sphere and in the stratosphere, respectively, prior to a nuclear explosion ($t = 0-$), and $A^*_{T,0}$ and $A^*_{S,0}$ were added to the troposphere and to the stratosphere, respectively, by a nuclear explosion which took place at $t = 0$, and that the total quantities of A in the troposphere and in the stratosphere have increased from $A_{T,0-}$ to $A_{T,0}$ and from $A_{S,0-}$ to $A_{S,0}$. Then we have the following relationships:

$$A_{T,0-} + A^*_{T,0} = A_{T,0} \quad (3)$$

$$A_{S,0-} + A^*_{S,0} = A_{S,0} \quad (4)$$

$$\left(\frac{B}{A}\right)_{T,0} = \frac{A_{T,0-} \times (B/A)_{T,0-} + A^*_{T,0} \times (y_B/y_A)}{A_{T,0-} + A^*_{T,0}} \quad (5)$$

and

$$\left(\frac{B}{A}\right)_{S,0} = \frac{A_{S,0-} \times (B/A)_{S,0-} + A^*_{S,0} \times (y_B/y_A)}{A_{S,0-} + A^*_{S,0}} \quad (6)$$

where y_B/y_A is the ratio of the fission products B and A freshly produced by the nuclear explosion. If $A^*_{T,0} \gg A_{T,0-}$ and $A^*_{S,0} \gg A_{S,0-}$, Eqs. 5 and 6 give $(B/A)_{T,0} \cong y_B/y_A$ and $(B/A)_{S,0} \cong y_B/y_A$. By introducing these values into Eq. 2, one obtains

$$(B/A)_{T,t} = (y_B/y_A) \times e^{-(\lambda_B - \lambda_A)t} \quad (7)$$

which corresponds to the empirical relationship shown in Eq. 1.

This indicates that a very large increase of Sr^{89} (and hence Ba^{140}) in the stratosphere must have resulted from the October 1958 hydrogen-bomb test series.

It is worthy of note that the Sr^{89} concentrations in rain and snow have remained fairly constant during the past few months, despite the fact that this nuclide decays with a half-life of 54 days. A marked increase in the rate of transfer of the fission products from the stratosphere to the troposphere in early spring months, which has recently been observed by Stewart *et al.* (*3*) and also by Kuroda (*2*), seems to compensate for the expected activity decrease due to Sr^{89} decay (*4, 5*).

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4. More detailed accounts of this work are in preparation.
5. This investigation was made possible by support from the U.S. Atomic Energy Commission. We are grateful to J. M. Bailey for collecting the rain samples.

6 April 1959

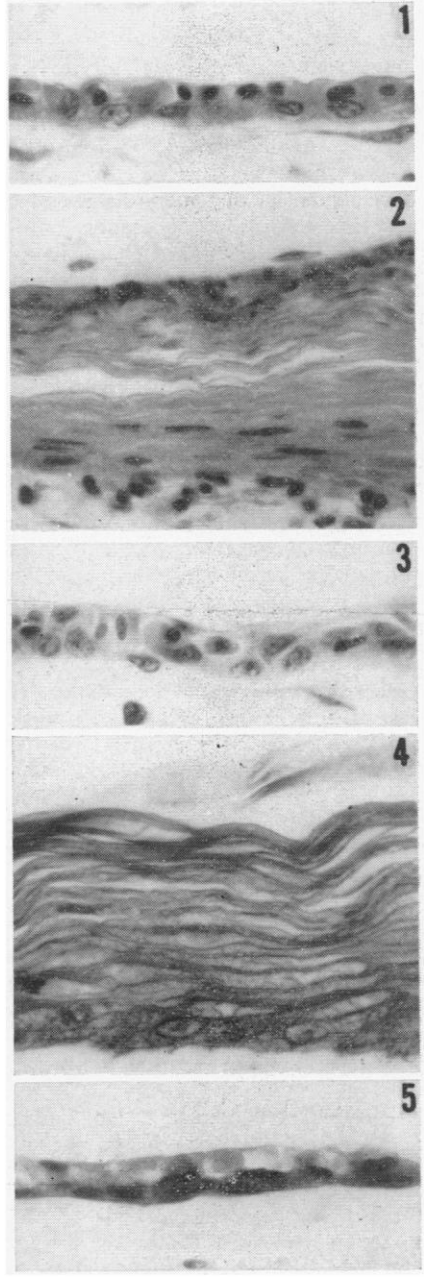
Etiology of Keratogenic Metaplasia in the Chorioallantoic Membrane

Abstract. The effects of elevated O_2 and CO_2 concentrations on the occurrence of experimental keratogenic metaplasia in the chorion of the chick embryo were examined. Exposure to oxygen resulted in advanced keratinization of the chorion; carbon dioxide at elevated concentrations, in mixtures with air or oxygen, repressed the appearance of metaplastic changes, and the chorion retained its respiratory characteristics. The evidence reported here suggests that reduction of the CO_2 content in the gaseous environment of the chorion is causally contributory to the onset of the metaplastic events.

As reported previously (*1*), explants of the chorioallantoic membrane from 8-day chick embryos grown for 8 to 10 days in vitro as organ cultures underwent striking metaplastic changes resulting in transformation of the one-cell-thick chorion into a stratified and keratinized epithelium. It was recently found (*2*) that a similar metaplasia could be consistently produced also *in ovo* by fenestrating embryonated eggs on the 8th day of development and incubating them with the shell-window open. In such eggs there was rapid vertical proliferation of chorionic cells in the exposed area and an alteration in their protein-synthesizing activities resulting in the transformation of the attenuated chorion into a multilayered, highly cornified structure (Figs. 1, 2). The onset of metaplastic changes depended, thus, on the following major conditions: (i) detachment of the chorion from the shell membrane; (ii) exposure of the detached chorion to atmospheric air—that is, to lower carbon dioxide and higher oxygen concentrations than those in the normal environment of this respiratory epithelium. The second of these conditions is discussed in this report.

To account for the effect of exposure to outside air two possibilities were considered: (i) release from inhibition by CO_2, due to a decrease in its relative concentration in the chorionic environment (in this case, similarly fenestrated eggs, when exposed to elevated levels of CO_2, should not show metaplastic changes); (ii) activation by O_2 at the relatively elevated level at which it occurs in outside air (if this is the cause, exposure of chorion to pure O_2 should result in metaplasia, and the advent of metaplasia should not be repressible by admixture of CO_2).

The possibility that CO_2 has an inhibitory effect was tested by incubating eggs, fenestrated on the 8th day of development (a ½-square-inch window was left open), for 10 days in saturation-humidity chambers constantly gassed with a mixture of air and 5- or 8-percent CO_2 (*3*). Similarly prepared eggs, gassed with air, served as controls. Neither the general development nor the viability of the embryos was noticeably affected. Histological examination of the chorionic epithelium failed to reveal metaplastic changes in any of the 28 eggs



Figs. 1–5. Sections through the chorion of the chorioallantoic membrane of 18-day chick embryos fenestrated on the 8th day of development and incubated in saturation-humidity chambers. In Fig. 1 the shell-window was sealed immediately following fenestration and the embryo was incubated in air. In the other figures the shell-window was left open and the egg was incubated (Fig. 2) in air; (Fig. 3) in air plus 8-percent CO_2; (Fig. 4) in O_2; (Fig. 5) in O_2 plus 8-percent CO_2. The sections were stained with hematoxylin and Biebrich scarlet (× 700).

maintained in these elevated-CO_2-air mixtures. The chorion retained its characteristic structure as a respiratory epithelium (Fig. 3). In contrast, all seven controls showed keratinization in the exposed area of chorion (Fig. 2). Evidently, in the presence of elevated concentrations of CO_2, the appearance of keratogenic changes in the appropriately prepared chorionic epithelium was completely prevented.

The effect of pure oxygen (*3*) was examined in fenestrated eggs prepared as described above and incubated till the 18th day in saturation-humidity chambers constantly gassed with oxygen. Neither the viability nor the general development of the embryos was noticeably affected. In all 35 eggs examined in this series, the exposed chorionic epithelium was found to have undergone a characteristic metaplasia into keratinforming, multilayered epithelium (Fig. 4). In comparison with controls gassed with air, metaplasia in oxygen-gassed eggs appeared somewhat earlier in development and progressed to a more advanced stage. It was concluded that exposure to O_2 created conditions favorable for the initiation and rapid progression of keratogenic metaplasia. Whether O_2 acted as an inducing agent in setting into motion the particular metabolic and morphogenetic systems resulting in keratogenesis is, at present, an open question.

Next, the response of the chorion to O_2 in the presence of CO_2 was examined in fenestrated eggs prepared as described above and constantly gassed with a mixture of 92-percent O_2 and 8-percent CO_2. It was assumed that absence of keratinization under these conditions would support the possibility that elevated levels of CO_2 have an inhibitory effect on this process. Of the ten eggs examined, none showed keratinization of the chorion, and the epithelium retained its attenuated, respiratory structure (Fig. 5). Thus, the presence of one part of CO_2 together with 11.5 parts of O_2 appeared to interfere with or inhibit the appearance of metaplastic changes.

These findings suggest that the presence of CO_2 at concentrations higher than atmospheric concentration restricts the ability of the chorion to undergo keratogenic changes. The removal of CO_2 inhibition appears, therefore, to play an important—though not exclusive—role in the etiology of keratogenic metaplasia. There are various indications that CO_2 at increased partial pressure may be a differentiation-controlling factor (*4*). It is thus not unlikely that, in normal development, CO_2 promotes the respiratory differentiation of the chorion, contributing thereby to its exclusion from other metabolic and developmental courses. Removing this gaseous control mechanism creates conditions favorable for a response of this tissue to other stimuli and for the display of new developmental potentialities. Under such circumstances, O_2 appears to stimulate the emergence of metabolic patterns resulting in keratogenic metaplasia. Other agents may, perhaps, provoke different developmental responses (*5*).

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Meetings

American College of Cardiology

The American College of Cardiology, a recent affiliate of the American Association for the Advancement of Science, was organized in 1949 to fulfill the need for a wholly professional body to promote and advance clinical cardiology and angiology and to study the treatment of cardiovascular disease. The objectives of the college are, first, to provide a meeting place for the exchange of information between people doing research in this and related fields and the clinical practitioner, second, to publish a journal in clinical cardiology. The college also set up and encouraged a workshop program under which masters in particular fields of cardiological investigation invite to their laboratories or wards groups of fellows of the college for a short, intensive period of work in the special techniques available. This workshop program has been enlarged until it reaches from coast to coast, and special groups are available at practically any time of the year.

The convention of the college takes place in the spring in some center of relatively high population and includes technical and scientific exhibits. The program usually covers a variety of subjects and lasts 4 or 5 days; each segment of the program ordinarily consists of a panel discussion by men working in a particular field. There is always an attempt to have on each panel a worker in basic science, several men from the area of clinical research, and others engaged in the clinical practice of cardiology who have a particular interest or reputation in that field.

There is an interim meeting each fall; this is ordinarily held in conjunction with the faculty of a university or teaching hospital in a more lightly populated area. At the interim meetings an attempt is made to study exhaustively one or two subjects in the field of cardiology or angiology.

A special feature of each of the meetings of the college is an evening session called a "fireside conference." Tables, eight or ten in number, are set up in a large ballroom, separated from each other by a distance of 10 or 15 feet. On each there is a placard giving the subject of discussion at that table—for instance, congenital heart disease, cardiac catheterization, use of enzymes in diagnosis, diet in heart disease, treatment of angina pectoris, phonocardiography, surgical treatment of acquired heart disease, pregnancy and heart disease, and so on. At each table sit a discussion leader and the visitors who are interested in that particular subject. The discussion is completely informal, and questions and answers are fired back and forth. One can leave the group at any time and wander over to another, and there is constant circulation between the tables. Fireside conferences are ordinarily planned to last 2 hours, from 8 to 10 o'clock in the evening, but in the experience of the college, they go on until well after midnight. When the room is closed at midnight, the discussions continue in the lobby and the coffee