Biological Sciences update
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Preserving lifesaving livers

Researchers have revolutionised the storability of human livers. **Liz Sheffield** explains how this greatly enhances the chances of these organs saving lives

More than 40 people die from liver disease in the UK every day. Since 1970, deaths due to liver disease have increased by 400%. It is the only major cause of death on the increase (see Figure 1) and is soon expected to overtake heart disease as the biggest cause of premature death. If liver disease is spotted sufficiently early, researchers estimate that lifestyle changes could prevent 90% of these fatalities (>60% of liver disease is alcohol-related). But that still leaves a lot of other people who have a life-threatening issue with this major organ. One intervention with a 75% survival rate after 5 years is transplantation.

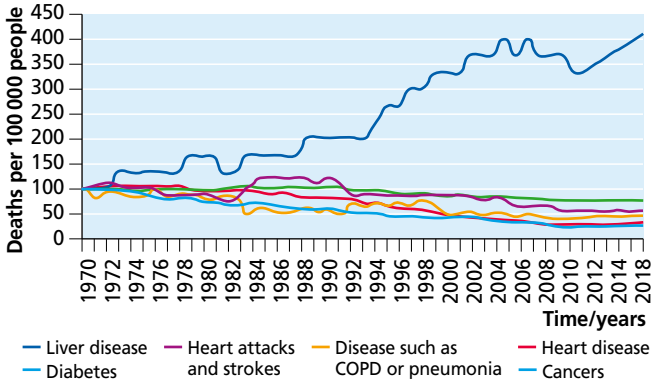

Figure 1 Standardised UK mortality rates

Liver transplantation

If transplants are a good option, why aren't more done? The most obvious answer is that donors (dead and alive) are vastly outnumbered by those needing a liver. But another constraint is that liver transplantation is problematic. Less than 3% of organ transplants involve livers — most are kidneys. The latter are not straightforward, but patients needing a kidney transplant can usually be kept stable with dialysis. There is no equivalent to dialysis for patients needing

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a liver, and the operation to install a donor liver is intricate and time-consuming (kidney transplant 2–3 h, liver transplant 4–8 h). Another constraint is that once removed from the body, organs rapidly deteriorate. Living donors can donate a quarter or half of their liver and expect their organ to regenerate to full size and function, but living donations account for less than 5% of transplants. The scarcity of people willing to donate part of their liver is one reason why intensive research has been in progress to find a way to extend the viability of removed livers.

Because livers, like the rest of our bodies, are about 70% water, they cannot be frozen without suffering irreparable damage. Water expands as it freezes, so when tissues are frozen, the membranes inside and around cells are damaged beyond repair. So, currently, there are only two options for a liver removed for transplant. One is to keep it cool (on ice, not frozen) which gives a window of about 8 h within which to effect the transplant. The other, recently developed, technique is to keep it at body temperature hooked up to a (very expensive) machine which perfuses it with oxygenated blood, anti-clotting drugs and nutrients. This extends the window to 12–24 h, but means that either the machine plus liver or the recipient needs to travel. The unpredictable nature of suitable donor availability and geographical constraints currently mean that there are huge losses of potentially life-saving livers.

Rats to the rescue

In 2014 researchers successfully transplanted rat livers that had been stored below 0°C into rats that subsequently recovered well. They used syringes to perfuse the livers — delivering oxygen and nutrients via capillaries. Then they supercooled the livers. First they added 3-O-methyl-D-glucose, a modified glucose compound, to the perfusion solution. This small molecule can pass through cell surface membranes, and it is taken up by the liver cells. But because it cannot be metabolised, it accumulates in the cells, acting as a protectant against the cold. The researchers also added polyethylene glycol — the active ingredient in antifreeze — which protects cell membranes and lowers the freezing point of solutions. Once perfused with this solution, the livers were cooled to –6°C without freezing — supercooled.

Human livers are 200 times larger than those of rats, and cannot be thoroughly perfused using syringes. The development of the perfusion machine mentioned above means that human livers can now be perfused, supercooled and stored without compromising their viability. This technique should vastly reduce the number of livers wasted and save many more lives until the day we can grow livers in the laboratory.

Activities

Sign up to be an organ donor (in 2020 'opt out' of donation comes into force in the UK but under-18s are one of the exempt groups): **https://tinyurl.com/y63pq7ke**

Consider becoming a living donor: **https://tinyurl.com/y65xxrla**

Find out how to look after your liver and talk to friends and relatives about how to look after theirs: **https://tinyurl.com/y63b6q3e**

Weblinks

'Supercool' method triples organ survival, 10 Sept 2019: **www.bbc.co.uk/news/health-49632609**

'Pioneering machine' for patients awaiting liver transplant, 11 Sept 2019: **https://tinyurl.com/y3h3coy9**

First UK live liver donation to a stranger takes place: **www.bbc.co.uk/news/health-21143602**

How does living liver donation work? Six things to know: **https://tinyurl.com/yyatctso**