tion of masculine reactions. This is not only due to a lack of female sex hormone, because removal of the ovaries and suitable replacement therapy with oestrogen and progesterone fails to evoke feminine responses.

The need for androgen at particular phases in the sexual development of the male was underlined in a different way by F. Neumann (Schering AG, Berlin), who described many experiments involving the use of a synthetic steroid, cyproterone acetate, which acts as an androgen antagonist. Exposure of foetal rats and dogs to the action of this substance, by treating the mother, prevents differentiation of the accessory sex glands and ducts of the males and can lead to the formation of a vagina. This condition provides the experimental counterpart of the clinical condition of testicular feminization. Another steroid, cyanotrimethylandrostenolone, is effective in disrupting the steroidogenic enzyme activity in the adrenal glands and, by causing overproduction of androgens, can reproduce the adrenogenital syndrome known in man.

ENZYMES

Facets of Phosphorylase

from our Molecular Biology Correspondent

DESPITE the obscurity of its physiological purpose, polynucleotide phosphorylase is an enzyme of great interest and utility for the biochemist, and it has been found to have some remarkable properties. The enzyme, as prepared from *E. coli* or *Micrococcus lysodeikticus*, is apparently a hexamer, with a molecular weight of some 200,000 or a little more. Work in Grunberg-Manago's laboratory has, however, recently unearthed a variant existing in certain strains of *E. coli* which has half this molecular weight (*Europ. J. Biochem.*, **8**, 577; 1969). The interesting feature of this mutant form is that it is entirely inactive in respect of polynucleotide synthesis (this being a role which the enzyme is in any case not thought to exercise in the cell). But the phosphorylase activity remains, though not without enzymological differences—notably requirement for a higher magnesium concentration, and inability to operate on high-molecular weight substrates. The mutant enzyme appears also to catalyse the exchange of phosphorus in the nucleoside diphosphates against pyrophosphate (although contamination with traces of another enzyme is not entirely excluded). Grunberg-Manago *et al.* refer to kinetic evidence that polynucleotide phosphorylase has two independent active sites, one concerned with polymerization, the other with attachment of nucleoside diphosphates. Moreover, the diphosphate is not a substrate or inhibitor for phosphorolysis, and they infer that the phosphorylase and polymerization sites are again separate entities. Whether the activity of the polymerization sites depends on the integrity of the quaternary structure, or whether a region common to both the polymerization and an association site is affected by the mutation, remains to be established.

From the same laboratory (Harvey *et al.*, *Europ. J. Biochem.*, **9**, 50; 1969) comes the observation of a transient state of very high viscosity during the polymerization reaction. The precise magnitude of the effect depends on a number of factors, including the enzyme concentration. The enzyme has been shown

to be free of detectable endonuclease contamination, and the sharp peak in the viscosity time curve cannot therefore be explained in these terms. There remain the possibilities that the enzyme possesses a hitherto undetected function, whereby it breaks down long chains to a limiting size, or that it forms cross-links by attaching to several segments of growing polynucleotide chains. The latter is perhaps the more likely explanation, since no polynucleotide intermediates of very high molecular weight have been observed.

A further ramification of polynucleotide phosphorylase activity concerns the circumstances in which an oligonucleotide primer is required for the polymerization reaction to proceed. In addition to the action of mild denaturants, limited proteolysis with trypsin was found by Klee and Singer to bring about conversion of phosphorylase of *M. lysodeikticus* from a primer-independent to a primer-requiring form. The basis of this transition has now been further studied by Klee (*J. Biol. Chem.*, **244**, 2558; 1969). Proteolysis was shown to involve the cleavage of only five or six peptide bonds, evidently with loss of some fragments of the chain, for the molecular weight of the modified enzyme was detectably decreased.

The most striking feature of the primer-dependent form is its ability to revert to the primer-independent condition on treatment with a thiol reagent, and the reversal of this effect by N-ethylmaleimide. Klee has now established that the trypsin-modified enzyme, unlike the native, possesses an appreciable free thiol content, amounting to 0.5 mole per mole of protein. After treatment with the thiol reagent, dithiothreitol, this increases to 1 mole per mole.

As with so many observations on polynucleotide phosphorylase, the interpretation is elusive. One cannot easily conceive of the basis for an all-or-nothing transition in enzymological behaviour accompanying a change in accessible thiol content of a half mole. It must be supposed in any event that proteolysis causes a change of conformation sufficient to alter the properties, that this is somehow reversed on reduction, and that insertion of a blocking group changes the conformation back once more.

CARCINOGENS

Herbal Medicines and Cancer

AFTER reading that Du Plessis *et al.* (*Nature*, **222**, 1198; 1968) detected the carcinogen dimethylnitrosamine in the fruit of *Solanum incanum* (used in the Transkei to curdle milk), Dr R. Schoental of the MRC Toxicology Research Unit, Carshalton, has been reminded of her own enquiries. She writes: During a short visit to East Africa in January, I made enquiries about the use of herbal medicines among patients suffering from oesophageal and naso-pharyngeal cancer, mostly in the Kenyatta National Hospital, Nairobi, the Mission Hospital, Shirati, Tanzania, and the New General Hospital, Kisumu, Kenya.

I came to suspect *Solanum incanum*. The Kenyans have several uses for the fruit. They cut it in half and apply it to the cut end of the umbilical cord of babies. Extracts are also used for bathing babies with sore buttocks. A hot leaf extract is drunk as a treatment for stomach ache. The ripe fruit, crushed in milk, is used as a treatment for worms. In Tanzania the root is