form and with a very large deletion that removes half of the spectrin-like region. The possibility to predict the evolution of the disease by protein (or DNA) analysis is important for the large proportion of affected children born in previously unaffected families, and also for constituting homogeneous patient groups for future therapeutic trials. If dystrophin is normal in quantity and quality, then the diagnosis of Duchenne or Becker muscular dystrophy can almost certainly be excluded[19]. Conversely, several recent reports show that some patients diagnosed as having spinal muscular atrophy or limb-girdle muscular dystrophy (both autosomal recessive diseases) in fact have deletions in the dystrophin gene[20,21].

Animals, models and therapy

A fascinating aspect of the dystrophin problem is the striking difference in phenotype between mice and humans that lack dystrophin. It is well known that the *mdx* mouse has no obvious clinical symptoms and was initially identified by G. Bulfield[22] on the basis of increased levels of pyruvate kinase in serum. The pathological findings in the *mdx* mouse were reviewed by G. Karpati (Montreal Neurological Institute). The *mdx* mouse shows extensive necrosis of muscle fibres from 15 to 80 days after birth, accompanied by active regeneration. Regenerated fibres can be recognized as they have central nuclei whereas normal muscle fibres have peripheral nuclei. After day 80, all fibres seem to be of the regenerated type and necrosis is much less conspicuous afterwards, as if the newly made fibres have become less sensitive to the lack of dystrophin.

One hypothesis would be that in mice a dystrophin-like protein (such as the one encoded by the new gene identified by Love *et al.*[1]) could replace the missing protein. This could be reminiscent of the mild phenotype in β-thalassaemia patients who express significant levels of fetal γ-globin. In fact, the *mdx* mouse has more muscle mass and appears stronger than the normal mouse! In contrast, in man the regenerative potential is rapidly exhausted by the continued necrosis. H. Blau (Stanford University), who has devised a method to prepare pure muscle satellite-cell populations, showed that even just a few months after birth, the replication potential of these cells (mononucleated myoblasts which can participate in regeneration and formation of new fibres) is less in Duchenne patients than in an older normal control, and at the age of 4 the replication potential is almost exhausted (less than 10 doublings). The dystrophic dog has a disease very similar to that of man, but heterogeneity of clinical evolution in the same sibship was reported[23].

Because of the high rate of new mutations in the dystrophin gene, genetic counselling and prenatal diagnosis will have only a limited effect on the incidence of the disease, and the design of efficient therapies is thus a major concern. The problem seems a formidable one because dystrophin is important in the structure of both skeletal and cardiac muscles. The demonstration by T.A. Partridge *et al.*[24] that injection of myoblasts from normal mouse into growing or regenerating muscle of *mdx* mouse can lead to substantial expression and correct localization of dystrophin in muscle fibres, in the injected muscle, generated considerable interest and hope in patients' associations. However, both in his paper and at the meeting, Partridge (Charing Cross and Westminster Medical School, London) stressed the numerous problems that should be dealt with for therapy in man: immune rejection (the successful implantation experiments were performed in immunodeficient *mdx*/nude mice); the production of a very large number of myogenic cells; the necessity of injection at multiple, probably closely spaced sites because dystrophin, like other muscle proteins[25] remains localized, within the fibre, close to the nuclei from which it is derived. Other approaches might be tested in subgroups of patients, for instance trying to boost expression of dystrophin in severe Becker patients. And Kunkel concluded in a rather optimistic mood that various therapeutic avenues might now be explored. □

J.L. Mandel is in the Institut de Chimie Biologique, Faculté de Médecine, INSERM U 184, 11 Rue Humann, 67085 Strasbourg Cedex, France.

1. Love, D.R. *et al. Nature* **339**, 55–58 (1989).
2. Koenig, M., Monaco, A.P. & Kunkel, L.M. *Cell* **53**, 219–228 (1988).
3. Lemaire, C., Heilig, R. & Mandel, J.L. *EMBO J.* **7**, 4157–4162 (1988).
4. Hoffman, E.P. & Kunkel, L.M. *Neuron* **2**, 1019–1029 (1989).
5. Watkins, S.C., Hoffman, E.P., Slayter, H.S. & Kunkel, L.M. *Nature* **333**, 863–866 (1988).
6. Campbell, K.P. & Kahl, S.D. *Nature* **338**, 259–262 (1989).
7. Nudel, U., Robzyk, K. & Yaffe, D. *Nature* **331**, 635–638 (1988).
8. Fenner, C.A., Koenig, M. & Kunkel, L.M. *Nature* **338**, 509–511 (1989).
9. Monaco, A.P. *et al. Genomics* **2**, 90–95 (1988).
10. Malhotra, S.B. *et al. Science* **242**, 755–759 (1988).
11. Baumbach, L.L. *et al. Neurology* **39**, 465–479 (1989).
12. Koenig, M. *et al. Am. J. hum. Genet.* (in the press).
13. Gospe, S.M. *et al. Neurology* (in the press).
14. Hu, X. *et al. Am. J. hum. Genet.* **44**, 855–863 (1989).
15. Den Dunnen, J.T. *et al. Nature* **329**, 640–642 (1987).
16. Chamberlain, J.F. *et al. Nucleic Acids Res.* **16**, 11141–11156 (1988).
17. Gibbs, R.A., Nguyen, P.N. & Caskey, C.T. *Nucleic Acids Res.* **17**, 2437–2448 (1989).
18. Chelly, J.I. *et al. Nature* **333**, 858–860 (1988).
19. Hoffman, E.P. *et al. N. Engl. J. Med.* **318**, 1363–1368 (1988).
20. Norman, A., Thomas, N., Coakley, J. & Harper, P. *Lancet* **i**, 466–468 (1989).
21. Lunt, P.W. *et al. Lancet* **i**, 46–47 (1989).
22. Bulfield, G., Siller, W.G., Wight, P.A. & Moore, K.L. *Proc. natn. Acad. Sci. U.S.A.* **81**, 1189–1192 (1984).
23. Cooper, B.J. *et al. Nature* **334**, 154–156 (1988).
24. Partridge, T.A. *et al. Nature* **337**, 176–179 (1989).
25. Pavlath, G.K., Rich, K., Webster, S.G. & Blau H.M. *Nature* **337**, 570–573 (1989).

DAEDALUS

Boring and crazing

To propagate through a solid, a crack must find from somewhere the energy needed to form its growing surfaces. If its surface-energy were ever zero, a crack could spread and ramify spontaneously. This actually happens when water is forced into a viscous material with which it is thermodynamically miscible. A convoluted aqueous intrusion of fractal complexity is formed.

This principle, says Daedalus, has powerful implications for geotechnology. What would happen to a borehole if a liquid pumped into it had zero interfacial energy with the local rock? The pressurized liquid would effortlessly penetrate and extend all the microcracks in the rock, crazing them into sub-cracks and sub-sub-cracks as it went. The result would be a sort of fractal tree root structure, radiating out in all directions from the borehole.

DREADCO's chemists initially recommended hydrofluoric acid for this job. It actually dissolves most rocks with evolution of heat, implying not merely a zero interfacial energy, but one strongly negative. But Daedalus distrusts this most corrosive and treacherous of acids, and prefers liquids that only just dissolve rock, or merely resemble it so closely that the interfacial energy vanishes. For silicate-based rocks and clays, compositions of hydrofluosilicic acid and sodium silicate solution ('water glass') seem promising.

When perfected, the new borehole technology will have wide and wonderful applications. Just bore your hole, line it, and pump a suitable DREADCO fracture fluid into it. From the bottom of the hole a fractally convoluted web of cracks and crevices will spread outwards until every element of the local rock is within an arbitrarily short distance of a crack. If the rock is water-bearing, the result is an ideally efficient well. If it is dry, the hole would make a perfect soak-away drain or wastewater-disposal pit. And if it contains valuable minerals, such holes provide a perfect way of getting at them. Many metals occur at such low concentration in an ore body that open-cast mining is very wasteful. A few holes bored into the deposit, and pressurized till their fracture trees intersect, will do the job much more neatly. An ore solvent pumped down one hole and extracted from its neighbour will travel a fractally complex path, passing arbitrarily close to every particle of ore. With no environmental damage, this elegant mine will swiftly extract all the ore in even a very dilute deposit.

Fracture fluid will even help to bore the initial holes; as a drill lubricant it will reduce the power needed and heat generated almost to zero. A version matched to the surface-energy of teeth could thus bring about a humane revolution in dentistry.

David Jones