that in addition to this mechanism also other mechanisms may play a rôle in this process of immunity. The following facts seem to us to favor such a conclusion. (1) The curve representing the rise and fall in the mitotic proliferation in the guinea pig thyroid glands shows a maximum in the first few days of the injections and then declines at a time when neutralizing substances can not yet have developed (see footnote 3-a). (2) The curves representing the first stage of increasing stimulation and the following stage of decline are in principle similar in the case of the anterior pituitary hormone and of iodine preparations acting as stimulants. It appears improbable that the acquired resistance to the effects of iodine is due to the development of iodine-neutralizing substances, able to act in vitro. Moreover, in the rat the maximum stimulation is reached as early as five days following the beginning of the injections and then a rapid decline sets in, at a time therefore too early for the development of neutralizing substances (see footnote 2-c). (3) There is known already a mechanism counteracting the thyroid stimulating effect of anterior pituitary hormone and initiated through the injection of anterior pituitary extract which is not dependent on the action of substances neutralizing the hormone in vitro. It consists in an increase in the production of thyroid hormone. The latter tends to lower the level of reactivity of the thyroid gland to all stimuli so far tested, such as the removal of a great portion of the thyroid gland,<sup>9</sup> administration of KI<sup>10</sup> and injection of anterior pituitary extract.<sup>11</sup> (4) There is reason for assuming that the neutralizing substances develop in response to the injection of a protein from which the thyroid stimulating hormone of cattle anterior pituitary could not be separated so far; this protein is foreign to rat or guinea pig. We may tentatively assume that a less complex chemical group attached to this protein functions as the hormone proper. An excess of the animal's own thyroid stimulating hormone would therefore not lead to the production of a hormone-neutralizing substance, although it may activate other antagonistic mechanisms, such as the one mentioned under No. 3. (5) In the case of mouse tumors it has been possible to show that the relative immunity, which develops against the action of substances inhibiting tumor growth, such as colloidal metals and hirudin, depends upon a combination of two processes, one residing in the organism and a second one developing in the affected tumor cells themselves.<sup>12</sup> It is probable that

<sup>9</sup> Leo Loeb, Jour. Med. Res., 41: 481, 1920.

10 S. H. Gray and I. Rabinovitch, Am. Jour. Path., 5: 485, 1929.

11 Leo Loeb, R. B. Bassett and Hilda Friedman, Proc. Soc. Exp. Biol. and Med., 28: 209, 1930. <sup>12</sup> M. S. Fleisher, Miguel Vera and Leo Loeb, Jour.

we have to deal with a similar combination of mechanisms also in the case of the thyroid-stimulating hormone of the anterior pituitary. We may assume that the change which takes place in the stimulated acinus cells of the thyroid gland alters their response to the subsequent application of the same kind of stimuli. The intensity of reaction must necessarily decrease in the course of continued application of stimuli; otherwise the results of stimulation would accumulate in geometric progression.

Retrogressive changes during long-continued injections of anterior pituitary extracts are not limited to the thyroid gland; the changes produced in the ovary of the guinea pig also disappear and at about the same time as those in the thyroid. In this connection it may be stated that in experiments with Hilda Friedman, we have found it impossible so far to separate the stimulating effect of the anterior pituitary on the thyroid from the effects of this substance on the ovary of the guinea pig. The latter consist in atresia of the follicles, in the formation of interstitial gland and of pseudocorpora lutea of theca interna origin (see footnote 3-b). The term "thyrotropic" hormone does not therefore seem suitable for a substance which invariably also exerts "gonadotropic" functions. The term "thyroid stimulating" characterizes this hormone sufficiently without implying that it is specifically "thyrotropic."

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## RETENTION OF CARBON DIOXIDE GAS IN THE INTERCELLULAR ATMOSPHERE OF PEARS AND APPLES

THE use of carbon dioxide other than as a refrigerant offers many possibilities in the field of horticultural science. The recent work of Brooks et al.<sup>1</sup> has indicated its value in preventing fungal infection and in the retardation of the respiratory processes during transportation of perishable fruit and vegetables. Kidd and West<sup>2</sup> have shown that in the gas storage of apples under certain controlled conditions carbon dioxide markedly increased the storage life of the fruit. Results obtained by Harley and Fisher<sup>3</sup>

Agr., 1932. <sup>2</sup> F. Kidd and C. West, "Gas Storage of Fruit. III. <sup>4</sup> F. Kidd and C. West, "Jour Pomol. and Hort. Sci., 11: 149, 1933.

<sup>3</sup>C. P. Harley and D. F. Fisher, "A Study of the Internal Atmospheres of Apples in Relation to Soft Scald," Proc. Amer. Soc. Hort. Sci., 271, 1930.

Exp. Med., 20: 522, 1914; M. S. Fleisher and Leo Loeb, Jour. Exp. Med., 21: 155, 1915. <sup>1</sup> C. Brooks, E. V. Miller, C. O. Bratley, J. S. Cooley,

P. V. Mook and H. B. Johnson, "Effect of Solid and Gaseous Carbon Dioxide upon Transit Diseases of Cer-tain Fruits and Vegetables," *Tech. Bul.* 318, U. S. Dept.

and by Brooks and Harley<sup>4</sup> have indicated that control of soft scald might be obtained by subjection of the fruit to an atmosphere of carbon dioxide prior to storage at low temperature.

Some work was undertaken during the current season in comparing the effectiveness of carbon dioxide treatment with that of precooling in the retardation of the ripening processes of fruit prior to storage at  $32^{\circ}$  F. A question arose as to the concentration of the gas in the intercellular atmospheres immediately following treatment and also as to the retentive capacity of various tissues for this gas. This short communication is a partial answer to some of these questions.

## EXPERIMENTAL

Packed boxes of Bosc pears and Jonathan apples were placed in a suitable container immediately following harvest and treated with 35 per cent. carbon dioxide for 24 hours at 65° F. A representative number of untreated fruits were immediately sampled,



FIG. 1. Carbon dioxide concentrations of the intercellular atmospheres at definite periods following removal of the fruit from treatment with 35 per cent.  $CO_2$  for 24 hours at 65° F. Wenatchee, Wash. 1933.

<sup>4</sup> C. Brooks and C. P. Harley, "Studies on Soft Scald and Soggy Breakdown of Apples." Submitted for publication in *Jour. Agr. Research.* 1934. and an analysis made of the gases in the intercellular spaces of the tissues. The gases were withdrawn from the tissues by a modification of the apparatus described by Magness<sup>5</sup> and analyzed in a Bonnier-Mangin gas analysis apparatus.

This sampling procedure was repeated on the gastreated fruit immediately following and at stated intervals after the fruit had been removed to the ordinary atmosphere. Data and results are summarized in Fig. 1.

It is interesting to note that carbon dioxide is absorbed to a much greater extent in Bosc pear than in Jonathan apple tissues. In an atmosphere of 35 per cent. of this gas, apples had an intercellular carbon dioxide concentration of nearly 50 per cent. and pears 80 per cent. at the end of the gas treatment. Fig. 1 offers a graphic picture of the speed with which this excess carbon dioxide gas is removed from the intercellular spaces. Approximately 70 per cent. of the accumulated carbon dioxide in the tissues has been lost within eight hours after removal from the gas treatment. The carbon dioxide concentration of the intercellular atmospheres of both the pear and apple show a normal value within 14 hours after removal from gas treatment.

The fact that fruits of this kind have such a short retentive capacity for carbon dioxide must be considered in problems of precooling as well as in those involving respiratory changes. The supposition is suggested that fruit responses to non-lethal carbon dioxide gas treatments are confined largely to the actual period while under such treatment. Respiration and ripening data at hand bear out this suggestion.

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<sup>5</sup> J. R. Magness, "Composition of Gases in the Intercellular Spaces of Apples and Potatoes," Bot. Gaz., 70: 308, 1920.