

FIG. 1

Abelsdorff (1896). The data of Köttgen and Abelsdorff are for the monkey, the dog, the cat and the rabbit, all of which are in agreement. They are also in approximate agreement with rough measurements for a human eye made by Koenig, and it is reasonable to assume that the substance is identical in all mammals. The curves in Fig. 1 are essentially those plotted by Hecht and Williams except that I have included two values for absorption of visual purple at 420 mμ and 440 mμ, which Hecht and Williams discard. When these two points are included the shift toward the red is less evident. While there is a considerable variation in the values for these points it seems that they may be safely included in the data.

In Fig. 2, the absorption spectrum measurements

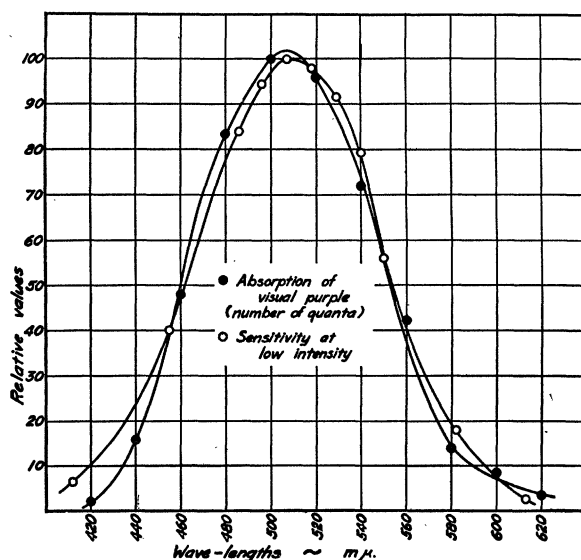


FIG. 2

are converted into relative number of quanta by multiplying by the wave-length and then by a comparison factor to bring the maximum value at 500 mμ into agreement with maximum sensitivity of the eye, at 507 mμ. The two sets of data are now in rather good agreement, but a separate curve has been drawn through each. The maximum of the absorption curve as drawn is at the same wave-length as the maximum of sensitivity, but about 2 per cent. above. Consequently, the points have all been lowered 2 per cent. in Fig. 3. In the latter figure are also included the

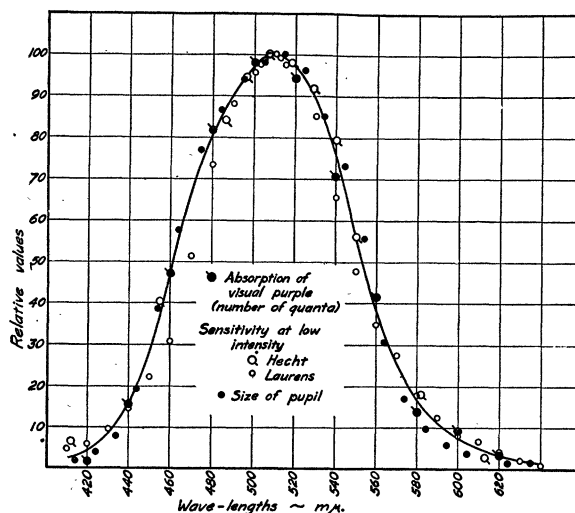


FIG. 3

data of Laursen<sup>5</sup> (1923) for pupil size as related to wave-length for the dark-adapted eye at low intensity, and also his measurements<sup>6</sup> (1924) of the spectral sensitivity of the human eye under similar conditions. The former, which constitute a purely objective measurement of the spectral response of the retina, agree very well with the recalculated absorption spectrum data, while the latter deviate somewhat from all the rest. With the exception of Laursen's spectral sensitivity measurements which were obtained for only two subjects, the data are in very close agreement. The alleged displacement toward the red has completely disappeared, and there is no further need for Kundt's rule.

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### ON THE SPIROCHETICIDAL ACTION OF THE ARSPHENAMINES ON SPIROCHETA PALLIDA IN VITRO<sup>1</sup>

SOON after the discovery of arsphenamine, it was reported that the substance had no direct spirocheti-

<sup>5</sup> H. Laursen, *Am. Jour. Physiol.*, 64: 97, 1923.

<sup>6</sup> H. Laursen, *Am. Jour. Physiol.*, 67: 348, 1924.

<sup>1</sup> From the Syphilis Division of the Department of Medicine, Johns Hopkins University Medical School, Baltimore, and the U. S. Public Health Service, Washington.

cidal action on *S. pallida* *in vitro*. This observation has been generally accepted, and the mechanism whereby the drug exerts its therapeutic action in syphilis has been a problem of long standing. It is usually assumed that its therapeutic effect rests on its conversion *in vivo* to some other actively spirocheticidal substance.

Contrary to this general impression, we have found that arsphenamine, neoarsphenamine, silver arsphenamine and "arsenoxide" (metaminoparhydroxyphenylarsenoxide) effect a complete immobilization *in vitro* of virulent *S. pallida* (Nichols strain) obtained from rabbit testicular chancres. Moreover, these immobilized organisms are non-infectious for rabbits, as shown both by testicular inoculation and by subsequent lymph node transfer, and are presumably dead.

The rate at which this antispirechetical action proceeds, and the minimal effective concentration of the arsenical, depend on numerous variables. Thus, there is a large positive temperature coefficient in the range 23° to 37° C. Serum, tissue particles and, in particular, a tissue mash, all *inhibit* the antispirechetical effect, perhaps because they combine with the arsphenamines. The degree of aerobiasis seems to have but little effect.

Under appropriate experimental conditions, arsphenamine and neoarsphenamine have a definite spirocheticidal effect *in vitro* within eight hours in at least 1:250,000 dilution; and "arsenoxide" immobilizes the organisms in dilutions of at least one million. It is of interest that these concentrations are of the same order of magnitude as those attained *in vivo* after the therapeutic administration of these drugs.

Experiments are now in progress to ascertain to what extent oxidation products of the arsphenamines, formed under the conditions of the experiment, contribute to their antispirechetical action. It is further obvious that *in vitro* results have no necessary implication with respect to the therapeutic action of the arsphenamines *in vivo*. Nevertheless, the current concept that the arsphenamines are converted only *in vivo* to a directly spirocheticidal agent is based on their supposed inactivity when added to the organisms *in vitro*. Since that initial premise is apparently in error, it becomes advisable to reinvestigate the possibility, first, that the therapeutic action of the arsphenamines may rest in part on a spirocheticidal effect similar to that observed *in vitro*, and second, that this spirocheticidal action may be an intrinsic property of the arsphenamines *per se*, rather than of degradation products liberated *in vitro* or *in vivo*. Although the arsphenamines are undoubtedly converted to other substances *in vivo* in the course of their elimination, such conversion may perhaps not be an essential preliminary to their therapeutic action.

Several other implications of possible practical importance may be pointed out. As will be described in a following paper, the immobilizing activity of a given arsenical can be assayed by a simple *in vitro* experiment. It becomes of interest to ascertain the degree of correlation between antispirechetical activity as determined by this *in vitro* test, and therapeutic activity as determined in infected rabbits. Finally, the *in vitro* technique should facilitate the study of the chemical nature of the reaction between arsphenamines and spirochetes, and the development of new therapeutic agents with more favorable therapeutic:toxic ratios. Work along these several lines of investigation is now in progress.

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### A RELATION BETWEEN THE AVERAGE MASS OF THE FIXED STARS AND THE COSMIC CONSTANTS

THE physics of the universe is essentially characterized by the three following relations which are fulfilled as to the order of magnitude:<sup>1</sup>

- (1)  $N = (R/a)^2$
- (2)  $T = 1/u$
- (3)  $R/a = e^2/(f m_p m)$

$R$  and  $T$  being the radius and the age of the universe,  $N$  the total number of protons and neutrons,  $u$  Hubble's constant (500 km/sec. per mega-parsec. =  $1.6 \times 10^{-17}$  sec.<sup>-1</sup>),  $f$  Newton's gravitational constant,  $e$  the fundamental charge,  $m_p$  and  $m$  the masses of the proton and the electron, respectively, and  $a$  the classical radius of the electron ( $e^2/(mc^2)$ ).

A further relation might be added to the above three connecting  $M$ , the average mass of a fixed star, with the cosmical constants. It has the simple form

$$(4) f M^2 = N e^2.$$

If we assume that equations (3) and (4) are fulfilled not only as to the order of magnitude, but exactly,<sup>2</sup> we arrive at a remarkable result. Dividing equation (4) by equation (1) written in the form

$$R^2 = N a^2,$$

we find

$$(5) (f M^2)/R^2 = e^2/a^2.$$

According to this formula the gravitational force which two fixed stars of average mass exert upon each other, at a distance equal to the radius of the universe, is as large as the electrostatic force acting between two fundamental charges at a distance equal to the classical radius of the electron.

<sup>1</sup> Cf. P. Jordan, *Naturwiss.*, 25: 513, 1937; A. Haas, *Naturwiss.*, 25: 733, 1937.

<sup>2</sup> Cf. *Physical Review*, 53: 207, 1938, Abstract of the Chicago meeting of the American Physical Society, No. 25.