A Better Chance for Kidney Transplantation

Since 1975 there has been an improvement in the success rate of kidney transplant operations, according to Paul Terasaki of the University of California School of Medicine at Los Angeles. The most significant factor contributing to the improvement is the increased number of transplant recipients who receive blood transfusions before surgery. Terasaki says, "There is a nationwide tendency to transfuse patients that is reflected in an increased [kidney transplant] survival."

Terasaki was reporting data accumulated by the UCLA transplant registry, which contains information about some 30,000 patients who have received new kidneys at medical centers in the United States and Canada. Earlier analysis of the registry data had shown that the percentage of transplanted cadaver kidneys that survived at least 1 year declined from 65 percent to about 45 percent between 1966 and 1974. (Transplants of cadaver kidneys from unrelated donors constitute about 70 percent of the total number, which is now about 4500 per year.)

In the early 1970's transfusions were considered a contraindication for kidney transplantation because they might induce the production of antibodies that would increase the risk of graft rejection. However, by the mid-1970's, data acquired by Terasaki and Gerhard Opelz, also of the UCLA School of Medicine, indicated that transfusions actually improved graft survival. Since then numerous studies have confirmed this conclusion. Terasaki says, "Forty-eight independent sets of data all gave the same effect."

As a result there has been a progressive increase in the percentage of transplant recipients who are given blood transfusions before they receive their new kidneys. According to the UCLA workers, about half were transfused in 1977, but by the end of 1980 this number had grown to about 90 percent. Exactly paralleling this increase was that of 1-year graft survival which can go as high as 70 percent for cadaver kidneys. Medical centers that do the most transplants tend to have the best results, but the transfusion effect is a general one.

According to Terasaki, there is a strong possibility that transfusions improve transplant survival by making it easier to identify those patients most likely to reject their grafts. The transfusions do induce in some patients the production of antibodies that attack the tissues of potential kidney donors. These antibodies are detected in the pretransplant tests and, if many different kinds are present, it may be difficult or impossible to find a kidney that will not be rejected. As Benjamin Barnes of Harvard Medical School described this situation, "We may be eliminating patients from transplantation rather than preparing them for it." Nevertheless, those patients will be spared from surgery that will not help them and the government, which bears practically all the costs for the treatment of kidney disease, will be spared an unnecessary expense.

—Jean L. Marx

A Boundary for the Quasars?

Roughly 15 billion years ago, the universe suddenly filled with quasars. They turned on everywhere, all at once, each with the brilliance of a thousand normal galaxies. Then, almost immediately, they began to die out. Because of their great distance and the finite speed of light, we see them now as they were billions of years ago. But today they are gone.

These are the implications of a recently completed quasar survey conducted over the past 8 years by Maarten Schmidt of the California Institute of Technology and Richard F. Green of the University of Arizona. Schmidt discovered the first quasar in 1963.

Their survey shows that the density of quasars rises rapidly with increasing redshift. Schmidt points out that if quasars were actually close by, with redshifts caused by something other than cosmic expansion (as some astronomers have suggested), the Milky Way would have to lie at the center of a quasar-free hole. In other words, he said at the AAAS meeting, the earth would have to occupy a privileged position in the universe, which violates everything astronomers have learned since Copernicus. Schmidt, like most astronomers, chooses to believe instead that quasars lie far away.

Surprisingly, the count found no quasars with a redshift greater than 3.53 (that is, with their spectral wavelengths shifted by more than 353 percent). An extrapolation of the numbers found at smaller redshifts implies that Schmidt and Green should have seen plenty of quasars beyond 3.53. So translating redshifts into distance and time, this boundary probably marks the era when quasars first turned on, Schmidt said. If so, it happened about 5 billion years after the big bang.

A consensus is growing among theorists that quasars are (or were) supermassive black holes at the cores of otherwise normal galaxies. They were bright because material being swept toward the holes was violently compressed and heated, giving up much of its mass as radiant energy before finally falling in. Presumably the quasars turned on when the galaxies formed, so perhaps this boundary also marks the period of galaxy formation. (Interestingly, Schmidt and Green's quasars showed little of the clumping seen among galaxies today. On the other hand, the statistics are poor, so clumping isn't necessarily ruled out.) Perhaps each quasar faded out as the central black hole finished sweeping up everything in its vicinity. It may be that many of the galaxies we see today harbor supermassive black holes—dead quasars—in their centers. There is growing evidence that just such a black hole, albeit somewhat less than quasar size, lies at the center of our own galaxy.***—M. Mitchell Waldrop***

A New Look Inside the Sickle Erythrocyte

Scientists may have to rethink the mechanism by which erythrocytes from individuals with sickle cell disease are believed to block blood vessels in the light of new findings by Constance T. Noguchi and Alan N. Schechter of the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK). Their results may explain why the disease is more severe in some patients than in others.

Sickle cell disease involves a sub-

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stitution of the amino acid valine for glutamic acid on each of the two β chains of the hemoglobin molecule, producing an abnormal molecule called hemoglobin S (HbS). Because of this mutation, HbS molecules that have given up their oxygen to tissues polymerize inside the erythrocyte and form long needle-like structures that distort the cell and reduce the flexibility required to pass through capillaries (*Science*, 30 January 1981, p. 468). Normal hemoglobin does not polymerize under any conditions and previous studies in vitro had shown that oxygenated HbS also does not polymerize.

Noguchi and Schechter, working with Dennis Torchia of the National Institute of Dental Research, have developed a new technique in which natural abundance carbon-13 nuclear magnetic resonance spectrometry is used to examine HbS inside individual erythrocytes. They have found that, on the whole, the behavior of HbS within the erythrocyte is very similar to its behavior in vitro—with one surprising exception. They observed that some of the HbS remains polymerized in the erythrocytes even when the cells are more than 90 percent saturated with oxygen.

The explanation for this unexpected aggregation was provided by Allen P. Minton of NIADDK, and involves the nonideality of protein solutions. All laws governing behavior in solution require the activity of the solute. In dilute solutions, the activity is generally equal to the concentration, which is used in place of activity since it is easier to measure. If solutions were ideal, activity would always equal concentration. In the real world, however, solutions are nonideal, and activity increases much faster than concentration. The effect is magnified for very large molecules, such as proteins. For HbS at the concentrations in the erythrocyte, Minton has found that the activity is 97, which means that HbS behaves chemically as though it were almost 100 times more concentrated than it actually is. In simple terms, this means that fewer molecules are necessary to initiate polymer formation—about half as many as previously predicted—and polymerization can be observed at lower concentrations.

The conventional view of sickling is that erythrocytes in individuals under stress lose flexibility after they have given up their oxygen in capillaries, but before they reach the venous system to return to the lungs for reoxygenation. The new results suggest that, even though oxygenated cells appear normal, they may have already lost some of their flexibility because of the presence of small amounts of polymer. They may thus be trapped in arterioles and sphincters even before they enter capillaries. Schechter speculates that individuals with the most severe form of the disease may have the greatest amount of polymerization in oxygenated cells.

—Thomas H. Maugh II

Extinctions: Iridium and Who Went When

The extinction of the dinosaurs must be a matter that is entirely separate from the marine extinctions of about the same time, if one researcher's interpretation of new findings in Montana is correct. The discovery near dinosaur fossils of traces of a supposed asteroid impact suggests that terrestrial fauna, including the dinosaurs, did not share the catastrophic end met by many marine species.

Paleontologists have always had trouble comparing observations from widely separated places. Did the dinosaurs in New Mexico disappear at the same time as those in Montana? Did microscopic plants and animals floating in the ocean become extinct exactly when the last dinosaurs died out? If widespread extinctions of many species occurred simultaneously, then they might have had a common, perhaps catastrophic, cause.

Paleontologist William Clemens and geologist Walter Alvarez, both of the University of California at Berkeley, presented the first direct evidence that, if an asteroid did hit Earth about 65 million years ago, it fell after the last of the dinosaurs disappeared. The postulated impact, as evidenced by a thin sediment layer rich in the element iridium, does coincide with the sudden disappearance of species that inhabited the surface of the ocean. Many scientists now accept the decimation of life in the sea by an asteroid impact as a reasonable working hypothesis (*Science*, 20 November 1981, p. 896). But the only other known iridium layer deposited in nonmarine sediments had no fossils nearby for comparison.

Clemens and Alvarez found the iridium layer at a well-studied site in northeastern Montana called Hell Creek. To a paleontologist, depth in the ground can be read as time—the deeper he digs, the older are the things he finds. At Hell Creek the youngest dinosaur fossil, the femur of a *Tyrannosaurus rex*, was found at a level about 3 meters below the iridium layer, which is at the base of a coal layer. Not only did the dinosaurs of the Cretaceous Period seem to have disappeared before the dust from the asteroid impact settled to the earth, Clemens said, but fossils of vertebrates typical of the next geological epoch, the Paleocene, were found at a level about 2 meters below the iridium layer. A single pollen sample taken from about 1.5 meters below the layer does contain Cretaceous species, but it lacks the pollen most typical of the period, indicating that the flora was in a transitional state.

Clemens and Alvarez politely disagree about the importance of the apparent gap between the iridium layer and the fossil evidence of major extinctions. The preliminary iridium analyses "argue strongly against the catastrophe hypothesis" of terrestrial extinctions, Clemens said. Alvarez emphasized the close proximity of the two events. The gap could represent a period of 10,000 years or less after millions of years of dinosaur dominance, Alvarez said.

Nevertheless, paleontologists are excited about the iridium layer as a time marker. However it got there, if it was deposited on both the sea floor and the land in the same geological instant, then paleontologists can use it to determine the order of events at widely separated locations. For example, it might be used to correlate the disappearance of the dinosaurs up and down central North America, where the gradual withdrawal of the central seaway may have forced the progressive retreat and eventual extinction of the North American dinosaurs. Paleontologists are also hopeful that the new data will help to finally break the connection in the public mind between asteroids and dinosaurs. The two never belonged together in the first place, they say.

—Richard A. Kerr