from mosquitoes represents one positive pool of 47 pools tested; over 400 mosquito pools from the endemic area remain to be examined.

The habitats in Mexico where these strains of VEE virus were recovered include secondary forest, mangrove, and a small patch of rain forest dominated by canopy-forming trees, all bordering a lagoon off the Gulf of Mexico coast at the village of Sontecomapan, Veracruz. These areas are in a narrow strip of coastal lowland immediately north of a small range of volcanic mountains surrounding Lake Catemaco, approximately 500 km southeast of Mexico City and 160 km southeast of the city of Veracruz. Whether VEE virus has a wider geographic distribution extending into more populated areas of the eastern coastal lowlands of Mexico and whether the virus has only recently moved to Mexico or has been endemic there for many years must be determined by future studies. Nevertheless, its presence constitutes a potential threat to the health of man and certain domestic animals in Mexico, and if carried northward, perhaps by migrating birds, it could also become a threat to inhabitants of the United States.

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4. These investigations were performed by collaboration among persons from Cornell University Medical College, the Pan American Health Organization, the Government of the United States of Mexico, the Instituto de Virologia de la Secretaria de Salubridad y Asistencia and the Instituto de Salubridad y Enfermedades Tropicales of Mexico, and were supported in part by USPHS training grant No. 5-T1-AI-231 from the NIAID and in part by the Surgeon General, Department of the Army, under sponsorship of the Commission on Viral Infections of the Armed Forces Epidemiological Board. VEE, Mucambo, and Pixuna virus antiserums and their VEE antibody titers were kindly supplied by J. Casals, R. Shope, and R. McKinney.

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"Chromaffin" Cell: Electron Microscopic Identification in the Human Dermis

Abstract. *A granulated cell in human skin has an ultrastructure similar to that of chromaffin cells of the adrenal medulla. This cell is closely associated with unmyelinated axons and may be the site of peripheral store of noradrenaline.*

The presence of chromaffin cells (those cells containing adrenaline or noradrenaline) in the human dermis has been a matter of controversy. Adams-Ray and Nordenstam (*1*) and Burch and Phillips (*2*) treated chromated skin with the Sevki stain (*3*) and concluded that chromaffin cells are present. These cells, in their opinion, are distinguishable from mast cells and have staining characteristics similar to those of the medullary cells of the adrenal. In contrast, Mercantini (*4*) and Matz and Skinner (*5*) state that the staining characteristics attendant on the use of the Sevki stain are not only dissimilar to those described by Adams-Ray *et al.* but also do not allow differentiation of mast cells, the commonly present granulated cell in the dermis, and chromaffin cells. Thus far electron microscopic observations (*6*) have failed to demonstrate conclusive differences between the granules of the so-called chromaffin cells of the skin and mast cells.

The data from physiological observations (*7*) on the cutaneous vasculature suggest that peripheral stores of noradrenaline are present and that they are controlled by cholengeric, postganglionic sympathetic fibers.

The cell shown in Fig. 1, from the dermis of the axillary skin of an 11-month-old white boy, was found incidentally during a study of the ultrastructure of a reactive inflammatory skin lesion, juvenile xanthogranuloma. The lesion is formed of histologically dissimilar cells, histiocytes, and proliferating fibroblasts, and it does not contain granulated cells. This cell contains membrane-limited, electron-opaque granules that are 1000 ± 200 Å in diameter.

These granules are similar to those in the medullary cells in the human adrenal. They are smaller than the granules of human mast cells which average 5000 ± 2000 Å in diameter. The granules are concentrated at one pole of the cell, and adjacent to this pole there are three unmyelinated axons within a Schwann cell. The limiting membrane of two of these axons are in appositional contact with the cell membrane of the granulated cell.

The ultrastructure alone does not identify the pharmacological nature of the content of the granules. However, the similarity in structure to the noradrenaline-containing cells of the

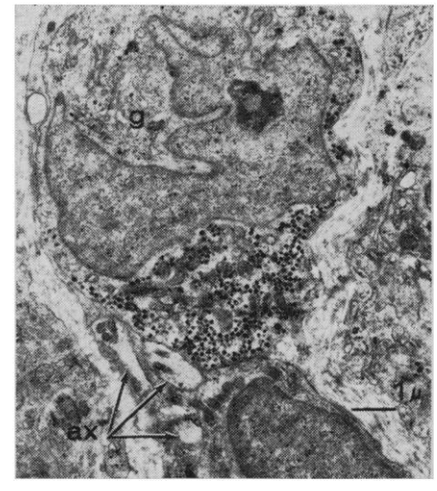

Fig. 1. The round electron-opaque secretory granules are concentrated amidst the mitochondria, at the lower pole of the cell. The arms of the irregularly shaped nucleus enclose the Golgi zone (*g*) wherein a few granules are seen. The three unmyelinated axons (*ax*) are within the adjacent Schwann cell.

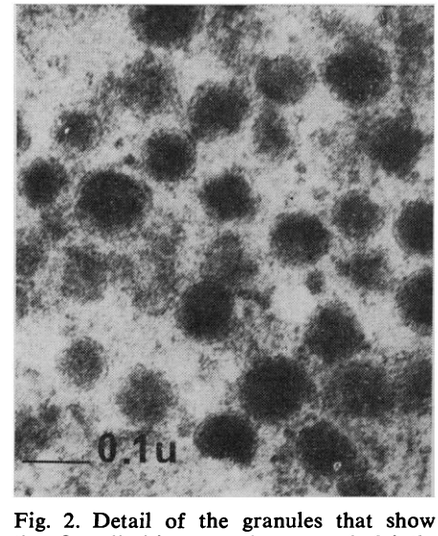

Fig. 2. Detail of the granules that show the fine limiting membrane and faintly granular matrix.

adrenal medulla and the close association with unmyelinated axons are certainly consistent with the physiological hypothesis requiring a peripheral store of noradrenaline.

Search for these cells in thin sections of human skin prepared for electron microscopy may be a time-consuming and disappointing task. Thus further observations may be dependent on incidental recognition during the course of other studies.

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Uracil: Failure To Restore DNA Synthesis While Relieving 5-Fluorouracil-Induced Inhibition

Abstract. *Growth inhibition of* Bacillus cereus *by 5-fluorouracil is abolished by the addition of uracil without the inhibition of DNA synthesis being relieved. The growth rate, protein, and RNA content of cells grown in the presence of 5-fluorouracil and uracil are unaffected until the cells contain only about 25 percent of their normal DNA content.*

The growth-inhibitory agent 5-fluorouracil (*1*) has been shown to inhibit DNA synthesis in Ehrlich ascites cells (*2*). The active form of the analog is believed to be 5-fluoro-2′-deoxyuridine-5′-monophosphate which acts as a competitive inhibitor of thymidylate synthetase (*3*). The conversion of the drug to the active metabolite and its effect on DNA synthesis in bacterial cells results in growth inhibition and "thymineless death" (*4*). In this report we suggest that the growth-inhibitory action of 5-fluorouracil can be dissociated from the drug's inhibition of DNA synthesis in *Bacillus cereus* by the addition of uracil together with 5-fluorouracil.

Bacillus cereus 569 H was grown at 37°C in the presence or absence of 5-fluorouracil (20 μg/ml; 0.16 μmole/ml). Growth was measured by changes in optical density (OD) in a Bausch and Lomb Spectronic colorimeter at 540 mμ. At zero time the drug was added to exponentially growing cells at OD_{540} of 0.3 (equivalent to 0.3 mg dry weight of bacteria per milliliter of culture) together with varying amounts of uracil. In some experiments radioactive nucleic acid precursors were also present. When the cells had grown to OD_{540} of 0.6, the appropriate analysis was performed. Total cell counts were determined by counting the cells, stained with methylene blue, in a Levy counting chamber. Viable counts were determined by pouring a portion of the cell suspension onto nutrient agar plates, incubating overnight at 37°C, and counting the resulting colonies. For control cells the increase in optical density at 540 mμ served as a true indicator of cell division and growth because the cell number at OD_{540} 0.6 was approximately double that at OD_{540} 0.3. In certain experiments growth and DNA synthesis were measured in the presence or absence of only 0.1 μg/ml of 5-fluorouracil added at OD_{540} of 0.02 and the cells grown to 0.64.

The uptake of 5-fluorouracil-2-C^{14} into the total nucleic acid fraction and the incorporation of labeled purines into DNA was measured by the membrane filtration procedure (*5*). Total DNA content was measured spectrophotometrically at 260 mμ in a Beckman DU spectrophotometer after removal of RNA by KOH, and by the Burton method (*6*) for measuring deoxyribose from DNA purine deoxyribosides.

Table 1 shows the time required by the cell suspensions to double in turbidity from an initial OD_{540} of 0.3 (equivalent to one generation time for control cells), the cellular content of radioactive 5-fluorouracil and DNA, and the total cell count when grown with various concentrations of uracil, 5-fluorouracil, and mixtures of the two.

5-Fluorouracil produced a marked depression of DNA synthesis. Cells grown during the period of inhibition (OD_{540} 0.3 to 0.6) synthesized only 16 percent of the normal amount of DNA. Added uracil had no effect on the DNA content of the cells. When the ratio of the molar concentration of uracil to that of 5-fluorouracil was equal to or greater than 1, the incorporation of 5-fluorouracil was diminished (but not abolished) and growth was indistinguishable from that of the control cells. The DNA content, however, was essentially unchanged from that of the 5-fluorouracil cultures and, even at a uracil to 5-fluorouracil ratio of 100, it was still greatly diminished when compared with control cells. The ultraviolet absorption method and the Burton method for DNA provided similar results. The similarity in total cell count between the cultures indicates that the reduction in DNA con-

Table 1. The effect of various concentrations of uracil (U), 5-fluorouracil (5-FU), and mixtures of both on the growth rate, DNA content, and cell count of *Bacillus cereus*.

Culture	U (μg/ml)	5-FU (μg/ml)	U : 5-FU (molar ratio)	Turbidity doubling time (min)	5-Fluorouracil-2-C^{14}		DNA		Cell count × 10^{-9} (per ml)
					Total 5-FU in cell* (μg per mg dry wt)	5-FU in RNA* (μg per mg RNA)	μg per mg dry wt	μg per mg dry wt (% increase)†	
Control				50			21.9	(100)	1.48
Control+ uracil	18			50			22.3	103	1.52
5-Fluoro-uracil		20		180	(100)	(100)	11.2	16	1.28
5-FU + U	1.8	20	0.1	90	94	83			
5-FU + U	18	20	1	55	15	8	10.6	12	
5-FU + U	180	20	10	55	2	1	11.0	15	1.34
5-FU + U	1800	20	100	55	0.7	0.2	11.6	20	

* Values expressed as a percentage of 5-FU culture. Actual values are 8.02 μg 5-FU per milligram of dry weight, and 13.9 μg 5-FU incorporated into RNA per milligram of RNA. † The value at OD_{540} 0.3 (9.1 μg DNA per milligram of dry weight) was subtracted from the DNA content at 0.6 and expressed as a percentage of the control.