amounts of DNA and careful controls with DNAs of known α-gene content, and so again restriction endonuclease mapping should prove simpler.

It is testimony to the remarkably rapid pace of progress of this area of research that a successful diagnosis, for δβ-thalassemia, has already been made by restriction mapping, by Orkin and his coworkers (*New Engl. J. Med.* **229,** 166; 1978). The analysis was performed to confirm the results of a chain synthetic ratio study, since the newer technique is obviously still in its infancy as a clinical tool. Orkin *et al.* were able to show that normal human DNA, digested with the restriction endonuclease *Hin*dIII, generates three β or δ globin-containing fragments. With DNA from an authentic case of δβ-homozygous thalassemia, two of these fragments were absent, but in the DNA from amniotic fibroblasts of the fetus diagnosed, these same two bands were present, though at lower intensity than in normal DNA. This obviously suggested δβ-thalassemia trait (heterozygous), the diagnosis established by chain synthetic ratios, and not δβ-homozygosity. Orkin and coworkers also demonstrated the feasibility of this procedure for diagnosing α-thalassemia. A single *Eco*RI DNA fragment containing all the α globin coding sequences in normal DNA was shown to be absent from placental DNA from a case of hydrops fetalis—the homozygous and lethal condition of α-thalassemia where all α globin genes have been deleted.

One potential complication in using restriction endonuclease mapping diagnostically is that any point mutation can potentially eliminate a restriction endonuclease cleavage site, or generate a new one. Thus, missing bands could potentially arise from such a mutation (which could be totally unrelated to globin genes), especially if the globin sequence as a consequence is now in a very large DNA fragment, which is known to transfer very inefficiently from gel to millipore filter, or in a very small DNA fragment, which binds poorly to the filter. While such variations in restriction endonuclease cleavage sites doubtless do exist, this problem should be solved by using a number of different enzymes. These procedures will doubtless become a major diagnostic tool for those thalassemias caused by gene deletions.

Mapping in detail

But restriction mapping diagnosis may not be limited to disease caused by such major deletions. More detailed mapping with a large array of restriction endonucleases may well reveal much more subtle defects, which may underlie the much more common conditions of β^0-and β^+-thalassemia. In these disorders it is known that no major deletions are present. As discussed by Nienhuis (*New Engl. J. Med.* **229,** 195; 1978) a restriction endonuclease of appropriate specificity has been found which could potentially enable homozygous sickle cell anaemia to be detected.

A detailed restriction map of the human genomic region containing the β and δ globin genes has recently been independently derived by two groups. The more detailed map comes from a collaborative study by R. Flavell, J. M. Kouter and E. de Boer in Amsterdam, and P. Little and R. Williamson, in London (*Cell* **15,** 25; 1978). Armed with a formidable arsenal of restriction endonucleases, they have been able to construct a remarkably detailed and unambiguous map of this region. Although they had a completely pure human β-globin cDNA probe which had been cloned in a baterial plasmid, they still faced the problem of distinguishing between fragments containing β globin or δ globin sequences. This problem was elegantly solved in the following way. *Eco*RI digestion of human DNA generates three β or δ globin containing fragments (the fourth is difficult to detect, as mentioned above). They suspected that two of these contained β-globin sequences, since they formed more stable hybrids with the β-globin probe. The human β-globin mRNA sequence predicts an *Eco*RI site at amino acid positions 121–122. A mutant haemoglobin, Hb O-Arab, has an amino acid substitution at position 121 (glutamic acid to lysine) which eliminates this *Eco*RI cleavage site. Hence, in *Eco*RI digests of DNA from such an individual, a new, large band, equal in size to the sum of the two normal presumptive β-globin containing fragments should appear, and this is precisely what was found, confirming the identity of the β-globin bands. The orientation of the coding sequences was also elegantly determined, by cutting the plasmid containing the β-globin cDNA probe with a mixture of *Eco*RI and *Hin*dIII. The different sized 3′ and 5′ sections of the β-globin sequence generated in this way could be used as probes to identify 3′ or 5′ coding regions in the genomic restriction fragments. The battery of restriction endonucleases, used singly and in combination, enabled the construction of a map, showing that the β- and δ-globin genes are separated by approximately 7,000 base pairs, and that both genes are transcribed from the same DNA strand. The β-globin gene contains an intervening sequence of 800-1,000 base pairs, within the sequence coding for amino acids 101–120. A similar intervening sequence is probably also present in the δ-gene.

A similar analysis of DNA from an individual homozygous for haemoglobin Lepore confirmed that this gene consists of a fusion of part of the δ and part of the β globin gene, with the probable deletion of 8.3 kb.

In the same issue of *Cell* (**15,** 15; 1978) J. G. Mears, F. Ramirez, D. Leibowitz and A. Bank

A hundred years ago

THE following statement with regard to Mr. Edison's recent invention appears in the *Times*:—It appears, from the New York papers, that a company has been started in New York called "The Edison Electric Light Company," with a capital of 300,000 dollars. The object of the company is stated generally to be "the production of heat, light, and power by electricity." The present object, however, is to supply a fund which is to assist Mr. Edison in carrying forward his experiments to a point where he shall give a positive demonstration of the powers of his new inventions. Precisely what these inventions are in all their details of transmission of force and the multiplication of the light derived from electricity, Mr. Edison has not yet told to anybody, fearing that the devices may be patented abroad. The invention, as to the use of electric lights, it is said, will not include the use of carbon points, as ordinarily known in electric lights, but instead the incandescence of a metal simpler and cheaper in every way. Mr. Edison has determined upon the general features of his light, its manner of production, &c.; but in many minor points connected with the distribution of the light for ordinary domestic and business purposes much work has yet to be done. It was at first supposed that 100,000 dollars would be a sufficient experimental fund, but the larger amount was finally determined upon.

THE French Government proposes to do an act of justice in raising the stipends of professors in science and medicine to the same amount as in the case of law and letters, 15,000 francs. Dr. Simplice, who writes on the subject in the *Union Médicale*, points out how unequally professors of pure science, as botany and chemistry, are rewarded as compared with, say, clinical professors, who can add enormously to their income by private practice. Dr. Simplice proposes that a maximum salary should be given to the former, and a minimum to the latter. This is a subject that calls for consideration here as well as in France.

From *Nature* **18,** 31 October, 705; 1878.