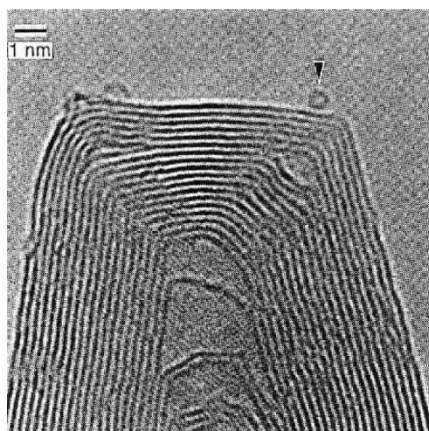


Smallest carbon nanotube

SIR — The discovery and synthesis of C_{60} molecules have led to an explosion of interest in the family of carbon structures and compounds. We have recently reported the discovery of carbon nanotubes¹, consisting of concentric sheets of carbon hexagons arranged in a helical manner, but with the ends capped by pentagons². The diameters of the tubes are in the nanometre range, with the smallest tube observed so far having a diameter of 2.2 nm. The structures consist of two to many layers. Recently, there has been speculation about the smallest possible carbon fibre whose diameter would correspond to the C_{60} molecule³, and which would have extremely interesting physical properties.

While observing the structure of car-



bon tubes in the transmission electron microscope, we have come across images that could indeed correspond to an isolated tube with the C_{60} diameter (see figure). The spherical hollow structure (arrow) has a shell with an outer diameter of approximately 0.8 nm, which could correspond to an image from a single C_{60} structure⁴. We do not think the structure is a single isolated C_{60} molecule because its contrast is comparable to that obtained from the {002} lattice fringes of the supporting polygonized carbon-tube structure, which is a large tube with many layers of carbon hexagons and hence large numbers of carbon atoms in a diffracting column compared with a single C_{60} molecule. So, we believe that what we are seeing is a tube with the diameter of a C_{60} molecule and the dimension of a few such units in the direction perpendicular to the plane of the image, being observed end-on. The observation of such spherical and elongated structures on the surface of tubes is fairly common, but this is the first time a single isolated structure has been found.

Such extremely small tubular structures could act as nucleation sites for the

growing tubes. Raft-like graphite layers are often seen in the form of incomplete layers on the surface of the tubular assemblies. In the very early stages of nucleation and growth, these rafts of carbon hexagons nucleated on the surface of graphitic sheets of the tube may curl up to form cylindrical shapes of small diameter, like the tube observed in the figure. It is, however, not possible to tell how actual growth proceeds on these structures to produce the completed layers or whether these structures are closed or open at their tube ends.

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Blood substitutes and infection

SIR — Increasing concern about blood-transmitted viral pathogens has spurred the development of a blood substitute that can effectively replace the oxygen-carrying capabilities of red blood cells. Chemically modified haemoglobins and recombinant human haemoglobin synthesized in *Escherichia coli*, *Saccharomyces cerevisiae* and in transgenic animals have been investigated as potential oxygen-carrying red-cell substitutes¹. They turn out not to be suitable because the oxygen affinity is too high to permit efficient tissue oxygenation, and the haemoglobin molecules are not stable. The dissociated $\alpha\beta$ -dimers are cleared rapidly by renal filtration, which can result in kidney damage.

Looker *et al.*² have now described a genetically engineered haemoglobin molecule incorporating many of the properties required for a red-cell substitute². The oxygen affinity of this molecule compares favourably with that of blood. Dissociation into $\alpha\beta$ -dimers does not occur as the two α -chains are linked together, and this eliminates the renal toxicity. The authors concluded that this engineered haemoglobin is a strong candidate for a safe blood substitute that could be used in the emergency resuscitation of trauma victims.

In our opinion, however, a red-cell substitute must fulfil at least one other important requirement. It must not stimulate bacterial growth, as does ex-

tracellular haemoglobin, because this will promote bacterial infection. In healthy people, most of the iron is located intracellularly as ferritin or as haemoglobin. This iron is normally not available to invading microorganisms. The small amount of extracellular iron that appears in the body is attached to transferrins (host iron-binding and transport proteins), thereby creating bacteriostatic conditions for microorganisms. Extracellular haemoglobin is usually not present in the circulation. Haemoglobin released by lysis of erythrocytes is immediately bound by the serum protein haptoglobin and transported to the liver. Free haemoglobin appears when haptoglobin is saturated. The free haemoglobin is oxidized and dissociates into globin and haem, and the haem molecules are bound by hemopexin and subsequently transported to the liver.

This clearance of extracellular haemoglobin from the circulation is an important defence factor against bacterial infections, as many pathogens possess iron-uptake systems that enable them to use the iron from extracellular haemoglobin. *Neisseria* species, *Haemophilus influenzae*, *Vibrio* species, *Bacteroides fragilis* and *E. coli* are examples of bacteria that are capable of using extracellular haemoglobin^{3,4}. Furthermore, haem-binding proteins of more or less the same molecular mass have been detected in several bacterial species^{5,6}, which could indicate that comparable haem-uptake systems are present in a wide range of microorganisms.

Sickle-cell anaemia, bartonellosis and trauma are examples of conditions where large amounts of haemoglobin may be present in the plasma and in which patients are unusually susceptible to infection⁷. Under these circumstances it is difficult to prove that this unusual susceptibility is due to the liberation of haemoglobin, but the idea that this is reasonable is strongly supported by experimental evidence showing that haemoglobin stimulates the growth of many bacteria in many different hosts⁴. For instance, non-fatal infections with *E. coli* in rats have been converted to fatal infections by adding haemoglobin and the lethal effect is eliminated by the simultaneous administration of haptoglobin⁸. If human recombinant haemoglobin behaves in the same way and promotes bacterial infections, then this will cause considerable problems, particularly in cases of emergency, when patients may have open non-sterile wounds. Therefore, elucidation of the structure–function relationship between the haemoglobin receptor of bacteria and haemoglobin metabolism is needed to provide a basis for understanding the mechanisms used by microorganisms for