TABLE I.
Effect of Aureomycin on Weight and Survival of Tuberculous Guinea Pigs.

Group	Avg wt start, g	Avg wt start treatment, g	Avg wt death, g	No. animals start	No. animals surviving 10 wks
A. Infected, aureomycin treated	501	556	440	12	5
B. Infected, untreated	471	529	552	11	10
C. Uninfected aureomycin treated	465	652	578	6	5

in the microscopic sections of tuberculous tissue from the 5 animals which survived the full 6 weeks of treatment, and tubercle bacilli were readily cultured from the lung in one of these animals.

All the animals treated with aureomycin showed definite evidence of local drug toxicity. There was marked fibrosis of the anterior abdominal wall, where the injections were given, and there were extensive peritoneal adhesions, which, in a few animals, constricted and partially obstructed loops of small intestine. This mechanical obstruction may have accounted for the weight loss in some of the treated animals. In 6 of the treated animals, intercellular material that stained blue with hematoxylin was observed in the liver, spleen, or renal medulla. In 2 of the treated animals, focal hepatitis and hepatic necrosis were observed.

The *in vitro* aureomycin sensitivity of the original organism used, when grown in a modified Dubos liquid medium, was 100 μg/cc. The sensitivity of the strain recovered from the guinea pig after 6 weeks of aureomycin treatment was unchanged.

These results confirm the findings of Steenken and Wolinsky,[1] who failed to influence favorably guinea pig tuberculosis using a considerably lower dosage of aureomycin. It is shown here that aureomycin given in parenteral per kg dosage approximately 10 times the maximum used for other infections in man fails to influence favorably the course of guinea pig tuberculosis, and, indeed, exhibits definite toxicity.

1 Steenken, W., Jr., and Wolinsky, E., *Am. Rev. Tuberc.*, 1949, **59**, 221.

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"Crystalline" Virus-Like Particles from Skin Papillomas Characterized by Intranuclear Inclusion Bodies.* (17328)

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This is a report of the observation with the electron microscope of virus-like bodies that have been obtained from skin papillomas. These papillomas are characterized by the presence of intranuclear inclusion bodies, and the elementary bodies obtained from them tend to be arranged in a crystalline-like pat-

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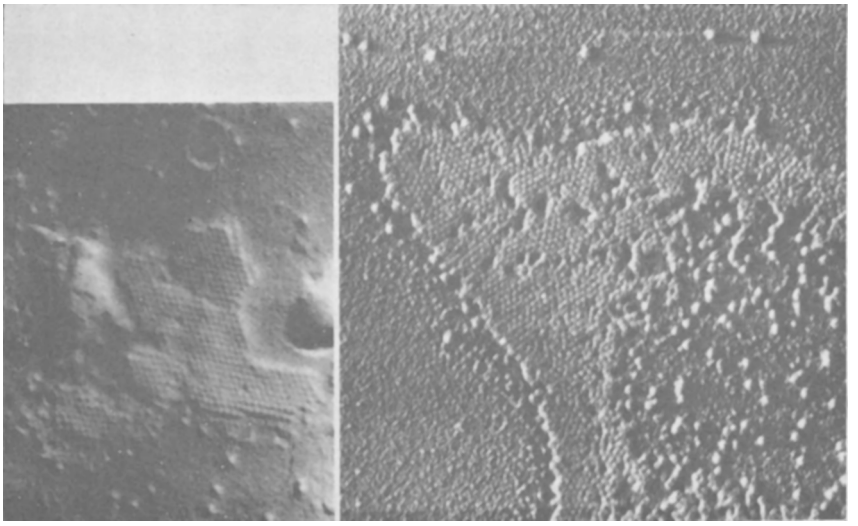

FIG. 1A. Electron micrograph of virus-like particles from intranuclear inclusion body papilloma. Note that particles are in crystalline-like array as well as free. Shadow cast with chromium, angle 1:7. Magnification 18,700 ×.

FIG. 1B. Same from another patient.

tern. Five such lesions were studied by electron microscopy. Four were obtained from the hands of children whose ages ranged from 2 to 12. These lesions differed from common warts in having a more pearly base and an erythematous halo, and were separated easily and completely from the underlying tissue with a curette. The fifth was a plantar wart obtained from a child 7 years old. It differed from the typical plantar wart in that there was no noteworthy hard hyperkeratotic top and very little surrounding callus. After a circular incision was made around the periphery this lesion also was easily and completely separated from the underlying tissue with a curette. Common warts from 9 patients, *molluscum contagiosum* lesions from 2 patients and one example of normal skin were similarly studied.

The preparation of the material was the same in all instances. Half of each lesion was fixed in formalin for tissue sections while the remainder was promptly ground with alundum and distilled water and subjected to clarifying centrifugation of the supernatant fluid at 2,000 r.p.m. for 5 minutes followed by centrifugation of the resulting supernatant fluid at 6,000 r.p.m. for 15 to 45 minutes. Small drops of the 6,000 r.p.m. supernatant fluid and the resuspended sediment were placed on collodion mounts for electron microscopy. These were shadow cast with chromium at an angle of 1:7.

Examination with the electron microscope (RCA type EMU) revealed spherical particles most abundantly in the 6,000 r.p.m. sediment of the suspension from the papillomas showing intranuclear inclusion bodies. These particles were frequently arranged in crystalline-like clusters or layers with an average diameter of 52 mμ and a range of 50 to 53 mμ (Fig. 1). Such an arrangement resembles that previously noted for crystalline plant viruses (Price, Williams, Wyckoff[1]). When these particles were not in crystal-like array, they averaged 68 mμ in diameter with a range of 56 to 80 mμ.

Control preparations of the *molluscum contagiosum* lesions revealed the characteristic brick-shaped elementary bodies previously noted by Boswell[2] (Fig. 2). These had an average length of 330 mμ with a range of 190 to 250 mμ. They were found most abundantly in the 6,000 r.p.m. sediment.

1 Price, W. C., Williams, R. C., Wyckoff, R. W. G., *Science*, 1945, **102**, 277.

2 Boswell, F. W., *Brit. J. Exp. Path.*, 1947, **128**, 253.

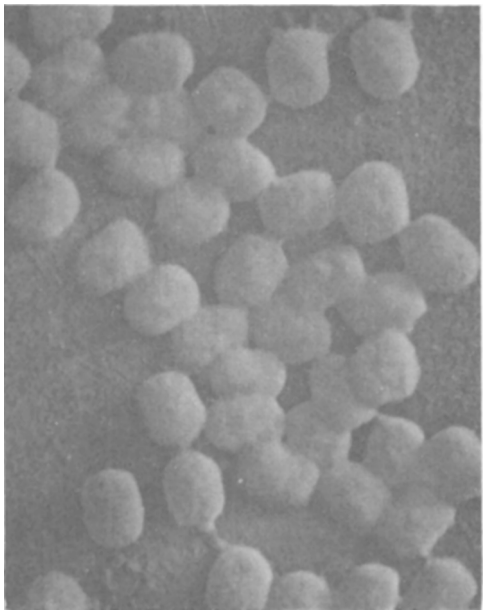

FIG. 2.
Electron micrograph of brick-shaped elementary bodies from molluscum contagiosum lesions. Magnification 35,000 ×.

These were also seen with the electron microscope in preparations made simply by touching the molluscum contagiosum lesions to the mount.

The common wart and normal skin preparations revealed no uniform particles, but merely amorphous scattered clumps of matter, collagen fibers, and spherical particles of varying diameter.

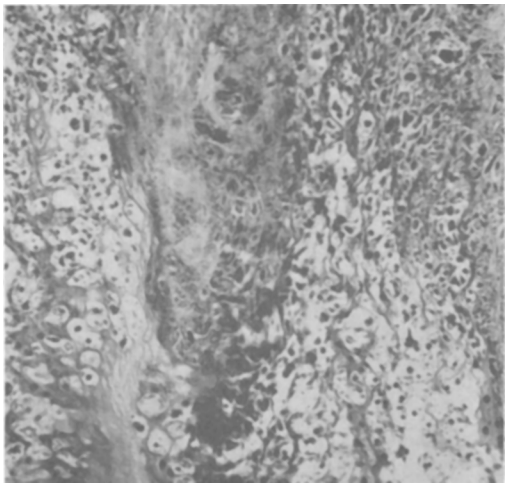

FIG. 4.
Higher power of a portion of Fig. 3—showing the prominent cytoplasmic bodies and looseness of lower cornified layers. Hematoxylin-eosin. Magnification × 65.

The histological appearance of the 5 papillomas yielding virus-like particles was similar (Fig. 3, 4, 5, 6). They showed irregular upgrowths of thickened epidermis overlying elongated papillae containing fine blood ves-

FIG. 3.
Papilloma yielding virus-like particles as shown in Fig. 1. Base is at bottom. Hematoxylin-eosin. Magnification × 30.

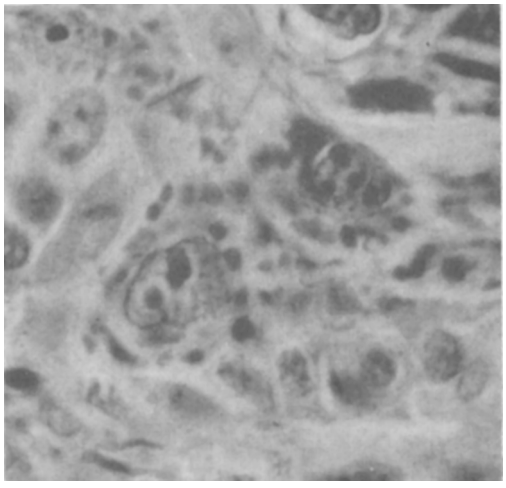

FIG. 5.
Same as Fig. 3. Note the single round intranuclear inclusion bodies photographing less black than the adjacent irregular chromatin masses. Solid cytoplasmic bodies are evident. Hematoxylin-eosin. Magnification × 1200.

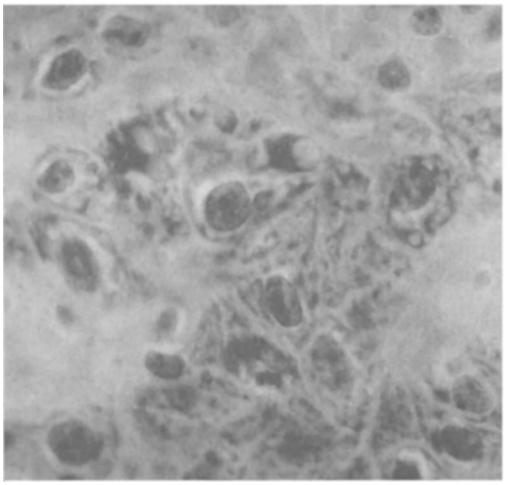

FIG. 6.
Same as Fig. 3. Both solid and vesicular cytoplasmic masses are conspicuous. Intranuclear inclusion bodies are also present. Hematoxylin-eosin. Magnification × 600.

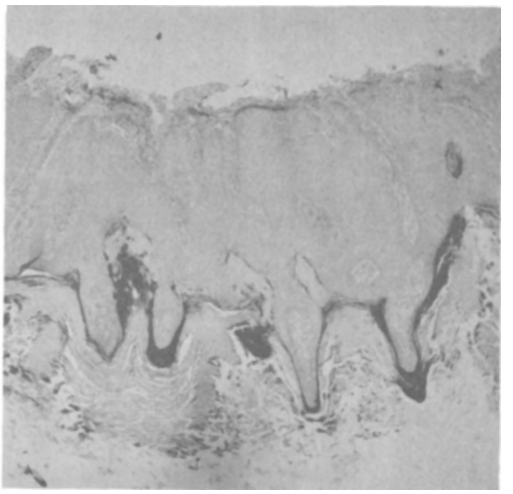

FIG. 7.
Common wart. Base is at bottom. Hematoxylin-eosin. Magnification × 30.

sels and delicate connective tissue. There was a great increase in the thickness of the stratum corneum with persistence of pyknotic nuclei in the lower layers where the keratinized substance was loosely arranged and not as compact as at the surface. Significantly, intranuclear inclusion bodies were present in a large proportion of the cells of the papillomas, but not of the adjacent epidermis. These were first seen in the layer directly over the basal-cells, and were evident in all of the more superficial layers. The inclusion bodies were round, stained with eosin and not hematoxylin; they were Feulgen negative and demonstrated little or no basophilia with methylene blue. Granules were present in the cytoplasm of the lowest row of cells that contained inclusion bodies. These granules when small were solid, but acquired a vacuole as they increased in size finally becoming oval or pointed in shape. Both the granules and the vesicular bodies stained with hematoxylin but had almost no affinity for the basic dye methylene blue and were Feulgen negative. At the level of the stratum granulosum they apparently became transformed into large solidly staining cytoplasmic bodies that persisted into the stratum corneum. Their affinity for hematoxylin was gradually replaced by a strong eosinophilia by the time they had reached the stratum corneum in the region showing the parakeratosis. No elementary bodies were seen in any of the stages in Giemsa preparations.

The lesions of *molluscum contagiosum* were classical: a localized zone of hyperplasia of the epidermis with eosinophilic bodies filling the cytoplasm, displacing the nuclei of the cells of the upper Malpighian layers and persisting into the stratum corneum where they eventually became hyaline and fragmented. The molluscum bodies were Feulgen positive. The common warts had the usual histological appearance (Fig. 7): papillomas composed of hyperplastic epidermis covering prolonged papillary processes bearing vessels and a delicate stroma. Considerable hyperkeratosis with variable parakeratosis was present.

Search through the accumulated material of the laboratory of surgical pathology of the New Haven Hospital revealed 31 other skin lesions histologically similar to that of the inclusion body papillomas described above. The ages of these patients ranged from 2½ to 68 years. There were also 158 typical verrucae from individuals 5 to 80 years of age.

Summary. Virus-like particles that tend to be arranged in a crystalline-like pattern have been observed by electron microscopy in a

TABLE I.

Clinical diagnosis	No.	Electron microscopy: Spherical particles	Electron microscopy: Spherical particles in crystalline-like array	Electron microscopy: Brick-shaped bodies	Pathology: Intranuclear inclusion bodies	Pathology: Molluscum bodies
Intranuclear inclusion body papilloma	5	5	4	—	5	—
Molluscum contagiosum	2	—	—	2	—	2
Common warts	9	—	—	—	—	—
Normal skin	1	—	—	—	—	—

study of suspensions of 5 skin papillomas. Histological examination of the same tissues revealed intranuclear inclusion bodies and characteristic cytoplasmic masses in the cells of the hyperplastic epidermis. Thirty-one lesions with similar histological appearance were encountered along with 158 typical verrucae in a review of surgical pathological material.

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Studies on the Thromboplastic Agent in Plasma. (17329)

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Thromboplastic preparations can conveniently be divided into two categories, those containing proteins and those which are lipids free from protein. In a recent study on the mode of action of Dicumarol[1] evidence was presented indicating that the thromboplastic agent in plasma responsible for the clotting of recalcified plasma had the physiological characteristics of a lipid thromboplastic agent. Further evidence has been obtained consistent with this view and will be presented in this paper. This evidence depends on a demonstration of a direct proportionality between the coagulation time obtained with the thromboplastic lipid and the coagulation time of a control sample of the same plasma which was recalcified and to which no thromboplastic agent was added. Such a relationship can be explained most simply on the basis that the thromboplastic agent in plasma has the characteristics of the lipid thromboplastic agent. Such a relationship also implies, as will be discussed later, a mutual dependence on some limiting factor found in plasma.

Methods. The thromboplastic lipid was prepared from beef brain as outlined in the previous study.[2] It was stabilized by adding hydroquinone to make up 1% of its weight. This substance is an antioxidant that prevents the autoxidation of the preparation and its subsequent loss of activity.[3] In assaying the thromboplastic lipid a 0.2% emulsion in 0.9% NaCl was prepared from the dry material. The coagulation times of recalcified dog plasma were determined at room temperature with and without the thromboplastic lipid on 22 different occasions extending over a four month period. The plasma was obtained by withdrawing 9 parts of blood from the femoral artery of an unanaesthetized dog

1 Lein, J., and Lein, P. S., *Am. J. Physiol.*, 1948, **155**, 394.

2 Hays, H. W., and Lein, J., *Arch. Biochem.*, 1945, **7**, 69.

3 Lein, J., and Lein, P. S., PROC. SOC. EXP. BIOL. AND MED., 1949, **70**, 446