purified $s_{20}° = ca\ 70 \times 10^{-13}$ from diseased embryos.[2] In such water preparations the E.S. and W.S. proteins appear to be present but because of factors not yet clear, boundaries are not obtained.

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Specific Chemotherapy of Experimental Staphylococcus Infections with Thiazol Derivatives of Sulfanilamide.

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Experimental and clinical experience has shown that staphylococcus infections are either uninfluenced, or at best, slightly affected by sulfanilamide, sulfanilyl dimethyl sulfanilamide;[1, 2] by prontosil;[3] by p-Amino-benzene-sulphonyl-4-aminobenzenesulphonedimethylamide (uleron);[1, 2] di-(p-formylaminophenyl) sulphone and di-(p-butylaminophenyl) sulphone.[4] On the other hand, sulfanilyl sulfanilamide and sulfapyridine seemed to have some curative effects on experimental staphylococcus infections in mice.[2, 5]

The relative ineffectiveness of present chemotherapeutic compounds against staphylococcic infections stimulated researches for compounds of greater efficiency against this organism.

Three new thiazol derivatives of sulfanilamide have recently been developed. 2-sulfanilamidothiazol (sulfathiazol), 2-sulfanilamidomethylthiazol (sulfamethylthiazol), and 2-sulfanilamidophenylthiazol (sulfaphenylthiazol) are analogues of sulfapyridine.

Sulfathiazol and sulfamethylthiazol have since been described by Fosbinder and Walter.[6] Like sulfapyridine the thiazol compounds are equivalent to or superior to sulfanilamide against *Streptococcus hemolyticus* and the various strains of pneumococci, but unlike either of these preparations they exert a marked effect upon staphylococci, both *in vitro*[7] and *in vivo*.

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1 Mellon, R. R., Shinn, L. E., and McBroom, J., PROC. SOC. EXP. BIOL. AND MED., 1937, **37**, 563.

2 Feinstone, W. H., Bliss, E. A., Ott, E., and Long, P. H., *Bull. Johns Hopkins Hosp.*, 1938, **62**, 565.

3 Levaditi, C., and Vaisman, A., *Compt. rend. Soc. de biol.*, 1935, **119**, 946.

4 Nitti, F., Bovet, D., and Hamon, V., *Compt. rend. Soc. de biol.*, 1938, **128**, 26.

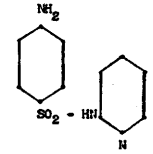
5 Whitby, L. E. H., *Lancet*, 1938, **2**, 1905.

6 Fosbinder, R. F., and Walter, L. A., *J. Am. Chem. Soc.*, 1939, **61**, 2033.

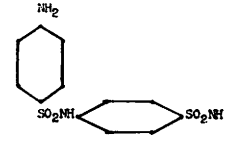
7 to be presented elsewhere.

The structural formulae for sulfanilamide, sulfapyridine, sulfanilyl sulfanilamide and each of the thiazol derivatives are as follows:

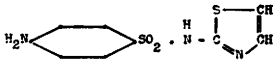
Sulfanilamide.



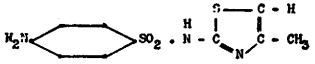
Sulfapyridine.



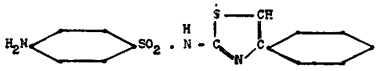
Sulfanilyl Sulfanilamide.



Sulfathiazol.



Sulfamethylthiazol.



Sulfophenylthiazol.

This communication represents a preliminary comparison of the efficacy of the thiazol compounds with that of sulfapyridine and sulfanilyl sulfanilamide in experimental staphylococcus infections in mice.

Method. Male albino mice of uniform age from a standard strain weighing between 19 and 21 g were infected by the intravenous injection (tail vein) of 0.2 cc of a saline suspension of a highly mouse virulent strain of *Staphylococcus aureus* representing roughly 800 million cocci. This strain (F.D.A.209) was obtained from a human case and kept in stock culture. The heavily abscessed kidneys of the infected animals were removed at the time of death for reculture on agar slants. Such transfers (usually 4) were carried out in successive groups of mice until the virulence developed was such that the above infection uniformly killed 100% of a series of at least 10 mice within 1 to 5 days. The culture of such virulence was used in all chemotherapeutic tests.

TABLE I.
Chemotherapy of Experimental *Staphylococcus aureus* Infections in Mice.

Preparation	Single dose, g/kg	Total dose, g/kg	Died before 20th day	Day on which death occurred (individual animals)	Pathologic findings
None (controls)			10/10	1,2,3,3,4,4,4,4,5,5	++ to ++++ (influenced by time of survival)
Sulfapyridine	1.0	18.0	6/10	5,6,6,11,12,16	++ +++ ++++ ++++
Sulfanilyl sulfanilamide	1.0	18.0	7/10	2,5,6,6,7,8,15	++ +++ ++++
Sulfathiazol	1.0	18.0	3/10	1½,4,12	0 0 0 + ++ ++ ++++
Sulfamethylthiazol	1.0	18.0	1/10	10	0 0 0 + + ++ ++ ++ +++
Sulfaphenylthiazol	1.0	18.0	5/10	8,13,14,16,19	++ +++ ++++ ++++ ++++

Key: 0 Kidneys pale, ⅘ normal size, no active abscess. No abscess in urinary tract. No abscess in knee joint.
\+ Same as 0 except that there is one apparently active pin point abscess on one kidney.
++ Same as 0 except that there are 2 or 3 pin point abscesses on one kidney that look active, but still show healing.
+++ Three or more abscesses on one or both kidneys. No abscess in urinary or genital tract. One knee joint abscess.
++++ Numerous abscesses on both kidneys. Abscess in urinary tract. Knee joint abscess.

TABLE II.
Chemotherapy of Experimental *Staphylococcus aureus* Infections in Mice.

Preparation	Single dose, g/kg	Total dose, g/kg	Died before 20th day	Day on which death occurred (individual animals)	Pathology* on 20th day, all animals	Culture† from kidney 20th day, all animals
None (controls)			10/10	1,2,2,2,3,3,4,4,4,6	++++	++++
Sulfapyridine	2.0	34.0	8/10	4,4,5,5,6,8,9,10	+++ ++++	+++ ++++
Sulfanilyl sulfanilamide	2.0	34.0	4/10	1,2,8,15	0 + ++ ++ ++ ++++	§
Sulfathiazol	2.0	34.0	3/10	3,14,16	0 0 0 0 + ++ +++	0 0 0 0 + ++ +++
Sulfamethylthiazol	2.0	34.0	1/10	12‡	0 0 + + + + +++ +++ ++++	0 0 0 0 0 + + + +
Sulfaphenylthiazol	2.0	34.0	6/10	9,9,10,10,13,14	++ +++ +++ ++++	++++ +++ ++++ ++++

* See key at foot of Table I.
† Key: 0 Negative. + 4 to 6 colonies. ++ 10 to 100 colonies. +++ 100 to 200 colonies. ++++ 200 or more colonies.
‡ Mouse died of starvation; one small abscess on heart.
§ No culture tests.

Treatment with all compounds was carried out at the following time intervals: 1½, 7, 24 and 32 hours after inoculation and once each day thereafter until death occurred, or up to and including the 15th day. The preparations were administered as suspension in ¼ to ½ cc of milk (per single dose) by means of the stomach tube.

In the first experiment, all surviving mice were killed and necropsied on the 20th day. The results of this study, based on the pathological findings, are shown in Table I.

A second experiment was carried out in similar manner except that on the 20th day one kidney was removed and cultured. The results of this study, based on pathologic and bacteriologic findings, are shown in Table II.

At necropsy there was a striking contrast in the gross appearance of the tissues of mice treated with sulfathiazol and sulfamethylthiazol as compared with mice which had received sulfapyridine or minimal doses of sulfanilyl sulfanilamide. In a significant number of animals treated with these two thiazol compounds the kidneys, prostate, liver and spleen were essentially normal except for a few scars from healed abscesses. In several mice to which sulfathiazol and sulfamethylthiazol had been administered no staphylococcus infection could be demonstrated by pathological or bacteriological methods.

Conclusions. Sulfathiazol and sulfamethylthiazol prolong the life of mice infected experimentally with a highly mouse virulent strain of *Staphylococcus aureus* and prevent the development and allow healing of abscesses in kidneys and other organs in a significant number of animals.

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Effectiveness of Neoarsphenamine, Sulfanilamide, Sulfapyridine in Marrow Cultures with Staphylococci and Alpha Streptococci.

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Edward and John LeCocq[1] have reported beneficial effects of therapy with neoarsphenamine in patients with osteomyelitis and bacteriemia due to the hemolytic *Staphylococcus aureus.* Using the

[1] LeCocq, E., *West. J. Surg.*, 1936, **44**, 655; LeCocq, John, personal communication.