1.04; *total,* 100.20 percent. The analysis, minus the insoluble residue and recalculated to 100 percent, compares favorably with the idealized formula $NaFe_3^{III}(PO^4)_2(OH)_4 \cdot 2H_2O$.

Wardite was recently shown to have the formula $NaAl_3(PO_4)_2(OH)_4 \cdot 2H_2O$ [Hurlbut, *Am. Mineralogist* 37, 849 (1952)]. Avelinoite, isostructural with wardite, is another example of substitution of trivalent iron for aluminum in a known mineral structure.

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A New and Physicochemically Well-Defined Group of Tumor-Promoting (Cocarcinogenic) Agents for Mouse Skin

In the course of our studies on the mechanism of experimental skin carcinogenesis [carried out since 1945; some of our previous papers are quoted in (*1*)], we have employed, as an aid, chemically and physicochemically well-defined nonpolar-polar substances as vehicles for the carcinogenic hydrocarbons. Some of these were naturally occurring, biologically active compounds; others were synthetic lipophilic-hydrophilic products, such as detergents and high polymers, especially carbowaxes (*2*). These substances were chosen by us partly because they have their principal counterparts in the living matter, and partly because these lipophilic-hydrophilic substances form a large group of well-defined compounds which, in regard to their physicochemical nature, can be arranged in systematic series. In addition, the interaction between certain nonpolar-polar compounds and biologically important proteins has been extensively investigated ***in vitro*** and partly also ***in vivo*** and constitutes now a fairly well-known field (*3*).

During our studies it appeared that some of these nonpolar-polar compounds—when used as carriers for the carcinogen—on the one hand delayed the development of tumors, whereas others greatly enhanced it and, on the other hand, caused different types of morphologic skin alterations. Therefore, and because the most powerful cocarcinogen now known, croton oil, contains many similar nonpolar-polar compounds, we decided to investigate whether some of our substances would have true cocarcinogenic properties.

The tumor-promoting property of an un-ionic detergent Span 20 (sorbitan monolaurate) was first studied by using Berenblum's technique (*4*). Two-month old male white mice of the same known ("anonymous") strain employed in all our previous studies were used. The animals were divided into three subgroups, 50 mice in each. The skins of the animals in group 1 received a single painting of 0.3 percent 9,10-dimethyl-1,2-benzanthracene dissolved in paraffin oil, but no additional treatment at all. Up to now—that is, 24 wk after the application—no tumors have developed, and all mice are alive. The mice in group 2 were painted twice daily during these 24 wk with pure Span 20; no tumors have developed in this group either. The animals in group 3 received a single painting of 0.3 percent 9,10-dimethyl-1,2-benzanthracene in paraffin oil, and then the same area of the skin of the back was painted twice daily with Span 20. In this group local cutaneous tumors began to appear at the end of the fifth week, and after 24 wk of treatment, 21 of the 50 mice have together 34 tumors. All mice were kept under similar conditions. Precautions were taken to avoid sources of methodical errors.

Large series of this kind of well-defined lipophilic-hydrophilic substances, having cocarcinogenic properties, are now being tested by us. The results available today point in the same positive direction, and a number of the compounds are highly potent cocarcinogens, even stronger than croton oil. Thus, another un-ionic detergent, Tween 60 (polyoxyetheylene sorbitan monostearate), for instance, showed significantly stronger tumor-promoting property than Span 20. When Tween 60 was used as a cocarcinogen in the aforementioned way, more than 70 percent of the animals developed skin tumors in 16 wk. The substances containing longer carbon chains appear to be stronger cocarcinogens. Further, the morphologic alterations seen in the skin of mice painted *only* with the nonpolar-polar compounds vary according to the compound used. In addition, the changes astonishingly closely resemble the alterations that are described as the "early response of the mouse skin to carcinogens." By changing the character of the lipophilic-hydrophilic solution, it was possible to induce alterations of different intensity in both the epidermis and the dermis (*5*).

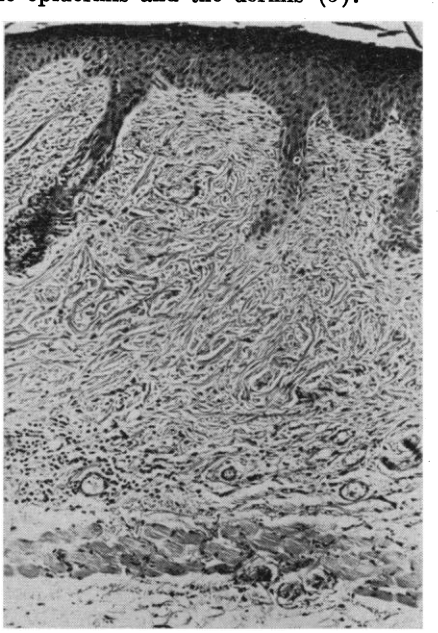

Fig. 1. Skin (right side of the back) of Mouse No. 54 after 2 wk of twice daily painting with Span 20 only. Thickening and distinct alterations in epidermis. Significant changes in dermis, collagenosis, dilated capillaries, and so forth. H + E. (×85)

The cocarcinogenic power of the individual substance, on the one hand, and the nature as well as the intensity of the morphologic changes that it induced in the skin, on the other hand, seem to be dependent, for example, on the position of the compound in the hydrophile-lipophile balance value series (*6*) when certain un-ionic synthetic detergents were used. The mechanism of the physicochemical and morphologic alterations in the cutaneous structures is now being studied, considering especially the property of nonpolar-polar substances to alter (and degenerate) various proteins as well as the binding of water, which seems to be one of the features of the induced change. In this connection we want to draw attention to the influence (*3*) of nonpolar-polar compounds on proteins, for example, denaturation with resulting liberation of biologically—and possibly also for the tumorigenesis—important —SH— and other groups, changes in solubility, alterations in molecular weight and shape, changes in antigenity and susceptibility to enzymatic digestion as well as changes in x-ray diffraction patterns and infrared absorption spectra. Interesting also is the appearance of fiber formation in various cutaneous structures as a result of treatment with nonpolar-polar compounds (the same phenomenon is well-known from studies *in vitro*).

Our present experiments with these compounds have given us the impression that the histologic changes seen in connection with the "early response of the mouse skin to carcinogens" are, for the most part, only comparatively nonspecific phenomena running parallel to the still unknown process of carcinogenesis, or being merely a reflection of this occurrence. Apparently the processes in the various structures of the skin also run parallel to each other, none being the real cause of the others. By varying the character of the cocarcinogenic nonpolar-polar compound (and thereby the quality and localization of the morphologic and chemical alterations) and the concentration of the carcinogen, it may be possible to induce skin tumors under more strictly controlled conditions than hitherto. In this way we are now trying to investigate which chemical and morphologic alterations are really necessary for the production of experimental skin tumors in mice and what is necessary for the achievement of a cocarcinogenic effect as well as the interaction between the stromal and parenchymal alterations during tumorigenesis.

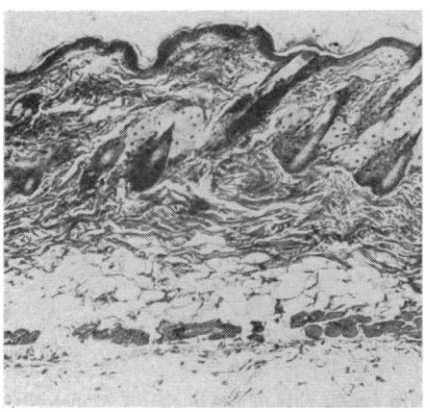

Fig. 2. Skin (left side of the back) of mouse No. 54; no treatment at all. Normal appearance. This specimen was taken at the same time that the specimen in Fig. 1 was taken. H + E. (× 85)

The results of the protein-chemical findings, as well as the details of histologic findings, will be reported elsewhere.

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Living Out "Future" Experience under Hypnosis

Rubenstein and Newman in their article, "The living out of 'future' experiences under hypnosis" [*Science* **119**, 472 (1954)] raise some issues that may require clarification. In describing a technique that deals with the projections of hypnotic subjects' experiences into a future time, they have presented a clinical modification of a time-progression and fantasy-projection technique recently reported upon by Israeli [*J. Clin. and Exptl, Hypnosis* **2**, 49 (1953)]. Although their report is of considerable interest with respect to personality study and projection in general, the authors do not make it clear that the technique they employed was one of *time* distortion rather than one of *age* alteration. Nevertheless, from their observations, they conclude that, since this type of projection appears to be essentially a fantasy, perhaps hypnotic age regression, too, is a fantasy. In view of the fact that the authors deal with time and not age as a variable within the framework of their hypnotic experiments, it appears dubious that their extension and generalization of findings to include alterations in age variables, particularly age regression, is meaningful.

It must be pointed out that there is a definitive difference between hypnotic *age* "regression" and "progression" and *time* "regression" and "progression." With alterations in time, recent experimental experience indicates that the subject tends to alter his perception of the world around him in the same manner that he does in all basic expressions of projection—that is, in a manner consistent with his inner personality organization. Clinical techniques, such as the