about 200 times as stimulant as ephedrine. 4. The depression of the dog's ureter which appears after the use of the more concentrated solutions of ephedrine hydrochloride, invariably follows a rather extended period of stimulation, a period in which tonus, rate and amplitude of contraction, either singly or collectively, may be increased.

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Cell Proliferation Response to Sulphydryl in Man.*

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Hammett[1] has shown in studies from this Institute that the radicle –SH is the essential stimulus to cell division in normal growth by cell number in certain plants and paramecia. Extension of this work to a mammal (rat) has shown that solutions containing this radicle, stimulate cell division in the healing of wounds.[2] This report embodies the work on man.

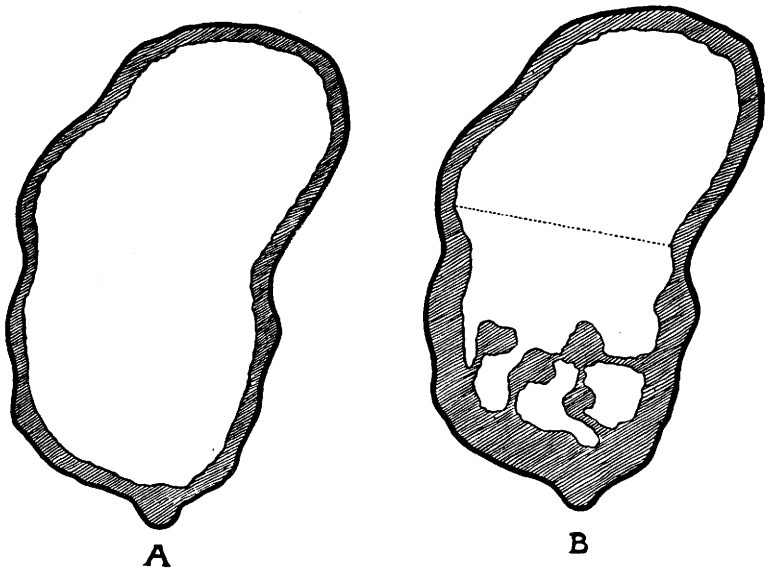
A male, 76 years old, fracture upper third of the thigh, had an ordinary varicose leg ulcer on the same leg, one half way between the knee and ankle. This ulcer was divided in half by a dam of adhesive plaster and one part treated with a solution of thio-glucose,[2] while the other half was treated by painting with 5% mercurochrome solution. The ulcer had existed for over 10 years, had never healed despite numerous and various treatments and with short periods of improvement, continued to progress. At the end of 24 hours, the ulcer was sharply divided by a growth in the sulphydryl treated part consisting not only of granulations but also of thin, translucent, ground-glass-like epithelium growing in from the edges and in islands in the ulcer. The original depth of 1/8 to 1/16 inch had filled to the surface with granulations at points devoid of epithelium to almost the point of exuberance. The other half of the ulcer showed no progress.

A woman, 74 years old, with a fracture of the hip, developed a

* Since these experiments were done, increased cell proliferation in root tips has been obtained with the same compound, *viz.*, thio-glucose.

[1] Hammett, F. S., *Protoplasma*, 1929, vii, 297; *Trans. Am. Philosoph. Soc.*, 1929, lxviii, 151.

[2] Hammett, F. S., and Reimann, S. P., *J. Exp. Med.*, 1929, l, 445.



A. Exact shape of leg ulcer obtained by tracing. Reduced approximately one-half. Shaded part is the newer epithelium blending into surrounding skin.
B. Twenty-four hours later. Lower part treated with thio-glucose solution. Shaded areas epithelium. No idea of depth is given in illustration but in the lower part the unshaded areas are healthy appearing granulations flush with or slightly above the general surface level. Exact shape, reduced approximately one-half.

typical decubitus ulcer over the sacrum. This was treated for 3 weeks by various standard methods with hardly any improvement. The edges were undermined to a depth of one-quarter inch. Application of wet dressings of thio-glucose solution stimulated healing to the extent that over one-quarter of the circumference had grown fast to the underlying granulations in 24 hours and a growth of approximately 1/16 of an inch of epithelium occurred around the rims. Because of the presence of abundant superficial pus, treatment was discontinued temporarily.

A man, 62 years old, suffered from "trophic" ulcer over the head of the fifth metatarsal, right foot. The wound looked like an old, chronic, calloused gastric ulcer about ¾ inch in diameter and ¾ inch deep. Various methods of treatment over a period of 6 weeks hardly influenced its status. Wet dressings of thio-glucose solution for 48 hours resulted in a wound ½ inch in diameter and about ¼ inch deep, growth occurring not only of granulations but also of epithelium. There was abundant surface pus.

A man, 66 years old, had 2 varicose ulcers, one on each side of the left ankle. Healing had begun on the internal one but was markedly stimulated by application of thio-glucose for 48 hours, whereupon

the surface pus again appeared in abundance and the treatment was discontinued.

The main interest at this Institute in these results, lies not so much in their obvious practical application as in the demonstration, the essential validity of the sulphydryl theory of growth by increase in cell number as proved in plants, uni-cellular animals and the rat.[1]

As far as the clinical use of this radicle is concerned in the stimulation of healing, many practical details remain to be investigated. Thio-glucose apparently stimulates bacteria as well as cells and the presence of this surface infection of itself inhibits healing.[3]

Perhaps thio-phenol or thio-cresol or some similar compounds will answer this objection. There are also investigations necessary as to the advantages of drip methods, applications on gauze, etc. In root tips, Hammett[4] has found that cells stimulated to rapid division by sulphydryl compounds are quite small in size. This is probably because the nuclei are stimulated to divide before the cytoplasm has a chance to absorb ordinary nutrition and reach its normal size. This may perhaps be "poor healing" because of the smallness of the newly divided cells.

A few preliminary experiments on other wounds have shown that it is advantageous to use sulphydryl solution for about 24 hours with intervals of 2 or 3 days between, when wet dressings of boric acid solution or other similar substances can be applied. Under such circumstances several wounds have healed in spurts, so to speak.

Summary: Thio-glucose in solutions of 1 to 10,000 applied as wet dressings, stimulates the growth of both granulation tissue and epithelium in wounds. Many details await investigation before this can be put to its most advantageous practical use. The evidence here presented is further proof of the sulphydryl theory of growth by increase in cell number.

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[3] Carrel, A., and Hartmann, A., *J. Exp. Med.*, 1916, xxiv, 429.

[4] Hammett, F. S., *Protoplasma*, 1929, in press.