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ORIGINAL ARTICLES

MYCOPLASMA IN LESIONS OF PEMPHIGUS

by

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Lesions of pemphigus arise on skin and superficial mucosae and are also found in mucosae of esophagus and stomach, lungs, lymph nodes and channels (Fig. 1), kidneys and spleen. All lesions contain the forms described below. The disease begins in nucleus of cells of rete malpighii and extends to cytoplasm (Fig. 2) and cell periphery. Nuclear changes are: complete or partial loss of nuclear membrane; conversion into dense mass of amorphous material; conversion into thin mass of amorphous material containing bodies, filaments, vacuoles; complete or partial filling with edema or vacuoles. In cytoplasm, amorphous material is usually less dense, bodies smaller, filaments thinner, and all stain more faintly than the same forms in nucleus. Nuclear contents first appear in cytoplasm as bud or perinuclear corona. Forms collect at cell periphery, increasing its density, there by producing the Tzanck cell (Fig. 3). Forms may extend from cell periphery into extracellular fluid as streams, for a distance of at least 80 microns (Fig. 4). Entire cell is ultimately converted into amorphous material, bodies, filaments, rings, vacuoles, which float freely in extracellular fluid (Fig. 5).

Amorphous material (Figs. 1, 2, 3, 7) has no limiting membrane, is of uneven density, is basophilic, eosinophilic, amphoteric. Its optical density is a measure of its thickness, which varies very considerably, sometimes within same mass. Amorphous material, unless very thin or very thick, always contains bodies, filaments, rings, vacuoles. Amorphous material photographically opaque with Wratten 58B or 61 green filters, can often be shown to possess forms present in less opaque material by use of Wratten 15 deep-yellow filter.

Bodies (Figs. 4, 5, 6) range in size from barely perceptible dots to approximately 1.3 mu in diameter. They are more often oval than circular and more commonly eosinophilic than basophilic. Larger bodies stain more intensely than smaller. Bodies occur singly, doubly and in short straight, curved, angulated chains of 2 to 7 elements united by thin filaments. While individual bodies in a chain are usually of approxima-

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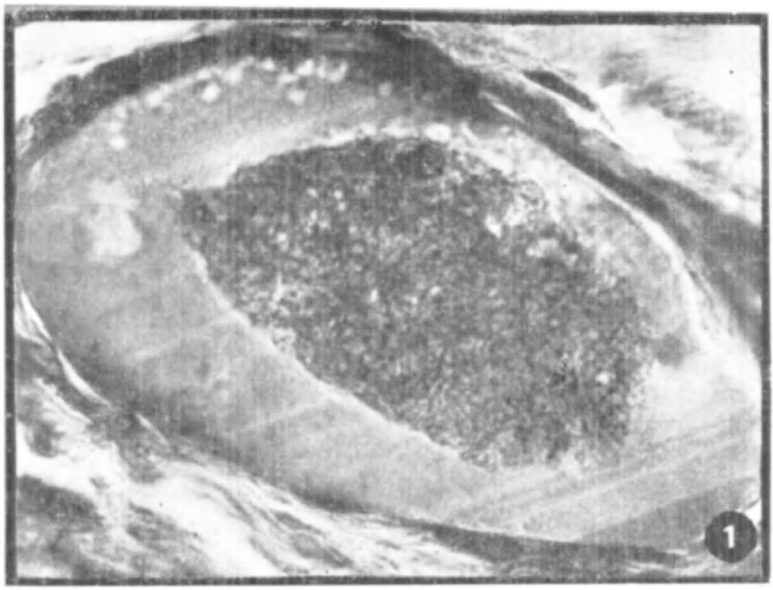
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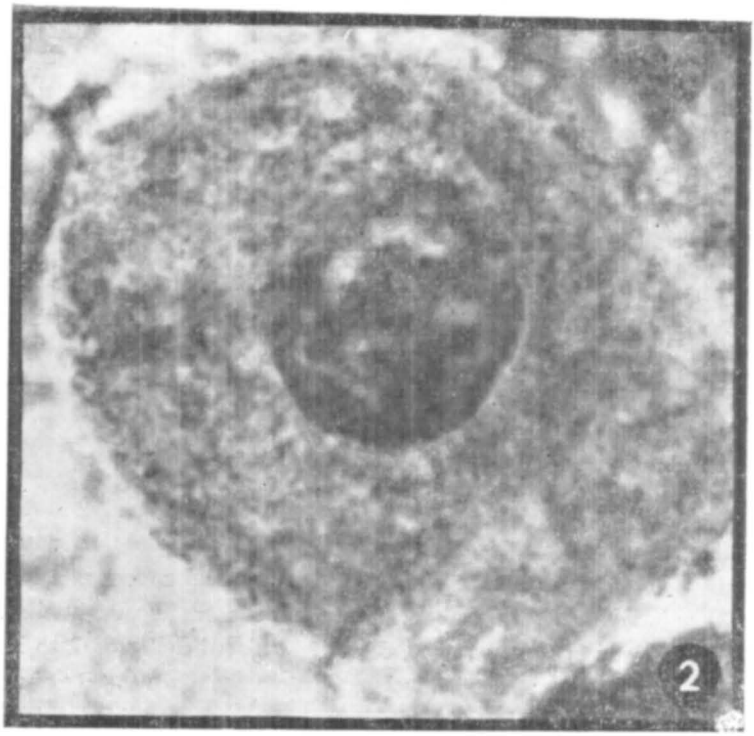
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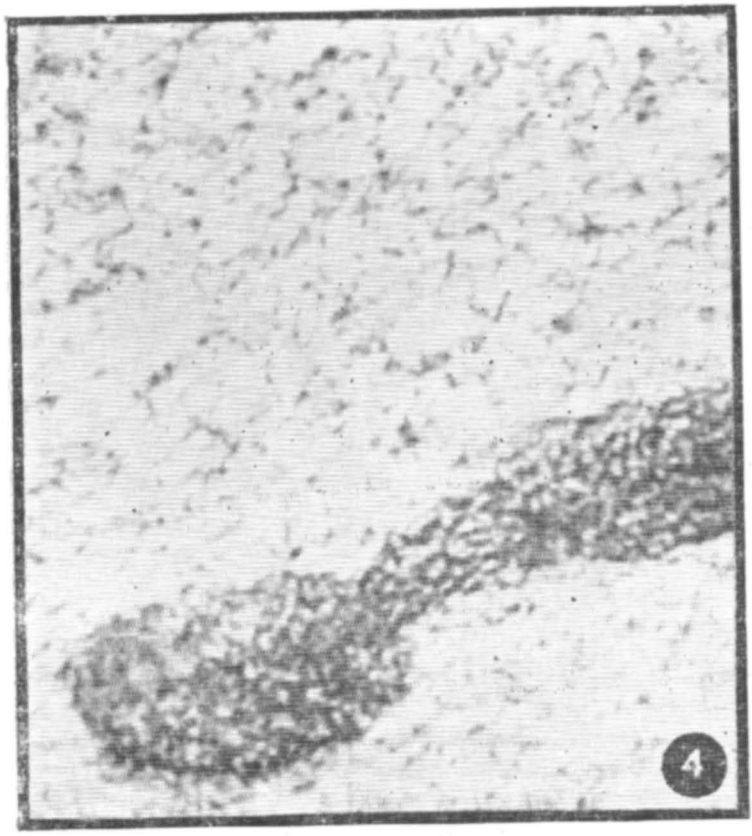
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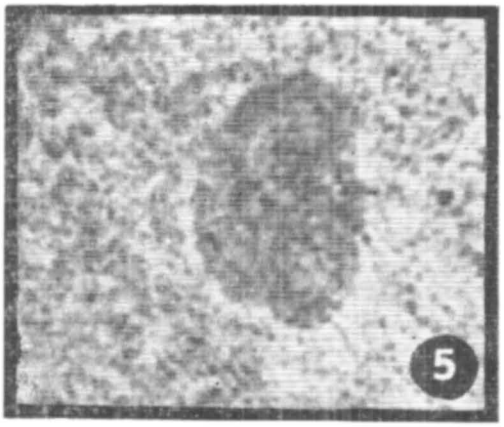
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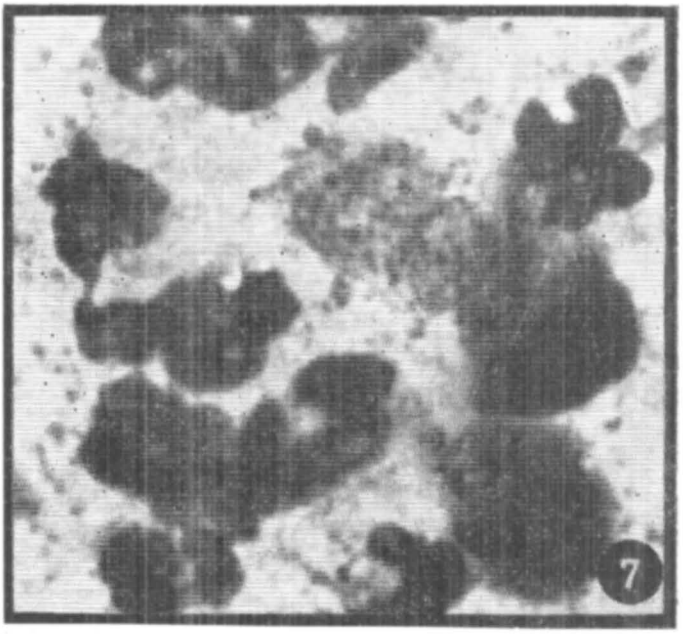
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tely equal size, this is not always, so. Most single bodies also possess filaments, much thinner than the body, arising from opposite ends of long axis of body. Such filaments often terminate, at a distance approximating diameter of body, in a "daughter" body, smaller and more faintly stained than "parent" body, to which filaments are attached. In its turn, filaments arise from "daughter" body. The two bodies of a doublet are usually of equal size and are closely applied to each other. Two identical bodies, joined by a filament, make shortest possible chain. Filaments are seldom straight, vary considerably in thickness from barely perceptible to short bands about 1 mu wide and contain oval or circular condensations, denser and usually wider than the filament (Fig. 4). Such condensations appear to be precursors of the bodies, whose shape is more uniform and which stain more intensely than the condensations.

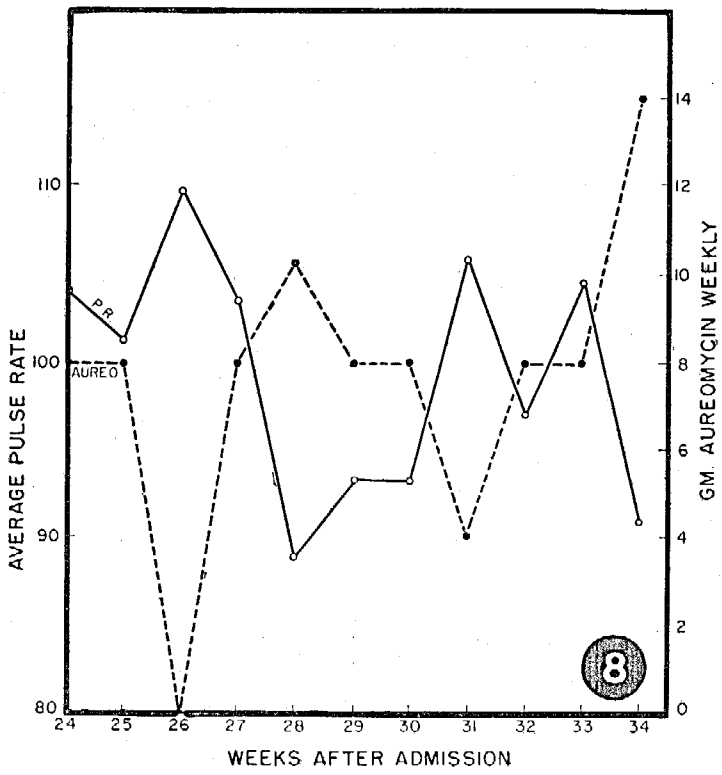
Rings (Figs. 4, 5, 6, 7) range in diamenter from approximately 500 millimicrons to 2 mu. They are more commonly oval than circular and some are crescentic. Staining properties are same as those of bodies. Periphery of ring may be of uniform density and thickness. In most rings, periphery is uneven in thickness and in staining density, thicker parts staining more intensely. Denser areas of periphery often contain one or more bodies. When two bodies only are present, they are usually placed at opposite ends of long axis of ring. A single body at periphery gives ring appearance of signet ring. All rings are not empty structures. Many contain bodies, approximately 400 millimicrons in diameter, centrally placed, and connected to periphery by very thin filaments which divide ring into roughly equal areas. Short filaments, ending in a "daughter" body, may arise from a "parent" body in periphery of ring. Size and close apposition of bodies in periphery of ring sometimes deforms it, producing triangular or quadrilateral shape. Rings may be found in length of a chain of bodies and filaments. Chains and clumps of rings seldom occur extracellularly in blister fluids but are common in nucleus and cytoplasm of cells and in amorphous material.

Vacuoles (Figs. 1, 2, 6) are round or oval areas, ranging in size from 2 mu to approximately 20 mu in diameter. They are found in nucleus and cytoplasm of cells and in amorphous material, particularly in denser portions. They may occupy all or part of cell nucleus. Walls are denser than material in which they occur and may be sufficiently thick to include rings, in addition to amorphous material, bodies, filaments. Vacuoles seldom appear empty. They usually contain, in varying proportions, amorphous material, bodies, filaments, rings. Contents may be stained more lightly than, or equally with, walls. In large dense masses of amorphous material, leukocytes, completely converted into amorphous material, bodies, filaments, rings, may be found in vacuoles.

Polymorphonuclears (Fig. 6), eosinophils and mononuclears phagocytize, and are destroyed by, forms. Polymorphonuclears and eosinophils are strongly attracted to forms and, generally, coexist. Polymorphonuclears are more commonly found either preceding, or at the first appearance of, forms and eosinophils in lesions of longer duration. Attachment of polymorphonuclears to periphery of epidermal cells, in

process of destruction by forms, produces partial or complete rosettes, strongly resembling those in positive LE preparations (Fig. 7).

Red blood cells are destroyed by forms. Earliest stages of destruction are: intact cell membrane shows narrow, often beaded zone of increased density; cells are filled with amorphous material, bodies, filaments, rings, vacuoles, relative proportions of which vary among cells; blood pigment is not seen. Later, cells, recognizable only by greatly deformed shape, are much, reduced in number. Cell membrane is usually incomplete, enabling forms filling cell to merge freely with those packing intercellular spaces. Finally, cells are completely replaced by forms. Mononuclears in autopsy tissues may contain brown pigment, intimately mixed with forms and containing ferric iron. With impending death, aggregates of forms, often surrounded by clear or partly clear zones, appear on surface of red blood cells (Fig. 3, (11)). Forms, in blister fluid and autopsy spleen of pemphigus, can be transmitted to, and maintained by serial passage in, brains of X-irradiated mice (1, 2, 3, 4, 5). Neutralization experiments (3, 4, 5) link transmissible agent with pemphigus. Mycoplasma was cultured from necrotic lesions at site of inoculation (5). Pathological reaction in brain is identical with that described by Findlay (6) for rolling disease, which was not seen in any mouse. Forms inocula used in mouse experiments are identical, morphologically and tinctorially with: those of cultured mycoplasma (7); those present in epithelial cells from which T-strains were cultured (8, 16); those in lesions in brain of X-irradiated mice inoculted



with cultures of mycoplasma isolated from X-irradiated mouse brains carrying serial passage of pemphigus agent and uninoculated, X-irradiated mouse brain, respectively. Additional links of forms present in human lesions with mycoplasma are: effect upon red blood cells (12, 13, 14, 15); aggregation at cell periphery (9, 10); striking improvement of clinical pemphigus by chlortetracycline hydrochloride (Fig. 8) and its resistance to penicillin, streptomycin and sulfonamides (5).

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ILLUSTRATIONS

Fig. 1 is section of corium in pemphigus vegetans, stained with hematoxylin and eosin. Figs. 2,4,6,7 are smears of spontaneously-arising blister fluids of pemphigus vulgaris in three different persons. Figs. 3 and 5 are smears of blister fluids induced by application of cantharides to normal-appearing skin of person from whom Figs. 2 and 6 were prepared. All blister fluids were stained with Wright. Magnification of Figs. 1–7 is x 2500. Forms, not illustrated, were present in the blister fluids of pemphigus patient from whom Fig. 8 was prepared.

Fig. 1 Lymph channel filled with forms, of which amorphous material surrounds closely-packed bodies; filaments, rings, vacuole, 6 mu by 4 mu, in amorphous material contains faintly-stained forms. Forms in amorphous material are more evident in denser areas.

Fig. 2 Epidermal cell, 35 mu by 29 mu. Nuclear membrane partly beaded, partly absent. Short chains of bodies and filaments enter cytoplasm from bodies producing beads in membrane. Where latter is absent, forms in nucleus blend imperceptibly with those filling cytoplasm. Cell membrane is absent.

Fig. 3 Epidermal cell. Vacuoles and chains of rings in nucleus. Nuclear membrane irregularly thickened and beaded. Small bud of forms connects thinkened nuclear membrane with cell periphery, to which dense masses of forms are attached.

Fig. 4 Cell nucleus, 16 mu by 16 mu. Nuclear membrane partly beaded, partly absent. Nuclear forms stream in to extracelluiar fluid. Thin, faintly-stained extracellular filaments contain condensations and bodies.

Fig. 5 Very advanced stage of destruction of nucleus by forms. Latter blend imperceptibly with those surrounding nucleus. Bodies and filaments in extracellular fluid show superb chains and vary considerably in size and staining density. Nuclear membrane absent.

Fig. 6 Polymorphonuclear, 14 mu diameter. Clump (? colony), 6 mu diameter, of forms in cytoplasm. Ring in nucleus contains central body with attached filaments. Concentration of forms at cell periphery.

Fig. 7 Advanced stage of destruction of cell by forms. "Signet ring" at periphery of nucleus. Cytoplasm filled with thin amorphous material containing faintly-stained bodies, filaments, rings. Numerous polymorphonuclears on surface of, and surrounding, cell. Nuclear and cell membranes absent.

Fig. 8 Reciprocal relation of average weekly pulse rates and total weekly intravenous dose of chlortetracycline hydrochloride.

"ART WORK WAS PERFORMED BY Mr. Molton Funk of the Department of Illustration, Downstate Medical Centre, State University of New York.

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