trypsin depends on the initial concentration, and is found to follow it in a manner consistent with a simple dimerization of the enzyme. Correcting for this effect, it is possible to determine the heats of binding of specific inhibitors, by using large molar excesses of the ligand, so that the binding sites are always saturated. It emerges that the heat of binding is in all cases dependent on enzyme concentration, and it can be inferred that the dimer has little or no affinity for the inhibitor. These results, which refer to pH 7.8, at which the enzyme slowly autolyses, differ in various respects from those reported by other workers, using different methods, all, however, in more acid conditions. Shiao and Sturtevant suggest that at their pH they are observing cannibalistic enzyme-substrate complexes, and the inhibitors are in competition with this interaction. The affinity of the monomeric enzyme for the inhibitors is compounded of a large negative enthalpy and a sizable negative entropy, even when the ligand is uncharged. It is likely that a change in enzyme conformation (induced fit) is responsible for a considerable part of both.

A more complex system has been studied by Ross and Ginsburg (*ibid.*, 4690). This involves the binding of feedback inhibitors, which control its activity *in vivo*, to the twelve-subunit enzyme, glutamine synthetase. Twelve molecules each of tryptophan and 5'-AMP are bound by each protein molecule, indicating that all subunits are functionally equivalent. The heats of binding of the two ligands separately were measured, and also that of both together. The contributions of the two interactions are strictly additive, and this is good evidence that the sites for tryptophan and AMP are separate entities. The binding of either ligand is accompanied by a large entropy change, but one (AMP) is positive, the other negative. This curious phenomenon may be related to the induction of conformational changes by one or other ligand.

An interesting application of microcalorimetry in the polynucleotide field has also appeared (Scruggs and Ross, *J. Mol. Biol.*, **47**, 29; 1970). This concerns the binding of monomeric adenine derivatives to poly-U, a process that always has a 2:1 stoichiometry. The principal finding is that the enthalpy is always the same, irrespective of whether the monomeric species is adenine, adenosine or deoxyadenosine. This eliminates any involvement of the 2'-hydroxyl group, or any other part of the sugar, in the stabilization of the helix, at least in this prototypic system. The binding of a derivative containing an extra amino group in the purine ring, so that three hydrogen bonds can be formed with the pyrimidine, causes the enthalpy to become 3 kcalories/mole more negative. Knowing the melting temperatures of the complexes, the entropies of association can be derived, and are large and unfavourable, as one might expect for the immobilization of monomers.

GYNAECOLOGY

Test for Spontaneous Abortion

from our Medical Biochemistry Correspondent

IF it is true that a gynaecologist's practice is made up of women desperately anxious either to have babies or to avoid them, they may all be helped by some recent biochemical investigations. Genazzani *et al.* have

shown how women whose pregnancies are likely to end in spontaneous abortion can be distinguished by measuring the concentrations of human placental lactogen in their serum (*Lancet*, ii, 1385; 1969).

Human placental lactogen, discovered in 1962, is a polypeptide hormone produced by the placenta, and similar in structure and in some of its effects to pituitary growth hormone. Radioimmunoassay carried out on seventy-four women showed that concentrations of the lactogen steadily increase between the seventh and thirty-first weeks of normal pregnancies. This probably reflects the growth in size of the placenta at this time. In two cases the increase during several weeks was very similar to the mean increase for the group.

Of thirteen women with threatened abortion, who had been admitted to hospital with pain and vaginal bleeding, five experienced an increase in human placental lactogen comparable with the increase in the normal pregnancies. These women all completed their pregnancies successfully. Five of the thirteen admitted to hospital, however, had barely detectable concentrations of human placental lactogen and rapidly aborted. The other three had relatively low concentrations when admitted to hospital, and these rapidly decreased until the women aborted.

In cases when the human urinary chorionic gonadotrophin was also measured it turned out to be a very unreliable indicator of abortion. But the test for placental lactogen, in the early weeks of pregnancy at least, seems to be a good guide to the likelihood of spontaneous abortion, pointing out those patients for whom active therapeutic measures are necessary.

FORESTRY

Trees in Trouble

by our Botany Correspondent

BUTT rot is a problem that often occupies the plant pathologists of the Forestry Commission. Their latest manoeuvres against *Fomes annosus*, the fungal cause of the trouble, are described in *Forest Research* 1969 (HMSO, £1.12½). Resistant species of forest trees are being sought to counteract the problem of butt rot, which seems to loom on most acid mineral sites in Britain. A survey of the spread of the fungus in stands of different species has confirmed that infection is less extensive in grand fir, *Abies grandis*, than in some other species. This is a hopeful sign for those who thought that this species might prove to be resistant to butt rot. The aim of the work in progress is to identify species which can be recommended for planting on heavily infested soils.

Another disease which has made surprising progress in the past year is beech bark disease, which had been thought to be of little importance except in mature trees. But there have been two serious outbreaks in young crops in Britain, in the Queen Elizabeth Forest (Hampshire and Sussex) and in Savernake Forest (Wiltshire and Berkshire). Preliminary investigations have indicated that drought is not after all an important causal factor. The cause seems to be a combination of the beech coccus insect and fungi of the genus *Nectria*.

The enquiries which the Forestry Commission pathologists dealt with in 1969 have shown them that elm disease, caused by *Ceratocystis ulmi*, is on the increase,