the administration of equal dosages of the 3 sulfonamides and their combinations would result in greatly different drug concentrations in the living body. In accordance with the results of absorption-excretion studies, as exemplified in Fig. 1, sulfonamide mixtures give high and well sustained blood concentrations and should, therefore, prove at least of the same if not of higher antibacterial value when compared with the same dosage of any one of their individual components *in vivo*. Although this viewpoint is well supported by clinical experience,[2,3] it remains to be accurately investigated in therapeutic studies with experimental infections of laboratory animals.

Summary. 1. In continuation of experimental and clinical studies with mixtures of sulfonamides, the toxicity as well as the absorption and excretion of the combinations sulfadiazine-sulfathiazole, sulfadiazine-sulfamerazine, and sulfadiazine-sulfathiazole-sulfamerazine were investigated in albino rats.

2. These combinations of partial dosages proved significantly less toxic than any one of their separate constituents in equal or comparable total dosage. The mixture of 3 sulfonamides was less toxic than either combination of 2 drugs.

3. The low toxicity of sulfonamide mixtures was shown to be due to the prevention of renal obstruction, resulting from a pronounced diminution in the intratubular deposition of sulfonamide crystals.

4. Mixtures of sulfonamides were more completely absorbed and excreted than equal amounts of their individual constituents. Blood levels from mixtures were, therefore, distinctly higher than expected on the basis of mathematical computations from the values of single sulfonamides.

5. It was reasoned on the basis of these experimental studies that the use of a mixture containing 3 sulfonamides in human therapy would almost completely eliminate the possibility of concrement formation in the urinary tract at the routine dose level. Hence, it would also obviate the necessity for adjuvant alkali therapy.

The technical assistance of the Misses Helen and Ruth Salzberg and Miss Catherine Russell is gratefully acknowledged.

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Surface Striations of *Euglena gracilis* Revealed by Electron Microscopy.

VINCENT GROUPÉ. (Introduced by Geoffrey Rake.)

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In the course of studying a variety of microorganisms with the aid of electron microscopy using the shadow casting technic of Williams and Wyckoff[1] and the replica technic of Hillier and Baker[2] a definite pattern of surface striations on the pellicle of *Euglena gracilis* was clearly revealed. The presence of such surface striations on this species suggests the possibility that many or all of the species of *Euglena* possess these markings in varying degree inasmuch as prominent surface striations have been described for other species of *Euglena (e.g., E. viridis, E. oxyrus,* and *E. spirogyra.)*[3]

Bacteria-free cultures of 4 physiologically different species of *Euglena gracilis,* obtained through the courtesy of Dr. George W. Kidder, were maintained by serial passage on

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2 Hillier, J., and Baker, R. F., *J. Bact.*, 1946, **52**, 411.

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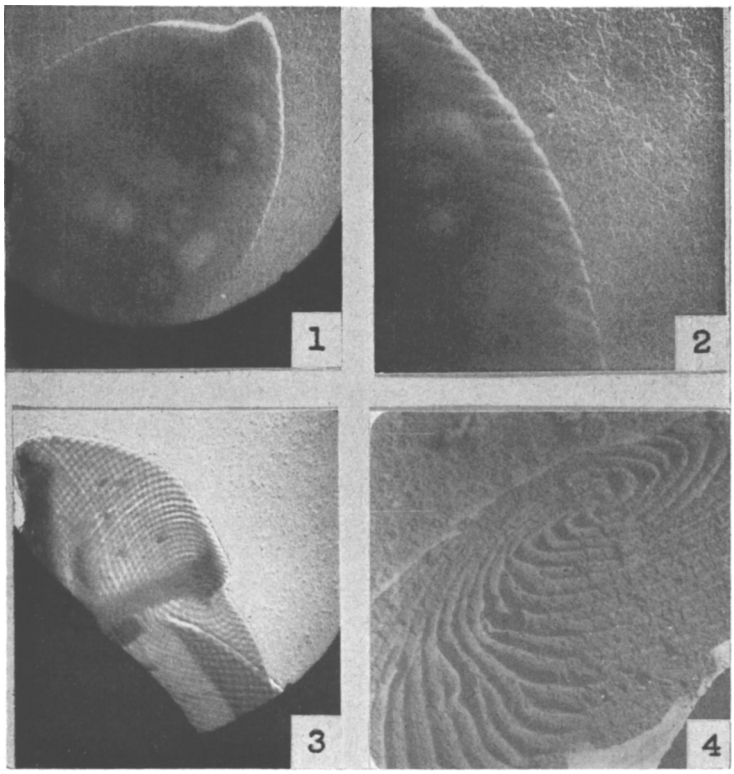

FIG. 1-4.
Electron Micrographs of *Euglena gracilis* Shadowed with Gold.
FIG. 1. Shadowed with 22.0 mg gold at the angle tangent 3/8.5. Magnification 3370 ×.
FIG. 2. Shadowed with 22.0 mg gold at the angle tangent 3/8.5. Magnification 7800 ×.
FIG. 3. Shadowed with 21 mg gold at the angle tangent 3/8.5. Magnification 3370 ×.
FIG. 4. Shadowed with 24 mg gold at the angle tangent 3/9. Magnification 8530 × (collodion replica).

tryptone acetate broth. Organisms for study were obtained from plate cultures of the various strains on tryptone acetate agar and were prepared for examination in the electron microscope using the replica technic of Hillier and Baker.[2] Specimens thus prepared were shadowed with gold according to the technic of Williams and Wyckoff[1] using a shadow casting device designed and built by Dr. H. Sidney Newcomer. An RCA electron microscope (Type EMU) was used throughout these studies.

It will be seen from the pictorial data presented in Fig. 1 and 2 that groove-like striations forming a regular pattern are present on the surface of *Euglena gracilis*. That these striations are located on the pellicle is evident from the micrograph presented in Fig. 3. It will be seen that the cell has ruptured allowing the protoplasm to escape and had left the pellicle virtually intact thus clearly revealing the pattern of striations on the membrane. Furthermore, it would appear that the striations originate from a central point located on the side of the pellicle and spiral outward and around the organism producing a pattern suggestive of a fingerprint. The structure of such a central point is shown in greater detail in the collodion replica of a portion of the surface of an organism pre-

sented in Fig. 4. A similar pattern of surface striations was observed on each of the 4 strains of *Euglena gracilis* studied.

Unfortunately, no intact flagella were observed and, although replicas of flagella were occasionally encountered, no evidence of structural differentiation was seen.

Summary. A regular pattern of groove-like striations was observed on the pellicle of *Euglena gracilis*.

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In vitro Sensitivity of *Brucella* to Streptomycin: Development of Resistance During Streptomycin Treatment.*

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Like many other species of bacteria brucella are remarkably sensitive *in vitro* to the action of streptomycin.[1-5] Experimental brucella infections in animals[1,3] have also been favorably influenced by the administration of streptomycin. However, the use of streptomycin in human brucella infections has not been attended by consistently favorable results.[4-8] The cause of this has not been elicited and there have been no reports in the literature of the development of resistance during the treatment of human brucella infections with streptomycin. The present report summarizes the results of numerous tests of the *in vitro* sensitivity of the 3 varieties of brucella to streptomycin. Studies are reported concerning a strain of *Br. abortus* which developed marked resistance to the action of streptomycin during the treatment of a patient having subacute bacterial endocarditis due to this organism.

Methods and Materials. The method of testing the *in vitro* sensitivity of 40 strains of brucella was as follows: a loopful of a 24-hour culture grown on a Bacto tryptose phosphate agar† slant was transferred to 10 ml of sterile tryptose phosphate broth so as to give a suspension with a turbidity equal to that of a barium sulfate No. 1 standard. This suspension was then serially diluted to 10^{-3} with tryptose phosphate broth. Pour plate colony counts indicated that this diluted suspension contained 30,000 to 300,000 viable cells per ml. Each of a series of 10 test tubes was inoculated with 4.4 ml of tryptose phosphate broth. To each of 9 tubes was added 0.1 ml of the 10^{-3} dilution of brucella. The 10th tube was used as a sterility control. To all but the sterility control was added 0.5 ml of streptomycin dissolved in sterile physiological saline, the amount of streptomycin added being sufficient to give a final concentration of 0.5 to 10 μg of streptomycin base per ml. The streptomycin solution

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† Difco Laboratories, Detroit.