The Panel is not aware of infections caused by bacteria more sensitive to this combination than eo either of its components.

Establishing efficacy would involve demonstrating that the clinical response to the combination is greater than to either agent used alone. No such evidence is available. *In vitro* studies of this combination have given variable results. The effects may be antagonistic, additive, or synergistic, and are unpredictable for any particular organism.

Thus, there is no evidence that each of the active ingredients contributes to the effect as claimed.

Documentation:

1. Erythromycin, oleandomycin and spiramycin—and their combinations with tetracycline. New Eng. J. Med. 257: 525–526, 1957. (Editorial)

2. Forfar, J. O., and A. F. MacCabe. Erythromycin, spiramycin, and oleandomycin. Britt. Med. J. 1: 581, 1957. (Correspondence)

3. Jones, W. F., Jr., and M. Finland. Antibiotic combinations; tetracycline, erythromycin, oleandomycin, and spiramycin, and combinations of tetracycline with each of the other three agents—comparisons of activity in vitro and antibacterial actions of blood after oral administration. New Eng. J. Med. 257: 482–491; 536–547, 1957.

4. Jones, W. F., Jr., R. L. Nichols, and M. Finland. Development of resistance and cross-resistance in vitro to erythromycin, carbomycin, spiramycin, oleandomycin and streptogramin. Proc. Soc. Exp. Biol. Med. 93: 388–393, 1956.

II. Favorable clinical response to Sigmamycin has been observed in the following categories and indications: infections of the respiratory tract and related structures and the genitourinary system, surgical infections, and miscellaneous (amebiasis and lymphogranuloma venereum have been found responsive to Sigmamycin). Dental infections caused by susceptible organisms are candidates for Sigmamycin therapy.

Evaluation: Ineffective as a fixed combination.

Comments: There is no evidence that each of the drugs present in this combination contributes to the effect as claimed. Although case reports can be found indicating favorable response, this response is similar to that expected following administration of tetracycline alone or, more rarely, oleandomycin.

Documentation: Informed judgment of the Panel.

III. In streptococcal infections, therapy should be continued for 10 days to minimize the possibility of the development of rheumatic fever or glomerulonephritis.

Evaluation: Ineffective as a fixed combination.

Comments: The Panel is not aware of convincing evidence that treatment with Sigmamcyin will prevent either of these conditions, regardless of the duration of therapy. More effective drugs are available for therapy of streptococcal infections.

Documentation: Informed judgment of the Panel.

Approved by WM. KIRBY,
Chairman.

APPENDIX IV

[From the New England Journal of Medicine, vol. 261, No. 26, Dec. 24, 1959, pp. 1318–1321]

FATAL CIRCLATORY COLLAPSE IN PREMATURE INFANTS RECEIVING CHLORAMPHENICOL *

(By Lafayette E. Burns, M.D.,† Joan E. Hodgman, M.D.,‡ and Alonzo B. Cass, M.D.,§ Los Angeles, Calif.)

A survey was made of premature infants born twenty-four hours or longer after spontaneous rupture of the fetal membranes, because of a higher mortality

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