of activity. The enzymic nature of the activity is indicated by its nondialyzability, thermolability (destruction at 60°C for 2 min), and optical specificity.

Of the sugars and derivatives studied here only mutarotase substrates have been reported to be "actively" reabsorbed by kidney (A,B,D) (*3*) or transported across cell membranes in response to insulin (A,B,C,D) (*4*). The nonsubstrates are reported not to be reabsorbed (H,I,J,K) (*3*) or thus transported (E,F,G,H,J) (*4*). Furthermore, phlorizin inhibits mutarotase at concentrations found in kidney (*5*) in "phlorizinized" animals. In such animals glucose reabsorption and oxidation (*6*) are blocked. The phosphorylation theory of glucose reabsorption is considered defective in that too high concentrations of phlorizin are required to inhibit kidney phosphatases.

A unitary theory of sugar transport applicable to transport of sugars into cells in response to insulin and reabsorption of sugars by kidney follows. Mutarotase in kidney catalyzes interconversion of various forms of sugar toward the equilibrium mixture during passage of the blood filtrate down the tubules. A preferentially absorbed form (PAF) of sugar passively diffuses into blood, where it must be present in lower concentration. As the filtrate continues down the tubule more PAF is produced by action of the enzyme and reabsorption proceeds. Since blood returning to the kidney must contain lowered concentrations of PAF, the theory demands that it be the same form that penetrates into cells in other parts of the body. Since insulin controls the transport of many sugars across cell membranes (*4*), mutarotase activity may be related to this action of insulin. PAF is probably neither the alpha nor the beta form of the sugar, since these are unquestionably present in sufficiently large amounts in many experimental situations where sugar transport occurs in response to insulin prior to addition of the hormone. It is suggested that PAF is a form of low abundance similar to or identical with the polarographically demonstrable mutarotational intermediate (*7*). Mutarotase, by controlling the rate of formation of a form of low abundance that penetrates into cells or that is a substrate for other enzymes, would control an important rate-limiting step in carbohydrate metabolism. Significantly, since the mutarotational system is going toward equilibrium, it is exergonic, the tubules are not required to expend energy, and the transport process although enzymatically controlled cannot properly be referred to as an "active" one.

Spontaneous uncatalyzed mutarotation could conceivably contribute to sugar transport to some degree in proportion to its rate and might become more important in organisms where metabolism or filtration rate is extremely slow. Fructose mutarotates at a much higher rate than glucose, and this may be a factor in its more effective utilization in diabetics.

The proposed theory suggests an involvement of mutarotase in diabetes mellitus and renal and phlorizin diabetes.

Experiments are in progress that are intended to elucidate a relationship between mutarotase and insulin.

Mutarotase occurs in animals, particularly in kidney, and is strongly inhibited by phlorizin. Sugars that are "actively" absorbed by kidney or transported across membranes into cells in response to insulin are mutarotase substrates. A unitary theory relating mutarotase to insulin and to sugar transport and reabsorption is described here.

ALBERT S. KESTON
New York University College of Medicine
New York 16

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Fire and the Australopithecines

In 1948, Raymond A. Dart [*Am. J. Phys. Anthrop.* 6, 259 (1948)] announced that the so-called "manapes" of South Africa, the Pleistocene Australopithecinae, were fire-users. Dart's claim rested on the supposed evidences of fire, in the form of ashes and charred bones, found at Makapan in association with the fossil remains of a newly-discovered variety of Australopithecine, which he consequently dubbed *Australopithecus prometheus*. Whether or not the Australopithecines actually employed fire is an important question when assessing their zoological status.

Owing to an unfortunate alteration, my brief report of Kenneth P. Oakley's studies of the geologic dating of the Australopithecinae [*Science* **119**, 863 (18 June 1954)] conveyed the erroneous impression that Oakley was inclined toward the view that these animals actually made use of fire; whereas, in fact, his position was quite the contrary. The printed sentence of my report, "Nor does the evidence support claims that the Australopithecines made any sort of tools, although they may have used ready-to-hand tools and weapons *or may have been fire-users*" (italics mine) should correctly read "Nor does the evidence support claims that the Australopithecines made any sort of tools (although they may have used ready-to-hand tools and weapons) *or were fire-users*" (italics mine).

Oakley's [*Am. J. Phys. Anthrop.* **12**, 9 (1954)] full statement on this point follows:

> The doubtful evidence of fire in the *Australopithecus* layer at Makapan is still *sub judice*, and even if confirmed could most readily be accounted for by a natural grass fire outside having ignited inflammable bat-guano at the entrance to the cave—there are in fact records of comparable fires having occurred in recent times.

This agrees with his earlier statements [in *An Appraisal of Anthropology Today,* Tax *et al.,* Eds. (Univ. of Chicago Press, 1953), pp. 29–30; *Weekly Evening Meeting Roy. Inst. Gr. Brit.* (20 Nov. 1953)] that the blackening of bones found at Makapan is due to manganese dioxide and is not due to charring, as claimed by Dart; furthermore, the other supposed indications of fire associated with the remains of *A. prometheus* were so equivocal as to leave Oakley unsatisfied that there was any evidence of hearths in that geologic layer.

Thus Oakley's critical studies of the Makapan material reveal *A. prometheus* as an unfortunate misnomer. Whatever the final verdicts regarding the posture, the cerebral status, and other moot characters of the Australopithecinae, it appears reasonably certain that these animals had not captured fire.

WILLIAM L. STRAUS, JR.

Laboratory of Physical Anthropology,
The Johns Hopkins University, Baltimore, Maryland

8 August 1954.

Noncytopathogenic Variants of Poliomyelitis Viruses and Resistance to Superinfection in Tissue Culture*

In the first successful propagation of poliomyelitis virus in tissue culture in 1936, the virus multiplied in the nervous tissues but not in the visceral tissues of the same human embryos (*1*). Ever since unequivocal multiplication in nonnervous tissue was demonstrated 13 yr later (*2*), it had been an intriguing question why the 1936 experiments with nonnervous tissue had failed. Recent experiments have demonstrated that intracerebral passage in monkeys favors the segregation of variants that are devoid of cytopathogenic activity for fibroblasts growing out of monkey testicles in tissue culture but possess full cytopathogenic activity for epithelial cells derived from monkey kidney (*3, 4*). More recently I have found that from the nervous system of infected animals it is possible to segregate variants that have no cytopathogenic effect on epithelial cells derived from monkey kidney (*5*).

Since the "MV" strain of virus that was used in the 1936 cultivation experiments had had a large number of intercerebral passages in monkeys, it appeared possible that it might be a variant that lacked the property of multiplication in nonnervous tissue. A specimen of this virus that had been frozen for many years was found to have no cytopathogenic effect on epithelial cells derived from monkey kidney in any dilution tested, although intracerebral inoculation produced typical paralytic poliomyelitis in a monkey. The freshly passaged virus also produced no cytopathogenic effect on monkey kidney epithelial cells and four blind passages failed to yield a cytopathogenic agent, although in the third and fourth passages a few epithelial cells degenerated and fell off the glass within 4 days after inoculation, whereas the bulk of the growth remained unaffected for 10 to 12 days.

Last year, I observed that a strain of MEF_1 suckling mouse-adapted poliomyelitis virus derived from the viral progeny in a single suckling mouse at the end-point of an intracerebral titration exerted little or no cytopathogenic effect on monkey kidney cells, but after an incubation period of 7 to 12 days the majority of the epithelial cells that had been exposed to the virus (in dilutions up to 10^{-7} to 10^{-8}) had become resistant to the rapid cytopathogenic effect of the parent strain.

Similar tests performed with the MV virus revealed that, after an incubation period of 10 to 12 days in roller tubes, the epithelial cells derived from monkey kidney had acquired a limited resistance to the cytopathogenic effect of 100 TCD_{50} of the homotypic, Type 2 Y-SK strain. At 2 days after challenge, the epithelial cells in the control tubes, as well as in the tubes that received the higher dilutions of the MV virus, were completely destroyed. The epithelial cells in the tubes inoculated with the lower dilutions of MV virus showed little or no change at 2 days, but at 4 days almost all the cells were similarly destroyed. This limited resistance was not observed when a mixture of the "MV" and "Y-SK" viruses was added to normal epithelial cells or when the Y-SK virus was added 1 hr or 6 days after the addition of the MV virus.

It should be noted here that strict neurotropic variants that have recently been segregated in this laboratory from Type 1 and Type 3 viruses have conferred no such resistance on epithelial cells derived from monkey kidney, but it is possible that the challenge viruses may not have been added at the right time. Further work on the mechanism of the resistance produced by noncytopathogenic variants of poliomyelitis virus would be of the greatest interest particularly with respect to the possible operation of a phenomenon comparable to that of lysogenic phage.

ALBERT B. SABIN

The Children's Hospital Research Foundation,
University of Cincinnati College of Medicine
Cincinnati, Ohio

References and Notes

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