGS. 29—31.—Smaller doughnut-type particles.

Fig. 29.—Part of a lymphoblast from a cervical lymph node, revealing the differences in morphology, size, and location between the smaller (d) and larger (arrow) doughnut-type particles. × 60,640.

Fig. 30.—Particle (d) within endoplasmic reticulum of a cell from mesenteric lymph node. Also shown is a centriole (C). × 44,793.

Fig. 31.—Multilobed particle (d) from section of thymus. × 44,793.

FIGS. 32—33.—Parts of phagocytic reticular cells from a peripheral lymph node. Elongated cellular projections (p) surround groups of particles. In a few areas (arrows), the extensions appear to join. Several inclusion bodies (IB) are present in Figure 32. Figure 32: × 23,520. Figure 33: × 33,880.

Fig. 34.—Various inclusion bodies (IB) in a macrophage from a peripheral lymph node. One of the inclusion bodies (center) contains a group of particles with nucleoids. ×32,186.

Fig. 35.—Part of a macrophage from a mesenteric lymph node. Groups of particles appear within a cytoplasmic vacuole (arrow) and in an extracellular space (crossed arrow). Also present are several inclusion bodies (IB). × 22,344.

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Fig. 36.—Low power electron micrograph of thymus from a normal mouse, illustrating the structure of healthy lymphocytes (L) and a reticular cell (R), lower left. × 5480.

Fig. 37.—Low power electron micrograph of thymus from leukemic mouse, revealing typical cytopathic changes, such as pyknotic nuclei (N), destroyed mitochondria (m), and severed cell membranes (arrows). × 5200.

Fig. 38.—Low power electron micrograph of mesenteric lymph node from leukemic mouse. Lymphocytes (L) appear in a healthy morphologic condition. × 5206.

Fig. 39.—Low power electron micrograph of cervical lymph node, demonstrating the appearance of several necrotic cells (arrows). × 5480.
Fig. 40.—Low power electron micrograph of kidney. Part of the proximal convoluted tubule appears at lower right. Infiltrated cells and cellular debris are shown on the left. X 15,600.

Fig. 40a.—Enlargement of outlined area of Figure 40, demonstrating the presence of several particles with nucleoids. X 43,320.

Fig. 41.—Part of a cell from a peripheral lymph node, showing accumulation of small granules within the nucleus (arrow). Other granules, resembling ribosomes, are scattered within the cytoplasm and surround mitochondria (m). X 32,186.

Fig. 42.—Section of an inclusion body from spleen, containing an abundance of granules and partially destroyed mitochondria (m). X 23,716.
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