rest having been either destroyed by inadvertent oxidation or differentially partitioned between the various organic solvents employed. These traces may be readily removed by a small quantity of permutit—we use 30 grams per 5 kilos of glands—so that the final extract made from the whole glands contains less than 1: 2,000,000 parts of adrenalin when tested by the blood pressure or intestinal strip methods. Our extracts are made up to a final concentration of 40 grams of whole glands per cubic centimeter. We have prepared extracts for the past six months according to these modifications of the Swingle-Pfiffner technique, and the product is apparently as potent as any which has yet been reported.

Besides the general restorative effects on comatose adrenalectomized animals, which have previously been described, the cortico-adrenal extract produces significant changes in carbohydrate metabolism. For a period of several hours following injection of the hormone, the percentage of sugar in the blood gradually rises from the convulsive level to normal limits, or even higher. In a series of twenty cases this result has been consistently observed. Normal cats and rats also show slowly rising blood-sugar levels following administration of the extract. In man the material is apparently without effect on the blood sugar in small doses of one or two cubic centimeters; a larger dose—15 cc injected intramuscularly in a subject under basal conditions—produced a gradual rise from 90 to 115 milligrams in 4½ hours.

It should be emphasized that the above glycemic changes are not at all referable to adrenalin action. When injected in similar dilution and amount to that present in the cortical extracts—between 1: 2,000,000 and 1: 4,000,000 parts of adrenalin, in amounts up to 10 cc per kilo—adrenalin produces only a slight increase in the blood sugar, and a fall to the normal level occurs within an hour or so after the injection. The gradual augmentation of the blood-sugar level following injection of the cortico-adrenal extract, reaching a maximum six or eight hours after the injection, is in marked contrast to the effect of the medullary hormone. Also in contrast to the action of the cortico-adrenal hormone is the merely temporary effect of adrenalin in resuscitating prostrated adrenalectomized animals.

The hypoglycemic and convulsive reactions following insulin administration appear to be scarcely affected, even when large doses of the extract are given intraperitoneally or intracardially. When the material is given as a preliminary measure, an hour or so before the administration of insulin, the action of the latter also appears to be relatively unaffected. In this respect the well-known effect of adrenalin in alleviating the severe symptoms of insulin intoxication finds no parallel in the action of the new cortico-adrenal hormone.

The effect of the cortico-adrenal hormone on carbohydrate metabolism is apparently quantitative in nature. Although different lots of extract differ in potency, and the experimental animals vary in their resistance or susceptibility to the material, experiments performed at various times with a particular extract on the same animal indicate very clearly this quantitative effect. An injection of 10 cc per kilo causes approximately twice the percentage rise in blood sugar, as does one of 5 cc per kilo. In general, it may be said that the blood-sugar raising power of the hormone is a direct function of the amount of the substance injected and also of the elapsed time.

Numerous observers[3] have reported that the percentage of the non-protein nitrogen in the blood becomes remarkably elevated following removal of both adrenals. Hartman *et al.*[4] have recently observed that their cortical extract brings about a reduction in the blood urea of adrenalectomized cats. The high levels of blood non-protein nitrogen which we have observed in a large series of animals are, however, only slightly affected by large doses of the cortico-adrenal extract prepared according to the Swingle-Pfiffner method. The profound anhydremia which is observed in animals following adrenal extirpation, and the extensive circulatory changes which are brought about following injection of the cortico-adrenal extract must, however, be given careful consideration in connection with the observed changes in the carbohydrate and nitrogenous constituents of the blood.

Further blood changes and circulatory effects which we have observed to be produced by the extract, and also the influence of the hormone on body temperature, will be reported upon later.

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