of inhibition, less dichromate would be needed for an inhibition in cases where the enzyme concentration is decreased from that used in these particular experiments.

The effect of dichromate on growth of two strains of *Staphylococcus aureus* was followed turbidimetrically (at 450 mμ. on the Coleman spectrophotometer) and checked by duplicate pour-plate dilution counts. In synthetic medium[2] as little as 1 μg./ml. was very toxic to growth, whereas in nutrient broth approximately 10 times as much dichromate was needed to obtain equivalent inhibition. This was undoubtedly due to binding of the heavy metal ion by constituents of the nutrient broth.

Because of the extreme difficulty in ridding glassware of dichromate after cleaning in "cleaning solution" and its great toxicity for living cells and enzymes, it is believed highly advisable in laboratories dealing with such material to clean all glassware by another method, such as 10 per cent nitric acid, a detergent, or 1–5 per cent trisodium phosphate.

[2] The medium used was that of Landy and Dicken (2) with the omission of sodium acetate, asparagine, guanine, xanthine, uracil, and folic acid.

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Letters to the Editor

The Effect of Urethane on Lymphatic Leukemia in Rats

In 1925 Hawkins and Murphy reported from this Laboratory that urethane anesthesia (ethyl carbamate) caused a rapid increase in the CO_2 content and pH of the whole blood of rabbits to a point where there was a marked uncompensated alkalosis. This reached its maximum in 24 hours and persisted for 48 hours. Accompanying this change was a marked fall in the circulating lymphocytes, similar in extent to that following a relatively large exposure to X-ray (*J. exp. Med.*, 1925, **42**, 609). Recently an investigation has been undertaken to test the effect of urethane on the development of transplanted lymphatic leukemia and lymphosarcoma in rats. Since starting this study, our attention has been called to two articles which have appeared in British journals. Haddow and Sexton, in testing urethanes on experimental animal tumors, noted that the most striking effect was upon leukemic cells (*Nature, Lond.*, 1946, **157**, 500). In the second paper, Paterson, Haddow, Thomas, and Watkinson compared the effect of urethane with deep X-ray on human leukemia (*Lancet*, 1946, 11 May, 677). They noted that the chemical agent produced a remarkably similar effect on the blood count and the enlarged lymph nodes to that resulting from the application of the standard method of deep X-ray therapy.

The material for our test was a transplanted disease of rats, which manifests itself as generalized lymphatic leukemia if the malignant cells are injected intraperitoneally or as a localized lymphosarcoma when the cells are inoculated into the subcutaneous tissue of the groin. The leukemic type of the disease develops rapidly, with marked increase in the circulating lymphocytes and extensive involvement of the thymus and lymph nodes. Death results in 8 to 12 days. The groin inoculations result in rapidly growing tumors which attain very large size and cause death of the rats in 16 to 21 days.

Among 50 inoculated rats, given from 50 to 100 mg. of urethane/100 grams of body weight, repeated 4 times a week, only 3 developed leukemia (6 per cent). Among 41 controls of the same strain, inoculated with the same material but receiving no treatment, 33 developed fatal leukemia (80.4 per cent). Among 30 rats inoculated in the groin with leukemia cells, and given the urethane treatment, only 9 (30 per cent) developed progressive tumors, while 26 of the 30 controls (86.6 per cent) died of lymphosarcoma.

We have previously demonstrated that adrenalectomy renders rats much more susceptible to our strain of leukemia (*Science*, 1943, **98**, 568). Furthermore, adrenal cortical and pituitary adenotropic hormones retard or prevent the development of the disease (*Science*, 1944, **99**, 303). In the light of these observations it may prove significant that the adrenals of rats given urethane in the dosage employed above show about 33 per cent increase in weight over those from normal, untreated animals. A similar increase in weight of the adrenals has been noted in rats which develop resistance to inoculated leukemic cells without treatment. We are attempting to evaluate the part played by the adrenals by treating inoculated, adrenalectomized rats with urethane.

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Wild Pineapples in Venezuela

Although pineapples, *Ananas ananas* (L.) Cockerell (*A. sativus* Schult. f.) were known to have originated in the American tropics and have been reported growing in the wild state in Brazil, Surinam, and Paraguay (*Pflanzenfam.* (2nd ed.), 1930, p. 154), not until recent observations by the author and V. Badillo in the Parguasa region of the Estado Bolívar, and simultaneously by others in neighboring regions, have they been definitely known to be in the wild state in Venezuela. They grow

under a variety of conditions ranging from dense shade under warm, humid forest to edges of forest. There seem to exist several varieties or forms, differing in fruit size and taste and in leaf characters. Among the latter may be mentioned complete absence of thorns in leaves, more so than in the Smooth Cayenne cultivated variety. Others have thorns retrorsely and antrorsely oriented. One such variety differs so little from its relative, *Bromelia Pinguin* L., that only the expert natives (Piaroa Indians) could distinguish them. While only one variety growing wild was found sweet and palatable enough to be desirable, Piaroa Indians have had under cultivation since time immemorial some varieties which yield large, tasty fruits. The wild varieties have abundant seed, one ovary alone having yielded 14. This is in contrast to the present commercial varieties and the sparingly established Pan de Azúcar in P. R., which are largely seedless. Samples of all of these have been brought to the Institute of Tropical Agriculture, at Mayagüez, Puerto Rico, to be used for breeding purposes if they survive there.

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A Nutritional Concept of Cancer

While the etiology of cancer has been categorized under infection by a transmissible virus on the one hand and gene mutation on the other (not to mention a host of other hypotheses), there has been relatively little speculation on the biochemical mechanisms whereby any of these events could lead to the process recognized as neoplastic growth. Recent studies by Beadle, Tatum, and others, on the genetic control of biosynthetic reactions in the fungus, *Neurospora*, have provided a foundation for new concepts of the biological regulation of growth. In particular, a study by Ryan and Lederberg (*Proc. nat. Acad. Sci., Wash.*, 1946, 32, 163–173), on the "adaptation" of a *Neurospora* mutant deficient in the synthesis of leucine, has provided an experimental basis for speculative analogy with neoplasia.

Field strains of *Neurospora* will grow on medium containing only sugar, salts, and biotin, which is to say that the fungus is capable of manufacturing all other essential metabolites. As the result of mutations of single genes, the capacity for synthesis of various compounds may be lost. A similar process presumably accounts for the nutritional requirements of higher forms.

Following ultraviolent treatment, a mutant strain of *Neurospora*, #33757, has been isolated which is incapable of synthesizing leucine. As a consequence, this strain requires leucine, and its growth is quantitatively regulated by the available supply.

Occasionally, cultures of leucineless *Neurospora* grown on limiting amounts of this amino acid will "adapt"; that is, an exceptional fragment of the mycelium will grow autonomously, irrespective of the available leucine, and may under certain conditions overgrow the culture until the sugar is exhausted. By genetic analysis of crosses between adapted and wild strains, it has been shown that adaptation depends on the mutation, or reversion, of the leucineless gene to an allele capable of mediating the synthesis of leucine.

A culture of leucineless *Neurospora* has, then, two growth potentialities: a regulated growth corresponding to the leucine externally available to it, and, exceptionally, autonomous growth on the basis of a gene mutation leading to the synthesis of that metabolite.

If one correlates normal tissue cells with a culture of leucineless *Neurospora*, both regulated by their environment, a simple analogy for cancer is evident—the newly found capacity of a cell to synthesize an essential metabolite otherwise available only in limiting and regulatory amounts.

While the *Neurospora* experiments suggest a mutational origin for this capacity, virus infection, by providing a missing link for a blocked enzyme system, could play a corresponding role. A consequence of this simple concept is that cancer cells may be found to differ in their growth factor requirements from cells of normal origin when they are grown *in vitro*.

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Education and the Foundations of Science

It is no surprise that students and leading citizens should make as poor a showing on Dr. Ralph H. Ojemann's tests of their conception and appreciation of scientific research as that exhibited in his article (*Science*, 1946, **104**, 335–338). Dr. Ojemann has evidently presumed that a pupil who has studied sciences for some years will have learned what he calls "the basic concepts involved," including, especially, one which he identifies as "study through controlled variables" (which he also calls "the most dependable type of study"). Such a presumption is unfortunately not to be justified by reference to the laboratory or to popular textbooks. Rules and procedures are learned, more or less, as are the results they produce; but the idea or philosophy of the business is either wanting altogether, or else set forth without explanation or quite arbitrarily and dogmatically.

This, however, is no wonder. Suppose an explanation of the method of "controlled variables" were undertaken; if it were of scholarly competence, it would shortly lead to Mill's celebrated Methods of Experimental Enquiry, since this particular method is but an application of one or two of these. But alas—these themselves are far from rigorous, as the explanation would also demonstrate. Supposing that it was intended to seek farther for an explanation; the concept of method *per se* and of explanation *per se* would demand attention. These are chiefly logical and epistemological matters. But logical and epistemological matters are little considered in American education. It is then a matter of course that students and others, even though long devoted to science, should be at a loss when confronted with problems which presuppose competence in those unknown directions.