

manek and Grandmougin.⁵ There was also a secondary maximum at about 465 m μ . Spectrophotometric analysis of the pink sap which was extracted from 5 cells kept under these conditions for one hour, gave the same absorption maxima as the dye itself. The method of extraction is described in another paper.¹ That the cells were not irreversibly injured is shown by the fact that they lived for months afterwards in the laboratory and appeared normal.

These results confirm unpublished data on the penetration of these dyes into sap of freshly collected plants of *Valonia macrophysa* which the writer obtained in 1925 while in residence at Bermuda.

These experiments show, therefore, that the position of the dye system on the oxidation-reduction indicator scale as described by Clark, is the factor determining whether or not a dye is reduced by the cell, but that it is not the exclusive factor which determines the penetration of these dyes into living cells.

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Actions of Sodium Bismuthate.*

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The bismuth compounds in current use contain the bismuth as cation, or in basic form, and do not dependably penetrate the brain and appear in the cerebrospinal fluid. Compounds containing the bismuth as anion, or in acid form, have not been tried previously, but, on theoretical grounds, might be expected to penetrate the central nervous system more readily than those containing bismuth as cation, and thus be more valuable in neurosyphilis. Accordingly, we have explored the possibilities of sodium bismuthate and obtained results worthy of record at this time in order to indicate the desirability of further study of anionic bismuth.

¹ Clark, W. M., "The determination of H ions." Williams and Wilkens, Baltimore, 1928.

⁵ Formanek, J., and Grandmougin, E., *Untersuchungen und Nachweis organischen Farbstoffe auf Spektroskopischen Wege.* (Berlin), Julius Springer, 1908.

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Sodium bismuthate (NaBiO_3) is the sodium salt of bismuthic acid with a bismuth content of 74.5%. It is obtainable in the market as a yellowish brown powder and possesses very low solubility in all ordinary and special solvents. The solubility in water and 0.9% sodium chloride solution is about 1:10,000, and in whole serum, 1:5,000, and sufficient liberation of bismuth occurs to give a darkening with sulphide. The reaction of the watery suspension (marketed product) is strongly alkaline. Strong mineral acids and 85% lactic acid dissolve bismuthate readily, but weak organic acids (citric and acetic) only slightly.

The toxicity of bismuthate was found to be very low. Rabbits (5) tolerated doses of from 0.6 to 1 gm. per kilo intramuscularly, and mice and rats (9), from 42 to 90 mgm. per kilo hypodermically. A fatal dose has not been found. The compound has been injected as a suspension in water or in acacia solution, without evidence of irritation. Three rabbits receiving 0.018 gm. per kilo intravenously and 0.22 and 0.6 gm. per kilo intramuscularly, excreted variable though considerable daily quantities of bismuth (about 1.4 mgm.) in urine over long periods (up to 4 months), the absorption being slow and continuous. Of 8 guinea pigs, receiving 0.1 gm. per kilo intramuscularly, 4 showed the presence of unabsorbed bismuthate in the muscles till the end of 14 days, and the remaining guinea pigs showed no depots 19, 21 and 33 days after administration. All of these guinea pigs showed presence of bismuth in the brain, amounting to a median of 0.09 mgm. Bi per 100 gm. of brain after a sojourn of the bismuthate during from 5 to 33 days in the body. Five rabbits receiving from 18.5 to 47.6 mgm. bismuthate (13.8 to 35.5 mgm. Bi) per kilo intravenously showed the presence of bismuth in the brain in from 3 to 24 days after injection. A definite antisyphilitic action of the bismuthate was demonstrated in the experimental syphilis of rabbits as follows: Prevention of chancres occurred in a pair of rabbits receiving 0.032 and 1 gm. per kilo during 3 and 6 months, respectively, while the untreated, control pair showed fully developed lesions with spirochetes at the end of 16 to 30 days. In curative experiments on developed chancres, in pairs of rabbits, 0.4 gm. per kilo of bismuthate caused clearing of lesions at the end of 72 hours and healing at the end of 21 days, whereas the untreated controls healed at the end of 41 days. As further controls, treatments with bismuth sodium tartrate and neoarsphenamine, in both prophylactic and curative experiments, gave the usual beneficial results.

Thus, anionic bismuth possesses a destructive action on the syphi-

litic virus, just as does the cationic form, with the advantages of cerebral penetration and comparatively low toxicity, but a more soluble compound than the bismuthate would be desirable.

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A Demonstration of the Curability of Malignancy in Rats by a Low Pressure Environment.

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Previous workers¹ who have carried out experiments on the effect of lowered oxygen tension on malignant neoplasms have reported a retarded growth and an extensive necrosis but no positive cures. They evidently missed the time when the factors which ultimately may annihilate the cancer reach their highest potency. Our success is attributable to (1) an adequate period of exposure, (2) a gradual adaptation to successive steps of decreasing oxygen tension, and (3) an uninterrupted maintenance of the final pressure throughout the experiment. We are not prepared to emphasize the superiority of our method, the reduction of the total pressure, as compared with the adjustment of the oxygen tension at normal atmospheric pressure. We believe, however, that it is technically more convenient and that it affords a greater margin of safety.

Our low pressure chambers are improved models of the apparatus described previously by one of us.² The pressure is controlled automatically and is disturbed neither by any manipulation in the care of the animals nor by the removal and the replacement of individual rats. A series may therefore be continued for almost an unlimited time, although the maximal exposure time in our cancer work has been 6 weeks exclusive of the one week adaptation period. Our results for the first 2 weeks have closely corresponded to those of other investigators and we shall, therefore, in this report consider mainly those series which have lasted longer.

We have employed 2 pressure levels: 300 and 360 mm., corresponding in altitude to 25,000 and 20,000 feet respectively. With

¹ Warburg, O., *et al.*, *Klin. Wochenschr.*, 1926, v, 829. Campbell, J. A., and Cramer, W., *Lancet*, 1928, ccxiv, 828.

² Sundstroem, E. S., and Bloor, W. R., *J. Biol. Chem.*, 1920, xlv, 155.