Seal vaccination success

SIR—In providing evidence that the primary cause of the epizootic of distemper with high mortality among harbour seals (*Phoca vitulina*) in the North and Baltic seas was canine distemper virus (CDV) or a closely related morbillivirus[1], which has since been claimed to be a new morbillivirus christened phocine distemper virus (PDV)[2,3], we heralded our evaluation in seals of a subunit CDV vaccine, shown to be effective in dogs[4]. If seals can be protected by the vaccine, it would not only confirm the close relatedness between PDV and CDV, but it would also provide final proof for this morbillivirus as the primary cause of the recent epizootic in seals. We now report our initial success with two different vaccines.

We used animals belonging to a breeding group of harbour seals kept in isolation for many years. So far no signs of phocid distemper have been observed in this group. For ethical and practical reasons the study was limited to eight adult animals. Six of these were vaccinated twice intramuscularly at two-weekly intervals followed by a third vaccination four weeks later. Two received a candidate subunit iscom CDV vaccine, prepared in collaboration with Coopers Animal Health Ltd (Berkhamsted, UK) as previously described[4]; the other four were vaccinated with a candidate inactivated whole virus CDV vaccine, kindly provided by Duphar BV (Weesp, The Netherlands). The other two animals were sham-vaccinated with an antigen-free preparation.

Before vaccination, CDV-neutralizing serum antibodies were undetectable (titre below 10) in these animals. After the third vaccination all six CDV-vaccinated animals had antibody titres ranging from 300 to 1,000. Ten days later all eight animals were transferred to a closed swimming pool and challenged, intraperitoneally or oculo-nasally, with a suspension of organ material from seals that had died during the outbreak.

Given similarly, this material produced clinical disease and the development of CDV-neutralizing serum antibodies in dogs[5].

The two sham-vaccinated seals showed signs of acute respiratory disease and mucopurulent nasal discharge about two weeks after challenge and died on days 14 and 18. Viral antigen was detected in the spleens and/or lungs of both these animals with an enzyme-linked immunosorbent assay, using a monoclonal antibody which recognizes the F protein of both CDV and PDV[3-5]. No clinical signs were noted in any of the vaccinated animals (I. Visser, to be published). A threefold or higher (average 15-fold) increase in CDV-neutralizing serum antibody titres observed in all vaccinated animals two weeks after challenge suggests that some replication of PDV had taken place. As is often the case in the natural disease, CDV-neutralizing antibodies were not found in serum samples collected after the death of one of the two seals, probably because of the acute nature of the disease. The other had developed a CDV-neutralizing antibody titre of 30.

Although the number of animals studied is small, the data warrant the conclusion that seals can be protected from phocid distemper by vaccination with certain inactivated CDV vaccines. Since the disease was only produced in animals not vaccinated against canine distemper, the last of Koch's postulates has also been fulfilled, reconfirming that infection with CDV or a closely related morbillivirus is the primary cause of the epizootic.

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1. Osterhaus, A.D.M.E. & Vedder, E.J. *Nature* **335**, 20 (1988).
2. Kennedy, S., Smyth, J.A., McCullough, S.J., Allan, G.M. & McNeilly, F. *Nature* **335**, 404 (1988).
3. Mahy, B.W.J. *et al. Nature* **336**, 115 (1988).
4. De Vries, P., UytdeHaag, F.G.C.M. & Osterhaus, A.D.M.E. *J. gen. Virol.* **69**, 2071–2083 (1988).
5. Osterhaus, A., *et al. Nature* **335**, 403 (1988).

Superconducting single crystals

SIR—Were large single crystals of the high-temperature superconductors of the type $La_{2-x}A_xCuO_4$ available (where A represents Ba or Sr), their physical and structural properties might provide insight into the still unknown mechanism of high-temperature superconductivity. By use of the travelling-solvent floating-zone method[1], we have grown such crystals and determined their superconducting properties, which we report. The anisotropy of their magnetic and electrical properties will be described elsewhere.

Appropriate amounts of La_2O_3, CuO and $SrCO_3$ powders were mixed in ethanol, dried and calcined in air at 1123 K for 12 hours. The calcined powder was formed into a cylindrical shape, 6 mm in diameter by 50 mm in length, and compressed at a hydrostatic pressure of about 100 MPa. This rod was sintered at 1273–1473 K for 12 hours in oxygen gas and was then used as both the feed and the solvent rod. For crystal growth we used a double-ellipsoidal infrared heating furnace (Nichiden Machinery Ltd) heated by two 1.5-kW halogen lamps[1]. Growth conditions involved growth rates of 1.0–3.0 mm per hour, solvent compositions of 55–80 mol% CuO and a growth atmosphere of 0.2 MPa O_2 (to prevent vaporization of copper oxide from the melt zone).

A sample of $La_{2-x}Sr_xCuO_4$ in this way, using a solvent of 75 mol% CuO, is shown in Fig. 1. The black, lustreless region at one end comprises a two-phase mixture of La_2O_3 and $La_{2-x}Sr_xCuO_4$, but the remaining portion, black with a metallic lustre, is single-phase $La_{2-x}Sr_xCuO_4$. This region exhibits two facets parallel to the growth direction. Back-reflection Laue X-ray diffraction of these facets gives sharp diffraction spots, confirming the single-crystal nature, and reveals a fourfold rotation axis, identifying the crystallographic plane of the facets as (001). Although the samples contained some cracks, single crystals of about 6 mm in diameter by 15 mm in length could be obtained.

The lattice parameters of the tetragonal

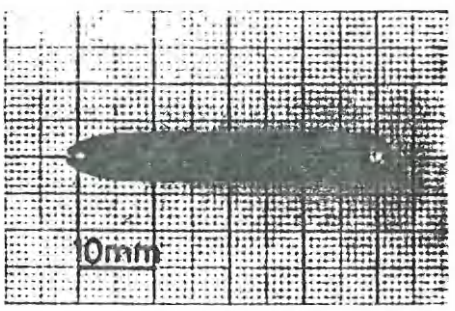

Fig. 1 Single crystal of $La_{2-x}Sr_xCuO_4$. Dimensions are ~ 6 mm diameter and 40 mm length.

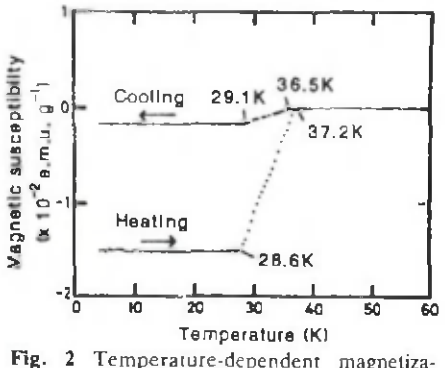

Fig. 2 Temperature-dependent magnetization of $La_{2-x}Sr_xCuO_4$ single crystals. The upper curve is for cooling in a field of 0.936 Oe; the lower curve is for heating in 0.936 Oe after cooling in zero field.