or brass, are hinged together along one edge and the hinge made light-tight by a backing of black paper. The free edges opposite the hinge are attached respectively to the inside jaws of the two slits. As the slits are caused to recede from or to approach each other these plates open and close like a book. When used as in the stellar interferometer the back of the book is directed away from the telescope objective and is out of the way of all other parts.

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SPECIAL ARTICLES

FURTHER OBSERVATIONS ON AN INHIBITOR PRINCIPLE ASSOCIATED WITH THE CAUSATIVE AGENT OF A CHICKEN TUMOR[1]

IN recent communications[2] attention has been called to certain evidence indicating the presence of an extractable principle in a chicken tumor, which tends to inhibit the activity of the causative agent in the transmission of this tumor. The present report deals with some additional properties of this inhibiting agent.

The most satisfactory source of this material has been found to be the desiccate of a relatively slow-growing Chicken Tumor I. A solution is prepared by extracting the desiccate with water, filtering through paper and then heating at 55° for 30 minutes to destroy the tumor-producing factor in the extract. This material, mixed with equal volumes of various concentrated, highly active fresh tumor extracts, shows a marked inhibiting action. The results of 69 test inoculations showed complete neutralization of the activity, with no tumor formation, in 59 cases (86 per cent.). The remaining 10 cases gave evidence of considerable inhibiting activity, in that the resultant tumors were, without exception, much smaller than the controls. The 30 control inoculations of the fresh extract in every instance resulted in actively growing tumors. It was further observed that heating of the extract to 65° or over damaged or destroyed the inhibiting action.

An extract of Chicken Tumor 10, a slow-growing fibrosarcoma, heated to 52° C, has been found to inhibit the development of Chicken Tumor I, a rapidly growing tumor. The results of 31 tests gave complete neutralization in 8 cases (26 per cent.), and the average size of the tumors in the remaining animals was definitely smaller than in the controls. The latter group showed 100 per cent. of actively growing tumors.

The outcome of the above experiments suggested that the inhibitors might not be so specific in their activity as the etiological agents. On the basis of this possibility, tests have been made on the action of the inhibitor on transplantable mouse sarcomas. One of the standard tumors, designated as 180, a sarcoma which gives a high percentage of takes and rarely if ever retrogresses when once established, was selected for the first test. Of 94 inoculations of tumor cell suspension, mixed with equal volumes of chicken tumor extract previously heated to 55° C, no tumors developed in 83 cases (88 per cent.). In the control group of 70 inoculations of the same tumor cell suspensions diluted with Ringer's solution, there were 15 cases (21 per cent.) which developed no tumors. Further controls with extracts of chicken liver and brain, with normal rabbit and chicken serum, and with the chicken tumor extract heated to over 65° C gave no significant variation in the number of takes or in the growth rate of the tumor from those shown by the other controls. The few tumors which occurred in the first group, resulting from the inoculation of tumor cells and inhibitor, were smaller than in the controls and tended to become stationary after the first week, or to grow very slowly.

Similar tests have been made on another mouse sarcoma, S/37, which is more rapidly growing than 180, generally killing the animal in from two to three weeks. An insufficient number of animals has been used to justify a final conclusion, but the general indications are that the chicken tumor extract reduces the number of takes and slows the development of the tumor in a significant percentage of inoculated animals. Additional tests are in progress with this tumor and on a mouse carcinoma and on a rabbit epithelioma. With the latter two neoplasms the preliminary experiments show little indication of any retarding action by the "inhibitor."

It is considered that the action of the inhibitor on the chicken tumor agent is probably a neutralizing phenomenon. With the mouse tumor the possibility exists that the result may be due to an incidental enzyme in the chicken tumor extract, which damages the tumor cells. The fact that the treated mouse tumor cells appear to multiply for a few days after

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

[2] Jas. B. Murphy, O. Helmer, A. Claude and E. Sturm, SCIENCE, 73, 266, 1931; Jas. B. Murphy, *Trans. Assoc. Amer. Physicians*, May, 1931 (in press); M. J. Sittenfield, A. S. Johnson and J. W. Jobling, *Proc. Soc. Exp. Biol. and Med.*, 28, 517, 1931.

inoculation and the absence of any signs of damage to the host tissues at the site of inoculation are, however, some indications that this is not the correct explanation.

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ERNEST STURM

HUMAN SERUM, AGE AND MULTIPLICATION OF HOMOLOGOUS FIBROBLASTS[1]

THE experiments of du Noüy[2] have shown that the rate of cicatrization of a sterile wound is a function not only of the area of the wound but also of the age of the patient. Simply stated, the area of the wounds being the same, the rate of repair is faster in young individuals than in old. Later work by Carrel and Ebeling,[3] and by Baker and Carrel,[4] has demonstrated that these findings may be explained on the basis of progressive physico-chemical changes which take place in the blood plasma during the lifetime of the individual. These authors have shown that the inhibiting action of homogenic and heterogenic serum on the growth of pure cultures of chicken fibroblasts is directly proportional to the age of the animal from which the serum is taken. This process of aging, which advances more rapidly during early life, is due, in part at any rate, not only to the loss of growth-activating substances, but also to an increase in concentration of inhibiting proteins and lipoids, particularly the latter. The curve representing the increase of these substances resembles the curve of the index of cicatrization, of du Noüy's formula, as a function of the age of the individual. After extraction of the lipoids, the remaining proteins are found to be far less inhibiting than the whole serum. Also, when the serum of an old fowl is diluted so that its protein concentration corresponds practically to that of a young fowl, its growth-inhibiting power, although markedly decreased, is still higher than that of the serum from the younger animal. Carrel[5] has also shown that the toxic substances which characterize old age are being continuously secreted by the tissues. Their progressive accumulation in the blood is not the result of lack of elimination from the circulation; it is rather an expression of the condition of the tissues. When the blood plasma was removed from old dogs by plasmaphaeresis, and was replaced by Tyrode solution, their serum was less inhibiting for a short time thereafter, but rapidly regained its former characteristics as the plasma was regenerated by the tissues. This recovery took place too rapidly to allow of a definite modification of the tissue cells.

The experiments here to be reported bring additional evidence of a confirmatory nature by demonstrating a striking contrast between the action of infant and adult sera on colonies of human fibroblasts cultivated *in vitro*. The fibroblasts were derived from a subcutaneous rheumatic nodule removed at biopsy from a seven year old male, and have been cultivated for three months in flasks on a medium consisting of a mixture of 20 per cent. adult human serum and 80 per cent. chick embryo tissue juice. When the experiments were made, this strain had been cultivated for almost two months and had been subdivided and transferred seven times. The cultures selected for the experiments were divided and the two halves of each were placed in separate flasks. One half of each was treated regularly with serum obtained from a 14 months old infant and the other half with serum from a 27 year old adult. In order to intensify the effect of the sera to be compared, the usual proportions were reversed so that the mixture consisted of 80 per cent. serum and 20 per cent. chick embryo juice. The results obtained from three such experiments which were made simultaneously, and with the same materials, have been averaged and presented in Fig. 1. It may readily be seen that the cultures

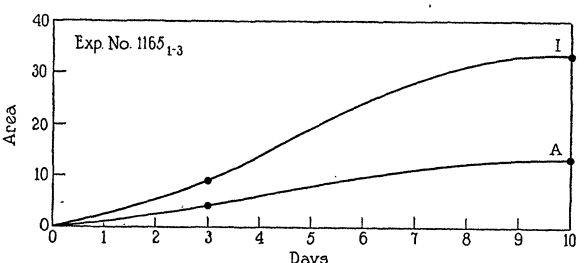

FIG. 1. Comparison of the rate of growth of human fibroblasts in the sera of a 14 months old infant and a 27 year old adult. I = infant's serum; A = adult serum.

treated with the infant's serum attained an area in ten days which was over 150 per cent. greater than that reached by those treated with adult serum.

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[1] From the Laboratories of The Rockefeller Institute for Medical Research.

[2] P. L. du Noüy, "Cicatrization of Wounds. III. The Relation between the Age of the Patient, the Area of the Wound, and the Index of Cicatrization," *J. Exper. Med.* 24: 461 (Nov.) 1916.

[3] A. Carrel and A. H. Ebeling, "Antagonistic Growth Principles of Serum and Their Relation to Old Age," *J. Exper. Med.* 38: 419 (Oct.) 1923.

[4] L. E. Baker and A. Carrel, "Effect of Age on Serum Lipoids and Proteins," *J. Exper. Med.* 45: 305 (Feb.) 1927.

[5] A. Carrel, "Diminution artificielle de la concentration des protéines du plasma pendant la vieillesse," *C. R. de la Soc. de biol.* 90: 1005 (April 12) 1924.