The Committee on Cell Cultures has recommended that serially cultivated human diploid cells should now be considered in the production of vaccines, as long as certain criteria are satisfied. The strain should be derived from normal human foetal tissue; cells should not show morphological, biochemical or chromosomal changes during propagation; they must be free from extraneous micro-organisms and must not induce tumours. The committee has also recommended that the cells used should give a high yield of the virus which is to be used for the production of vaccine. A number of field trials have already been carried out, and more than 200,000 people have received vaccines (produced from virus cultures in the human cell strain designated *WI*-38) against poliomyelitis, adenovirus 4, measles, rubella and rhinovirus. There have been no undesirable effects.

New Allosteric Hypothesis

from a Correspondent in Molecular Biology

THE Benesches give compelling evidence in favour of a hypothesis recently introduced by themselves to account for a number of hitherto mystifying features of haemoglobin chemistry in an article in *Proc. U.S. Nat. Acad. Sci.*, **56**, 1268 (1966). They also suggest that the new scheme may have a general bearing on the so called allosteric enzymes in which activation (or inhibition) is brought about by small concentrations of ligands, which may or may not be substrate molecules ("homotropic" or "heterotropic" systems). Haemoglobin represents the archetypal homotropic system, in which the binding of oxygen at one site increases the affinity at others, sterically remote from it. It is known that in haemoglobin species in which, for example, two haem groups are in the oxidized (ferric) state, the oxygen affinity of the remaining haems is increased. In effect, therefore, the oxidized haems act on their partners as though they themselves were permanently oxygenated.

The Benesches showed earlier that if a fully functional haemoglobin is mixed with a completely oxidized (ferric) haemoglobin, and if the conditions of temperature and ionic strength are properly chosen, the same type of enhancement of oxygen affinity occurs. They surmised that an interchange of sub-units is responsible according to the following scheme in which $(\alpha\beta)$ represents a sub-unit in the so called *R*-state (low oxygen affinity), $(\alpha\beta)^*$ a sub-unit in the *O*-state (high oxygen affinity) and $(\alpha\beta)^0$ an oxygenated sub-unit. (The concept of sites in two affinity states is central to the hypothesis formulated by Monod, Wyman and others.) A fully oxygenated tetramer is in dissociation equilibrium, $(\alpha\beta)_2^0 \rightleftharpoons 2(\alpha\beta)^0$. Exchange with deoxygenated sub-units then takes place, with formation of an *O*-state sub-unit: $(\alpha\beta)_2 + (\alpha\beta)^0 \rightleftharpoons (\alpha\beta)^* (\alpha\beta)^0 + (\alpha\beta)$, and this is followed by oxygenation: $(\alpha\beta)^* (\alpha\beta)^0 \rightarrow (\alpha\beta)_2^0$. Since the central step requires the oxygenated sub-unit $(\alpha\beta)^0$, it follows that only molecules capable of symmetrical dissociation in this way can participate in the reaction.

The Benesches have now shown that no exchange (as judged by the increase of oxygen affinity) occurs with myoglobin, with isolated haemoglobin α and β chains, or with the species β_4^A (which is found naturally as haemoglobin *H*). With oxidized *S* haemoglobin $(\alpha^A\beta^S)_2^+$ (where the + superscript indicates the ferric oxidation state), and with other such haemoglobins, the oxygen affinity was enhanced. An interesting corollary is the existence in solution of mixed species $(\alpha^A\beta^A)(\alpha^A\beta^S)$ which have not been observed experimentally. The results lend support to the idea that the mixed species are not observed simply because any fractionation procedure such as electrophoresis will displace the equilibrium between tetramers and dimers so as to reveal only the forms with extreme mobility $(\alpha^A\beta^A)_2$ and $(\alpha^A\beta^S)_2$. The work of Simon and Konigsberg is particularly interesting in this context (*Proc. U.S. Nat. Acad. Sci.*, **56**, 749; 1966). Covalent cross-links were introduced between the two β-chains of haemoglobin tetramers, thereby preventing dissociation into sub-units. It was found that although the oxygen uptake capacity remains unimpaired, the haem–haem interactions are completely annihilated. These workers suggest that the conformational change known to occur on oxygenation is prevented by the cross-links, but it is clear that sub-unit interchange would equally be impossible. It seems entirely reasonable to suggest that exchange of substrate-bearing sub-units with free sub-units may be responsible in general for the formation of states of high affinity. It has often been remarked that such enzyme systems, subject to control by ligand binding, appear all to be made up of sub-units in a state of reversible aggregation.

Lunar Orbiter II

THE photograph (right) is a view of the floor of the crater Copernicus from the south taken from a height of 45 km by *Lunar Orbiter* II five minutes after midnight (G.M.T.) on November 24, 1966. Copernicus is 96 km in diameter and 3·2 km deep, and the near rim of the crater is 53 km from the crater Fauth at the lower edge of the picture. The hills rising from the floor of Copernicus are 300 m high, and slope at 30 degrees or so.

The photograph above shows the neighbourhood of Copernicus taken by the 3·148 m reflecting telescope at Lick Observatory. Fauth is the double crater, shaped like a keyhole, near the bottom (south) edge of the photograph.