employ made possible the isolation of folic acid and of hormones such as ACTH and gastrin and of antibiotics. It is important, Professor Chain said, to have the right technique at the right time. As the isolation of penicillin required the technique of the then new freeze drying methods, so today's sophisticated genetical techniques are necessary to "nail down the locus of the defect" manifesting itself as disease.

The closer working of chemists with biochemists has led to discoveries in the field of natural product chemistry; for example, the elucidation of the structure of γ globulin, or the determination of the sequence of transfer RNA.

Although these results have increased the understanding of disease they have not contributed greatly to its therapy. If the biochemist is to help medicine further he must, Professor Chain suggested, consider again the importance of comparative biochemistry. Only by viewing the intact biological system, and with the aid of his advanced techniques and sophisticated tools, can the biochemist attempt to solve the problems of incurable disease.

Parliament in Britain

Hovercraft

Mr J. P. W. Mallalieu, Minister of State in the Ministry of Technology, defended his department's policy of concentrating on the design and production of hovercraft of 300–500 tons to follow the 160 ton SRN4. Replying to suggestions that 5,000 ton hover-ships for rapid trans-atlantic freight and passenger transport and 400 to 4,000 ton ships for communication between Scotland and northern Europe should be developed, Mr Mallalieu thought that problems associated with the smaller craft should be ironed out before work was started on larger ones. The minister said that he did not envisage active cooperation with the United States and Canada on very large ships but that a useful flow of information was being maintained. He hoped that the considerable amounts of money being spent on tracked hovercraft would keep Britain ahead in this field. (Oral answer, October 14.)

Concorde

The first prototype Concorde aircraft is expected to fly from Toulouse early in the new year and the second about six weeks later from Filton. Mr A. Wedgwood Benn gave an assurance that there would be no political interference with the technical development of Concorde. Replying to a question on the financial implications of the delay in the timing of the first flight, Mr Benn admitted that time is money, but said he believed that the in-service date would not be much affected by the initial delays.

Challenged about the danger to passengers in Concorde of exposure to galactic and solar radiation, Mr Benn stated that the estimated annual exposure of a Concorde crew member on North Atlantic routes is equivalent to the dose from between six and seven medical X-ray examinations. Concorde will carry an exposure monitoring device which will also give warning of the onset of exceptional solar flare radiation so that the aircraft can descend to avoid it. With this level of radiation no special shielding will be needed for the aircraft. (Oral and written answers, October 14.)

Cyclamates

In Britain, cyclamates used in all foods and drinks except ice-cream need only be labelled as permitted artificial sweeteners. Mr Hoy, Joint Parliamentary Secretary to the Ministry of Agriculture, Fisheries and Food, declared that there was no evidence to indicate that any further restrictions should be enforced. Reminded that in the United States the Food and Drug Administration is considering compulsory detailed labelling of all products containing cyclamates, Mr Hoy said that the use of cyclamates was much wider in the USA than in the UK. The Food Additives and Contaminants Committee and the Pharmacological Sub-Committee found that there was no risk to health at the likely level of consumption of cyclamates. Asked if he was aware that many doctors and scientists believe sugar to be far more harmful than cyclamates, Mr Hoy said he did not want to start another argument. (Oral answer, October 16.)

Fluoridation

Mr K. Robinson, former Minister of Health, outlined the progress being made with the fluoridation of water supplies. For some time Anglesey, Watford and Birmingham have been supplied with fluoridated water and this year five more fluoridation schemes have started. The total population receiving fluoridated water in England and Wales now exceeds two million. In order to demonstrate complete faith in the efficacy and safety of fluoridation, the Ministry of Health will for an indefinite time pay costs for local authorities if proceedings are brought against them on grounds of injury to health caused by fluoridation. (Written answer, October 14.)

Nobel Prizes for Medicine, 1968

Nobody will have been in the least surprised by this year's award of the Nobel Prize for Medicine to Dr M. W. Nirenberg of the National Institutes of Health at Bethesda, Professor H. G. Khorana of Wisconsin University and Professor R. H. Holley, until recently of Cornell University and now at the Salk Institute; for several years now, all three have been strongly tipped as eventual winners of the prize. They have, of course, been central figures in the deciphering of the genetic code; in other words, in the determination of which amino-acid or punctuation mark is specified by each of the 64 three-letter code words in DNA, and in the elucidation of the process whereby this code is translated during protein synthesis.

By 1960 the general outlines of the flow of information from DNA to RNA to protein had been established, but the prospects of deciphering the code were slim. At that time the only way seemed to be by correlating the sequence of amino-acids in a protein with the sequence of nucleotide bases in the DNA or RNA molecule that had specified the protein. But adequate methods for sequencing nucleic acids were not available. In 1961, however, Drs M. W. Nirenberg and J. H. Matthei revolutionized the position when they published their classic experiment which proved that cell free extracts of bacterial cells support protein synthesis and, furthermore, that when synthetic RNAs of known composition are added to these cell free systems, they specify short proteins which can easily be analysed. The classic result was that polyuracil, an RNA containing only uracil, specified a protein containing only one amino-acid, phenylalanine. The code word or codon for phenylalanine must therefore be a sequence of uracil residues.

Publication of the cell free system technique was the signal for a sharply contested race, notably between Nirenberg's group and that of Ochoa at New York University, which led to the assignment of most of the genetic code words. Hardly a month went by without either or both groups publishing new assignments in the *Proc. US Nat. Acad. Sci.* These experiments were chiefly done, however, with random co-polymers of two or three of the four RNA bases, so they yielded the composition, but not the sequence, of the bases in each codon. For example, a polymer containing much more adenine than cytosine promotes the incorporation of much more asparagine than histidine into a protein. The conclusion is that the code word for asparagine contains two As and one C, while that for histidine has two Cs and an A. But is the sequence of the histidine codon, for example, CCA, ACC or CAC ?

Two discoveries led to the answer. First, Nirenberg found that simply by adding trinucleotides—in other words, single codons—to ribosomes, part of the protein synthesizing machinery, the amino-acid specified by that codon was attached to the ribosome by its specific adapter RNA molecule, its transfer RNA. Trinucleotides of known sequence are relatively simple to synthesize and the trinucleotide binding technique is simpler than the classic cell free system, so that the order of bases in the code words was quickly determined. Secondly, by brilliant chemistry, Dr Khorana devised a method for synthesizing single codons and much longer DNA and RNA molecules of known sequence. In essence he began by synthesizing a double stranded DNA molecule containing twelve base pairs in a known sequence by sophisticated but straightforward organic chemistry. He then exploited two enzymes; the first was the DNA polymerase enzyme isolated from *E. coli* by Dr A. Kornberg, which replicates DNA *in vitro*. When this enzyme replicates short DNA molecules, it somehow slips when it reaches the end of the chain and repeats the replication. As a result, a short molecule of known sequence is converted into a much longer molecule of repeating units. This DNA can then be copied by a second enzyme RNA polymerase so that the end result is an RNA molecule of known sequence. With such methods Khorana's group have now synthesized molecules containing all 64 possible triplets of the four nucleic acid bases and all have been assigned functions specifying either amino-acids or stop and start signals. The latter ensure that when the information in an RNA molecule is translated into the sequence of amino-acids in a protein, the translation always begins at the beginning and ends at the end; in other words, the stop and start codons are the equivalents of capital letters and full stops in punctuation. Brenner's group at Cambridge had, of course, produced elegant but indirect genetic arguments for the assignment of stop signals which Khorana's group, with their synthetic codons, were able to confirm directly and unambiguously; they also quite unambiguously confirmed genetic evidence that each code word consists of only three nucleotide bases.

Professor Holley's outstanding achievement was the elucidation of the nucleotide base sequence of a transfer RNA molecule, an alanine transfer RNA from yeast, which was announced in 1964 after several years' laborious work. Transfer RNA molecules play the vital part of adapters during protein synthesis; they have two specific recognition sites, one for the specific amino-acid and the other for the codon which specifies that amino-acid. Holley's success depended basically on two discoveries. The first was finding a method for separating and purifying a particular species of transfer RNA from all the very similar molecules in the cell. When he began in the 1950s, most groups working on the problem were trying to devise chemical methods of separation but with conspicuous lack of success. Holley devised a physical method, known as counter current distribution, which relies on the differential solubility of various species of transfer RNAs in two phase solvent systems. Once over that hurdle he could get down to the sequencing itself. The crucial step was to devise a method of splitting the molecule into fairly large fragments the sequence of which could be determined; from these the sequence of the entire molecule could be pieced together. The trick Holley discovered was to use nuclease enzymes at unusually low temperatures so that instead of breaking down the molecule completely they broke it at certain susceptible points to yield large but analysable fragments. As with all pioneering work, once Holley had reported his successful methods others followed, and since 1964 nearly a dozen more transfer RNA molecules have been sequenced and techniques improved.

As soon as Holley's sequence of the 77 nucleotides in yeast alanine transfer RNA had been announced, Khorana, with his unique abilities and experience of synthesizing polynucleotides, started to synthesize the gene for yeast alanine transfer RNA. In progress reports earlier this year he described how about half of the molecule has been made so far and there is no reason to expect that any major snags will develop. Once the gene has been made it will be attached to a bacterial virus which will act as a carrier to introduce the gene into a bacterial cell where with luck it will function. While all this has been going on at Wisconsin, Nirenberg's group has developed its trinucleotide binding technique, which was so important for the determination of the sequence of code words, into an assay for the process of chain termination, the reading of the full stops in the genetic message. The preliminary results suggest the new technique will be as useful as its predecessors.

Apart from their Nobel prizes, Khorana and Nirenberg have something else to celebrate. On October 15 Columbia University announced that they were the joint winners of the $25,000 Louisa Gross Horwitz Prize.