

Potsdam numerical calculations) if additional stars, mostly those giving negative residuals, were rejected. Such an arbitrary exclusion of observations, however, is against the rules of the theory of errors, and it deprives the result of any value.

(10) In the publication of the 15-foot camera observations, secured by the Lick expedition of 1922, attention was drawn⁵ to a run in the residuals of the check star field (photographed on the nights before and after the eclipse). Since the origin and reality of these small residuals are quite doubtful, the observers based their final result (1''72) on the observed (uncorrected) star displacements D_1 . Freundlich, von Klüber, and von Brunn, on the other hand, give preference to the figure 2''05 obtained from the star displacements D_2 which are "corrected" for these uncertain residuals of the check field. It is true that this choice is a matter of personal judgment, but whatever the choice, the same procedure should be employed for both pairs of instruments used by the Lick expedition. The adoption of the Potsdam view-point would require that the observations secured with the Lick pair of 5-foot cameras⁶ be similarly "corrected" for the check-field residuals, and this would lead to a slightly smaller value (1''71). The mean of the results given by the two pairs of instruments would then be 1''9, which still agrees with Einstein's prediction within the limits of permissible observational error.

SUMMARY

The scale determination for the 28-foot camera, on which the published result of the Potsdam expedition is based, is unsatisfactory and should be rejected. A new reduction of the Potsdam measures, in which the scale correction is determined from the star observations, yields a result of $E = 1''.775 \pm 0''.13$ for the light deflection at the sun's limb, and considerably reduces the residuals of the observations. The objections of the Potsdam observers against the reduction of the 1922 observations are not valid, and there is no reason to change the results published by the Lick observers. The various measures of light deflection at the sun's edge thus far available are listed in the following table; their weighted mean is $1''.79 \pm ''06$.

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NORMAL TISSUES AS A POSSIBLE SOURCE OF INHIBITOR FOR TUMORS¹

THE presence of an inhibitor associated with the causative agent of a chicken tumor has been reported

⁵ *L. O. Bull.*, 11, 54, 1923.

⁶ *L. O. Bull.*, 13, 130, 1928.

¹ From the Laboratories of the Rockefeller Institute for Medical Research.

in recent communications. While the tumor agent is more or less species specific the inhibitor from the sarcoma has been found to affect definitely a transplanted sarcoma of mice. The results of these observations and others on the properties of the causative agent led to the suggestion that the mechanism involved in the induction and growth of the chicken tumor may be an unbalanced but similar mechanism to that which controls growth and differentiation of normal tissues. This conception led to attempts to separate the hypothetical stimulating and retarding factors from active normal tissues. We have discussed elsewhere the limited evidence indicating the possibility of inducing malignant transformation by means of the growth-augmenting factor. The present paper is a report of experiments which suggest that an inhibiting factor may be extracted from certain normal tissues.

The inhibitor or balancing factor might be expected to occur where there is a greater concentration of the stimulator. Therefore we have used active tissues as the source of our test materials. Preliminary experiments with extracts of whole fresh embryos and placenta of the mouse, treated in the same way as the chicken tumor extract, *i.e.*, heated to 55° C. for 30 minutes, had little influence on either transplantable carcinoma or sarcoma of the mouse. Profiting by the experiments with chickens, where the tumor desiccate yielded more definite amounts of the inhibitor, we changed the method to the following:

Method: The test tissues consisted principally of placenta, whole embryo, embryo skin and skinless embryo of the mouse. The tissues were macerated, spread in thin layers in a sterile dish, frozen and dried *in vacuo*. These desiccates were ground to a fine powder, extracted with a small amount of water, centrifuged and the supernatant fluid tested on tumors. The carcinoma used for inoculation was cut up into the usual size grafts and part of these immersed in the suspension made from the dried tissues and part in normal salt solution for controls. Usually two or three nicks were made in the grafts to give a greater area of exposure to the fluids. The time of contact allowed was only that required to load the grafts into trocars for inoculation. With the Crocker sarcoma 180 a suspension of the cells was made by forcing the tumor through a fine grill and 1 cc of the cells suspended in 3 cc of salt solution. This suspension was added to an equal amount of the tissue extract and 0.05 cc injected immediately into mice. For the controls the suspensions were diluted in the same proportion with Ringer's solution. The treated tumor was inoculated into one groin and the control into the other. Additional mice were inoculated with

the control material alone. In some experiments the suspensions prepared from dry tissues were heated at 52° for 30 minutes, but as this treatment had little effect on the results they will not be presented separately. The outcome of eight experiments in which desiccated skin from mouse embryos was the test material are given in Table I.

TABLE I

Material inoculated	Number inoculated	Number negative	Per cent. negative
Carcinoma No. 63 plus extract embryo skin	128	74	57.8
Carcinoma No. 63 plus Ringer's solution	164	29	17.7
Sarcoma No. 180 plus extract embryo skin	40	1	2.5
Sarcoma No. 180 plus Ringer's solution	59	0	0

The second material tested for possible inhibiting action was desiccated mouse placenta. The results with the two tumors are shown in Table II.

TABLE II

Material inoculated	Number inoculated	Number negative	Per cent. negative
Carcinoma No. 63 plus extract of placenta	158	98	62
Carcinoma No. 63 plus Ringer's solution	234	49	20.9
Sarcoma No. 180 plus extract of placenta	86	0	0
Sarcoma No. 180 plus Ringer's solution	129	1	0.7

The inhibiting action of the extracts was shown not only by the low percentage of takes resulting from inoculation of the carcinoma grafts treated with the extracts, but also by the fact that the tumors that did arise from these inoculations were on the average much smaller than the controls. It is evident that neither of these extracts tested had any retarding action on Mouse Sarcoma 180. Extracts of fresh tissues tested included whole embryo, embryo skin, skinless embryo and placenta; those of desiccated tissues, whole embryo and skinless embryo. None of these extracts, heated or unheated, had any significant effect on either of the tumors tested, nor on another sarcoma of the mouse (S/37). A few preliminary experiments on the local injection of these extracts about an established tumor have shown no evidence of retarding growth.

The principal value of the general observation is the possible light thrown on the nature of the mechanism involved in malignancy. The relation of this factor from normal tissues to the inhibitor from the

chicken sarcoma will be discussed in a subsequent paper when more definite information is available.

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ERNEST STURM

META-AMINO PARA-HYDROXY PHENYL ARSINE OXIDE AS AN ANTI- SYPHILITIC AGENT

THIS trivalent arsenical preparation, meta-amino para-hydroxy phenyl arsine oxide, studied by Ehrlich and Bertheim, later by Voegtlin and others, has generally been thought to be the most important effective breakdown product of the arsphenamines. It is relatively toxic and on this account its use has been heretofore limited to purely experimental fields. Our own theoretical interests led us to study this substance first as a trypanocide, then later in experimental syphilis. We soon found that in experimental trypanosomiasis, the therapeutic index was relatively very high compared to most other effective agents. In rabbit syphilis, we found the therapeutic index to be higher than for any other single antisyphilitic agent known to us. So far as we are aware, it had never received a trial in the treatment of human syphilis.

We have felt for some time that absolute toxicity alone is without special significance, but that the ratio of curative dose to the toxic dose furnishes real evidence of promise. On the basis of abundant data obtained in our laboratories, we readily enlisted the interest of Drs. W. F. Lorenz and W. J. Bleckwenn, of our Department of Neuropsychiatry, and Drs. O. H. and H. R. Foerster, R. L. McIntosh, and L. R. Wieder, of our Department of Dermatology. Complete reports of clinical investigations in the use of this drug will be made in due time by our clinical colleagues. Suffice it to say at this time that sixty patients have received, collectively, a total of seven hundred intravenous injections of this drug in quantities varying from 5 up to 130 milligrams per dose. The usual dosage ranges from 30 to 60 milligrams for the single dose.

Clinically, the results have been exceedingly promising, both in therapeutic effects and freedom from toxic manifestations. We fully realize the necessity, however, of a very careful and prolonged study before a full report can be made on questions of thoroughness of disinfection, optimal dosage, freedom from possible serious toxic manifestations, and practical utility in the treatment of syphilis in its several stages, when used alone and in conjunction with mercury or bismuth.

We have been designating this drug as "158," or more or less tentatively by the name *Mapharsen* from (m)eta-(a)mino-(p)ara-(h)ydroxy (ars)ine oxide. This drug was first prepared for us by Professor C. S. Hamilton, of the University of Nebraska, and later by the Research Department of Parke, Davis & Com-