

ABSTRACTS OF THE COMMUNICATIONS, PACIFIC COAST BRANCH.

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Note on the reestablishment of a tendency to metastasize in a Flexner-Jobling carcinoma.By **THEO. C. BURNETT** (by invitation).*[From the Rudolph Spreckels Physiological Laboratory of the University of California.]*

Owing to a misunderstanding on the part of the attendant, our strain of Flexner-Jobling tumor, which had been carried through nine generations since our experiments with cholesterol,¹ was destroyed during the Christmas holidays (1913). In order to repair this serious loss, we asked Dr. Peyton Rous for a new supply, that we might have tumors for future work. He very cordially responded to our demands, as was to be expected, but informed us that his strain had never metastasized, and expressed doubt as to the value of the tumors on that account.

February 21, 1914, we inoculated forty-seven white rats with the new tumor, which was Rous's twenty-first generation, new series. On March 14, thirty-nine, or eighty-three per cent., had well-marked tumors. Twenty-six of these were kept as "stock" and also served as controls, while thirteen were injected four times, at intervals of two or three days, with one cubic centimeter of a 2 per cent. emulsion of cholesterol. The injection was made on the opposite side to that of the tumor inoculation. By April 11 the tumors began to break down, and we were therefore obliged to kill some of the animals. By May 15 all had been killed. A post mortem was made on each rat, and the results were as follows:

Control rats. 26 killed, 9 metastases; 38.5 per cent.
Treated rats (cholesterol)... 12 killed, 9 metastases; 75 per cent.

A portion of one of these metastases was fixed and sectioned in

¹ Robertson and Burnett, *Jour. Exp. Med.*, Vol. 17, No. 3, 1913, p. 344.

the usual way, and the diagnosis confirmed microscopically by Professor G. Y. Rusk, of the department of pathology. In addition, seven rats were inoculated with pieces of a metastatic tumor from the mediastinum, and in fourteen days all had developed well-marked tumors.

Two facts seem evident. The tumor has again become a metastasizing tumor, and treatment with cholesterol has increased that tendency. The results from the treatment with cholesterol were to be expected from our former experiments. Why the tumor should spontaneously become more virulent (if we look upon the formation of metastases as an index of virulence) is not so clear. Haarland¹ has shown that mice transferred from Berlin to Christiana became refractory to Ehrlich's sarcoma, and explains it as due to change of diet from fats and proteins, to carbohydrates. This is in accord with the results of Van Alstyne and Beebe,² who find a non-carbohydrate diet of casein and lard reduces both the number of "takes" and the growth of the tumor. On the other hand, Danysz and Skszynski³ found a greater number of "takes" in animals fed on a vegetable diet, than in those fed on meat. Sweet, Corson-White and Saxon,⁴ using the Osborne-Mendel diet, which contains plenty of carbohydrate, found a retarding influence. Our rats have been fed the regular laboratory diet of rolled barley, bread, meat, and occasionally lettuce, of which they seem to be very fond. It would seem, then, rather difficult to explain this change in the tumor on the ground of a change in diet.

As to the strain of rats used, they were obtained from New York, and were all over one year of age. This fact may be significant.

There is another possibility that might be tentatively considered, namely, that in all these results of experimental diets we may be dealing with a common factor. If, as has been suggested, cholesterol is a cleavage product of some of the proteins, it may be we shall find here an explanation of some of the varying results of investigators. The diet used by Sweet, Corson-White

¹ Haarland, *Berl. klin. Woch.*, Vol. 44, 1907, p. 713.

² Van Alstyne and Beebe, *Jour. Med. Research*, Vol. 29, No. 2, 1913, p. 217.

³ Danysz and Skszynski, *Compt. Rend. de Soc. de Biol.*, Vol. 74, 1913, p. 1144.

⁴ Sweet, Corson-White and Saxon, *Jour. Biol. Chem.*, Vol. 15, No. 1, 1913, p. 181.

and Saxon is apparently a cholesterol-free diet and perhaps the same can be said for casein and lard, although the writer is by no means certain on this point. This is merely suggestive and further investigation along this line may prove it erroneous.

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Immunity tests in coccidioidal granuloma.

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In a case of coccidioidal granuloma studied no specific complement-fixing bodies or agglutinins could be found in the blood serum using cultures of *Coccidioides immitis* and emulsions of the same organism from human lesions as antigens. No specific skin reaction could be demonstrated. Precipitins, however, could be demonstrated in the serum even when diluted 1-160, when an extract of dried cultures of the organisms was used as precipitinogen. The precipitins were apparently specific since they could not be demonstrated when normal serum was tested with the same antigen or when the specific immune serum was tested with an antigen similarly prepared from the closely related organism *Blastomyces*.

The presence of specific precipitins in this infection must be verified by the examination of other cases. It is suggested that this reaction might be applied as a means of diagnosis in cases of deep seated infection where there are no discharging lesions from which the spherical doubly-contoured bodies can be demonstrated. It might also serve as a means of differentiating coccidioidal granuloma from blastomycosis in obscure cases.

Experiments are now being carried out to determine whether specific immune substances are formed in infected animals.