

followed by aqueous extraction of the precipitate. The extract, made up to a volume of 5.0 ml., was injected into a rabbit in daily doses of 1.0 ml. The Congo Red index was again taken as measure of the activity of the reticulo-endothelial system<sup>4</sup>. This index was determined before, and 24 or 48 hours after, the first injection; further determinations were made one day and about ten days after the last injection.

The resulting curves of the activity of the reticulo-endothelial system varied greatly (see accompanying graph). All healthy subjects yielded extracts that rapidly increased the rate at which the dye disappeared from the blood. This rise in the Congo Red index was followed, on cessation of the injections, by a return to the initial level. Normal human blood thus contains a positive restropic factor.

The blood of patients exhibiting various clinical conditions (other than malignant disease) yielded either positive or inactive extracts. Entirely different results were obtained with extracts of blood from cases of malignant disease. Such extracts rapidly lowered the index. This negative restropic effect is usually noticeable 24 hours after the first injection, but may take several days for its full development. Exceptions were noticed in two cases, one showing a tumour of the parotis, the other diagnosed as carcinoma of the ear; these extracts were inactive. No case of malignant disease so far examined has yielded positive extracts; no case of non-malignant disease so far examined has yielded negative extracts.

It would thus appear that human blood contains substances affecting the active mesenchyme in the manner previously described for pituitary extracts. The concentration and the nature of the restropic substances seem to be related to the condition of the subject. The positive restropic activity of the blood of healthy subjects may be absent in some clinical conditions, as yet undefined; in malignant disease it tends to be reversed. There is as yet no evidence to show whether the absence of positive restropic, and the presence of negative restropic, factors in cases of malignant disease have a causative or merely a symptomatic significance.

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<sup>1</sup> Wetzler-Ligeti, C., and Wiesner, B. P., *NATURE*, **140**, 892 (1937).

<sup>2</sup> Wetzler-Ligeti, C., and Wiesner, B. P., *Chem. and Ind., Proc. Biochem. Soc.*, **57**, 85 (Jan. 22, 1938).

<sup>3</sup> Wetzler-Ligeti, C., and Wiesner, B. P., *Endocrinology*, **22**, 693 (1938).

<sup>4</sup> Stern, K., and Wilhelm, R., *Z. Exper. Med.*, **97**, 354 (1935).

### Cytochrome Oxidase

IN a recent paper on the indophenol oxidase, now known as the cytochrome oxidase, Keilin and Hartree<sup>1</sup> repeat the statement which they made in an earlier paper<sup>2</sup> that "According to Harrison<sup>3</sup>, it is hardly necessary even to postulate the existence of an enzyme such as indophenol oxidase. The oxidation of *p*-phenylenediamine in muscle preparation he explains as a secondary or coupled oxidation by

means of a peroxidase or a hæmatin compound acting in conjunction with H<sub>2</sub>O<sub>2</sub> formed in a primary oxidation of substances such as glutathione or hypoxanthine". They then proceed to give arguments against this secondary oxidation theory, but the facts they quote merely show that the indophenol reaction of tissues is not *solely* due to secondary oxidation.

I was well aware of these considerations, but showed in a number of ways that the indophenol oxidase theory alone does not explain all the experimental facts relating to the indophenol reaction; for example, the production of a positive reaction on adding hypoxanthine to liver suspension, even in presence of cyanide, which is known to inhibit the activity of the indophenol oxidase. What I actually said in concluding my paper was: "I feel that the explanation of the indophenol reaction and its significance in cell oxidations is best accounted for by assuming a combined action of an indophenol oxidase, as suggested by Keilin, and the secondary oxidation mechanism suggested in this paper. These together afford a satisfactory explanation of the observed facts."

So far from not believing in the existence of an indophenol or cytochrome oxidase, I carried out experiments shortly afterwards to show the interaction of a dehydrogenase system (glucose dehydrogenase) with the cytochrome-oxidase system as postulated by Keilin. These experiments gave a positive result<sup>4</sup> and have recently been confirmed in this laboratory.

The amount of secondary oxidation by hydrogen peroxide occurring in the intact tissues is at present unknown, but there is no reason to believe that it is negligible; indeed Keilin and Hartree<sup>2</sup> have themselves recently extended the number of systems which are known to be capable of bringing about secondary oxidations.

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<sup>1</sup> Keilin, D., and Hartree, E. F., *Proc. Roy. Soc.*, B, **125**, 171 (1938).

<sup>2</sup> Keilin, D., and Hartree, E. F., *Proc. Roy. Soc.*, B, **119**, 114 (1936).

<sup>3</sup> Harrison, D. C., *Biochem. J.*, **23**, 982 (1929).

<sup>4</sup> Harrison, D. C., *Biochem. J.*, **25**, 1016 (1931).

### Dismissals of Scientists in Austria

BRITISH and other scientists will be interested to know the position of some of their colleagues in Austria since the recent annexation of that country. It is difficult to get reliable information, as the dismissals, arrests and other measures of repression are not officially published, and the state of affairs in the Austrian universities and technical schools changes from day to day. Nevertheless, it is possible to give a preliminary and incomplete account of what has been happening in the field of the natural sciences. It should be borne in mind that the state of affairs in other fields is likely to be worse, since the natural sciences do not touch on political questions, while philosophy, history, sociology, etc., do.

The following is a list of professors of the natural sciences who have been dismissed (lecturers and assistant professors are not included):

Prof. Emil Abel, physico-chemist, Technical High School of Vienna.