

more positive results may be obtained on routine examination without resorting to concentration of sputums.

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AN OVER-COMPLEX APPARATUS

THE ingenious device described by J. H. Wales in *SCIENCE* for June 15 (79: 7059, 545) for obtaining a constant flow of liquid from a vessel by means of a siphon float appears to involve a fallacious complexity. It is inferred that by floating an inner container A, in an outer vessel of liquid, the level of the liquid in A will remain at a nearly constant point because the inner vessel with its contents rises by flotation as the liquid in it is siphoned off.

This is scarcely a true picture. As the vessel A rises from loss of contents the level in B falls, and since the level in B always remains at a given height above the level of A the two levels will sink together. Any uniformity the system may have, therefore, is strictly dependent on the level in B, which is lowered in direct proportion to the volume of liquid removed. If the same liquid is used in each vessel, and if cost, restricted quantity or other limitation on the liquid in A need not be considered, where then is the advantage of the inner vessel? Exactly the same result would be attained if the float siphon were placed directly in B and A discarded altogether.

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SPECIAL ARTICLES

ON A SELECTIVE GAMETOGENIC EFFECT OF CERTAIN HYPOPHYSEAL EXTRACTS

It has been well established that the structure and function of the testis, both as regards its production of germ cells and of its internal secretion, rapidly degenerate after removal of the anterior hypophysis and that both functions are restored by the administration of implants or extracts of anterior hypophyseal substance. It is of special interest that, depending on their method of preparation, extracts of hypophyseal substance can be made which have relatively much more influence on the germinal than on the internally secreting mechanism of the testis.

The hypophyseal extracts here reported were those employed in another series of experiments for their synergic properties when added in vitro to pregnancy-prolan. By their use it was possible to markedly increase the limited effects of prolactin on normal immature females and to bring about the development of the ovary and ovulation in hypophysectomized females. These preparations were forty per cent. alcoholic extracts of desiccated anterior pituitary tissue, or trypsin-crepsin digests of such extracts. They maintained the germinal epithelium of the testis of hypophysectomized rats and, moreover, caused its repair after the profound regression encountered forty days after hypophysectomy, without effect on the internally secreting mechanism as mirrored by infantile seminal vesicles. Indeed, our results, which are to be published in detail elsewhere, show that the testis may increase threefold in weight though the seminal vesicles remain completely atrophic. In contrast to these results, the predominating effect of other gonadotropic preparations, whether from hypophysis, pregnant mares' serum, pregnant human

serum, urine or placenta, is on the internally secreting component of the testis—usually considered to be the Leydig tissue.

Entirely independently of these studies, Smith, Engle and Tyndale have recently shown that the substance in menopause urine, like the hypophyseal extracts here reported, differs from the substance in pregnancy urine in its stimulating effect on the germinal rather than on the interstitial testicular tissue, and by the combination of the substance in menopause with that in pregnancy urine Smith and Engle have also secured synergic effects in hypophysectomized females.

The possibility of preparing hypophyseal extracts which effect selectively the seminiferous epithelium, as does the substance in menopause urine, furnishes presumptive evidence of an underlying chemical similarity if not identity of the two substances and of a true hypophyseal origin of the menopause hormone.

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A NEW TYPE OF FEVER AGENT

THE increasing use of artificial fever in various diseased conditions is arousing interest in the production of fever by chemical means. In some cases, such as general paresis and some chronic infections, pyretic drugs owe their possible value to the temperature increase; in other conditions, such as obesity and perhaps psychic apathy, improvement may be ascribed to metabolic stimulation.

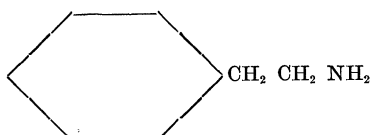
Fever results from metabolic increase under two

conditions only: (1) if the latter is extreme; (2) if the heat-loss mechanism is impaired. Pharmacologists recognize groups of drugs producing fever in either of these two ways.

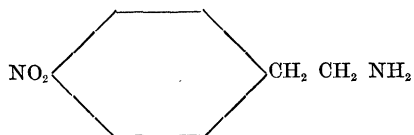
In the first place, the dinitro derivatives of phenol, cresol and naphthol seem to rely almost entirely on excess heat production for the creation of fever; the heat-dissipating measures attempted by the body are no match for the metabolic orgy induced.

On the other hand, sympathetic stimulants (adrenaline, ephedrine and, preeminent in this connection, beta-tetrahydronaphthylamine), while producing fever partly by calorogenic action, act chiefly by their propensities for saving heat. For instance, the blood flow through the body surface is greatly slowed and, as Gilman and I¹ have shown, the vapor pressure of the body decreases, permitting less escape of heat by evaporation of water from the body surfaces.

With the idea of developing a new field of synthetic fever-producing substances which might combine some virtues of each of the two above groups, I sought as a starting point a very simple nitro-aromatic sympathetic stimulant. Phenyl-ethylamine



represents the simplest type of sympathetic agent (Barger and Dale).² Eighteen years ago, I³ showed that this substance will produce a slight fever in dogs. Professor Arthur J. Hill, of the Department of Chemistry, has now kindly made for me a few grams of *p.* nitro-phenylethylamine,



a substance apparently never hitherto tested pharmacologically. This substance was at once found capable of raising the body temperature of guinea-pigs and rabbits by several degrees Fahrenheit within some fifteen to thirty minutes; two rabbits have exhibited as high a temperature as 107° F. with a dose of 120 mgm/K (Fig. 1). The therapeutic range is not wide, for in the guinea-pig, 70 mgm/K is ineffective, while the lethal dose is certainly less than 200 mgm/K.

¹ H. G. Barbour and A. Gilman, *Jour. Pharm. and Exp. Therap.*, 50: 277, 1934.

² G. Barger and H. H. Dale, *Jour. Physiol.*, 41: 19, 1910.

³ H. G. Barbour, *Jour. Pharm. and Exp. Therap.*, 8: 126, 1916.

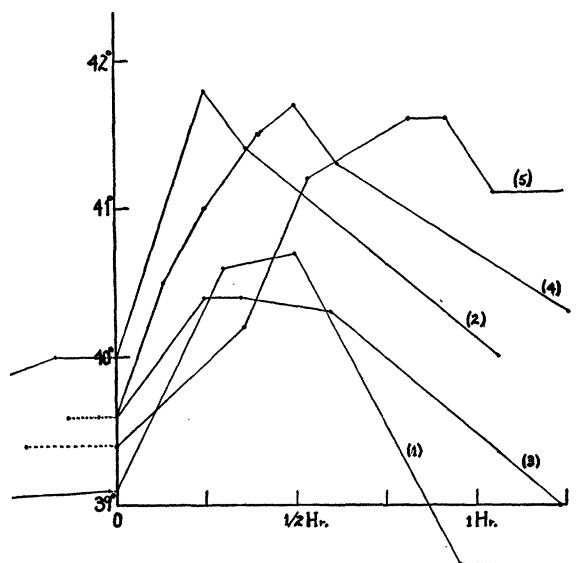


FIG. 1. Fever produced by *p.* nitro-phenylethylamine. Curves 1 and 2, guinea-pigs each given 90 mgm/K subcutaneously. Curve 3, 640 gram rabbit given 100 mgm/K. Curves 4 and 5, rabbits, 3 kilos each, each given 120 mgm/K. Ordinates: body temperature in degrees Centigrade; abscissae: time in hours. All injections at zero hour.

Animals given from 90 to 120 mgm/K subcutaneously begin within a very few minutes to show such symptoms as exophthalmos, dilation of the pupils, constriction of the ear vessels and general muscle tremors followed, especially in guinea-pigs, by visible shaking chills. Erection of the fur coat and increases in heart rate and in respiratory rate and depth also occur. The return of body temperature to normal is apparently associated with *complete recovery*.

A high degree of blood concentration is shown by the following determinations made by Dr. Ethel Buraack:

Serum specific gravity in a guinea-pig increased from 1.0219 to 1.0251 (14.6 per cent.); in a rabbit, from 1.0243 to 1.0252 (3.7 per cent.). Serum osmotic pressure in a guinea-pig increased from 0.826 to 0.977 (18.3 per cent.); in a rabbit, from 0.860 to 1.041 (21. per cent.).

The whole blood specific gravity of a rabbit (No. 5 in the chart) decreased from 1.0490 in six minutes to 1.0474, but in twenty minutes had risen to 1.0505, and in forty minutes to 1.0528, indicating an increase of 7.8 per cent. All these blood concentration phenomena tend to interfere with the loss of bodily heat. The fever curves of two guinea-pigs and three rabbits are presented in Fig. 1.

Professor Hill and I are outlining a program by which new chemicals are to be synthesized and pharmacologically tested in the promising field of fever-

producing agents typified by *p.* nitro-phenylethylamine.

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A SUGGESTED RELATIONSHIP BETWEEN THE PROTOPLASTIC BRIDGES AND VIRUS DISEASES IN PLANTS¹

THE virus of onion yellow dwarf has been transferred from diseased to healthy onions by the bites of more than 75 species of aphids. Very little, if any, difference has been noted between the feeding habits of the different species and their capacities to transmit the virus. The systemic nature and rapid spread of the virus of yellow dwarf in the growing onion has been demonstrated by means of several species of aphids. After the inoculation by the bites of infective aphids the spread of the virus through the tissues is very rapid and apparently in all directions. In following the course of the stylets of the aphid's beak it was occasionally observed, in the case of intercellular penetration, such as is exemplified by *Myzus persicae* Sulz. and *Aphis rumicis* Linn., that the content of a cell adjacent to the path of the stylets apparently had been partially extracted without the cell walls having been punctured.

In connection with the study of the tracts of the stylets, both intercellularly and intracellularly, through the tissues and the spread and effect of the virus, attention was also given to the protoplasmic bridges or plasmodesms between adjacent cells, with the thought in mind that these structures may function in the spread of the virus from cell to cell and also afford a means by which intercellular feeders are able to make contact with the protoplasm without piercing the cell wall.

In the onion and in all the other plants examined for plasmodesms, including more than a dozen of our common plants that have virus diseases, protoplasmic bridges were found to be prevalent in all the living tissues of the leaves and stems—the study of plasmodesms having been so far confined to these parts. In the onion they were found in the leaves, in the meristematic tissues of the bulb and in the flowering stalk. They were variable in size, ranging from only a very few to 60 or more microns in diameter. They connected the cells usually in all directions. In case of cells with thin walls, as in the meristematic tissues and in the tissues of leaves, the plasmodesms were undivided. They were single strands, whereas in case of cells with thick walls, as in the flowering stalk of the onion, the plasmodesms were usually divided into a number of delicate strands in the region of the

middle lamella of the cell wall. In all instances, however, the plasmodesms were visible under the ordinary high-power combinations of the microscope and therefore were ample in size to permit viruses and many other disease-producing agents to pass from cell to cell.

Each wall of a living cell was traversed by a number of plasmodesms. The number and distribution of the plasmodesms radiating in the different directions from a cell varied much according to the shape of the cell. In case of elongated rectangular cells the plasmodesms through the end walls were usually numerous, uniform in size and distribution and small and crowded, whereas those through the lateral walls were relatively few per unit area. The ones traversing the lateral walls varied somewhat in size, ranging from a few to many microns in diameter, and were irregularly distributed. Between irregularly shaped cells, where there is no distinction as to end and lateral walls, the plasmodesms through the different walls were similar in type and distribution. In character and distribution they were similar to those in the lateral walls of the elongated rectangular cells, except that they were more closely spaced. Even through those walls where there was the greatest sparsity of plasmodesms the stylets coursing, intercellularly, the region of the middle lamella could not penetrate very far without contacting plasmodesms unless they abruptly veered from their course. In case the plasmodesms are only incidentally encountered by the aphids during the feeding process these bridges are sufficiently numerous through any of the cell walls to be accessible and serve as a means by which the insect could inoculate the content of cells without having to pierce or rupture the cell walls. It is, therefore, quite plausible that these protoplasmic bridges have an important bearing relative to the intercellular movements, not only of solutions and other substances of various kinds which have to do with the normal functions of the plant, but also of viruses and other disease-producing agents as suggested by Samuel.

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¹Journal Paper No. J 162 of the Iowa Agricultural Experiment Station, Ames, Iowa. Project No. 135.