blinded or mentally retarded as a result of the same diseases.

The launching of the ambitious target 'Health for All by the Year 2000' is tied up in the developing world in the attempt to break the vicious circle of disease, meagre resources, the frustrating struggle to make the slightest dent in morbidity and mortality and the failure of the health services to participate effectively in social development. The challenge to WHO is to use these technological breakthroughs to the best advantage in the overall developmental process. The developing countries and WHO are committed to primary health care. Diagnosis has to be made first and foremost in the family, in terms which are simple enough to be understood but at the same time sufficiently discriminatory to indicate a line of action. The *rational* use of antibiotics at the primary health care and first referral levels is encouraged. In order to make a continued review of clinical diagnosis at these health care levels, WHO has invested heavily in the development of simple, rapid laboratory diagnostic techniques that can be used in the peripheral laboratory in the developing world. Another approach is the reinforcement of immunoprophylaxis which has proved to be extremely efficacious in preventing many communicable diseases. The WHO Expanded Programme on Immunization has selected the following target diseases: tetanus, diphtheria, pertussis, tuberculosis, poliomyelitis and measles.

In order to take full advantage of the latest findings in biomedical sciences, WHO launched a new Programme for Vaccine Development in 1984. The Programme is currently dealing with five diseases for which vaccines do not exist or for which vaccines have not proved entirely satisfactory in every environment. These diseases are tuberculosis, dengue, hepatitis A, acute respiratory virus diseases and diseases caused by encapsulated bacteria.

There are two other programmes that the Organization is fostering. One is the further development of simplified techniques for rapid diagnosis for case-management and monitoring of primary health care. The second programme which should be launched during 1985 aims at the rational designing of drugs built on defining the molecular structure of microbes.

Influenza hemagglutinin structure and antigenicity

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An influenza virus membrane contains two sorts of virus specified glycoproteins the majority of which are hemagglutinins (about 500–1000 per virus), the others are neuraminidase molecules (about 100–500 per virus). The more abundant hemagglutinins are the glycoproteins which interact with infectivity-neutralizing antibodies and because of their consequent importance in antigenic variation, their structure and their antigenicity are the topics of this contribution. The hemagglutinins of viruses of the H_3 antigenic subtype, the Hong Kong influenza viruses will be considered primarily because detailed information on the three-dimensional structure of a hemagglutinin is at present only available for the hemagglutinin of the 1968 Hong Kong virus. This molecule is a 220,000 dalton trimer of identical submits each made up of two disulphide-linked glycopolypeptide chains – HA_1 and HA_2. HA_1 contains 328 aminoacids and 6 asparagine-linked carbohydrate side-chains, and HA_2, 221 amino acids and a single carbohydrate side-chain. The hemagglutinin is associated with the virus membrane through a region of uncharged amino acids near the C-terminus of each HA_2 glycopolypeptide and can be released from this association by detergent extraction or proteolytic digestion. Digestion with bromelain at a single site, HA_2 175, releases the soluble trimer, BHA, crystals of which have been used to solve the structure of the molecule. X-ray crystallographic analyses indicate that the amino terminus of HA, as well as the carboxy-terminus of HA_2 is near the membrane of the virus. The HA_1 chain extends from this position through a fibrous region into a peripheral β-structure rich region and then returns to terminate about 30A from the virus membrane. The most prominent features of the submit composed of HA_2 residues are two antiparallel α-helices, one 29A long which proceeds distally from the membrane end of the molecule to connect through an extended chain with the other helix, the major component of the central fibrous stem of the molecule, which stretches 76A back towards the membrane. Hemagglutinins have two functions in virus infection; they bind virus particles to sialic acid-containing receptors and following endocytosis, they appear to mediate fusion between virus and endosomal membranes which results in transfer of the genome-transcriptase complex into the cytoplasm and initiation of virus replication. Probably as a consequence of inhibiting these functions antibodies neutralize virus infectivity and impose selection pressures which lead to the emergence of antigenic variants. In the Hong Kong viruses, following the initial pandemic of 1968, pandemics occurred in 1972 and 1975 and more limited epidemics in 1977 and 1979. On each occasion the viruses responsible were antigenically distinct from previous isolates and consequently were able to infect individuals in what had become a non-immune population. Nucleotide sequence analyses indicate that the amino acid differences detected in the hemagglutinins of these viruses are located almost exclusively in the distal HA, region of the molecule and because of this and the correspondence of their locations with those of substitutions found in monoclonal antibody-selected variant hemagglutinins, this conclusion is firmly based. The relationship of these substitutions to defined sites of antibody binding and to the regions of the molecule with specific functions were discussed.