

# SAFEGUARDING THE KIDNEY

Early detection and prompt treatment could prevent long-term health effects of acute kidney injury, a condition that commonly arises while people are in hospital. By **Michael Eisenstein**; infographic by **Alisdair Macdonald**

## A NEST OF NEPHRONS

The kidneys are responsible for filtering toxins and by-products of metabolism out of the blood. At the heart of this purification system are hundreds of thousands of tubular structures known as nephrons.

Blood flows into the kidneys through the renal artery.

Filtered blood leaves the kidney through the renal vein.

Toxins are expelled from the body in the urine through the ureter.

The functional units of the kidney — the nephrons — are clustered in segments known as renal pyramids.

Blood filters into a nephron from a bundle of blood vessels called the glomerulus.

The nephron tubules are formed of epithelial cells that aid the reabsorption of essential liquids and electrolytes back into the blood.

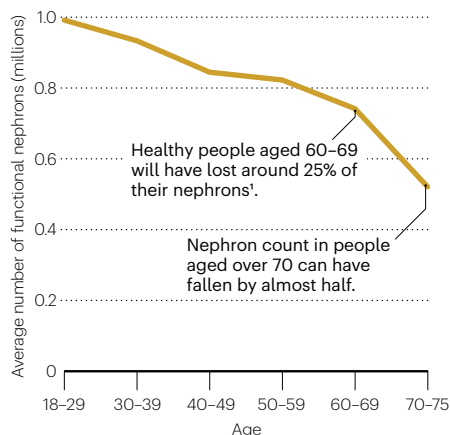
Remaining waste is deposited from the nephron into the collecting duct and expelled as urine.

1M

The average person begins their life with around one million nephrons in each kidney\*, but this can vary considerably.

### Nephron count

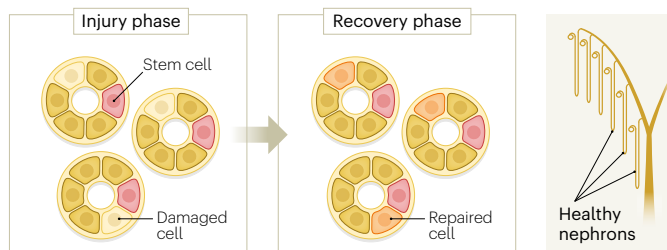
Everybody is born with a finite number of nephrons, which then declines as we age. This means that older people are more vulnerable to the effects of nephron damage, because they typically have fewer healthy nephrons at the onset of injury.



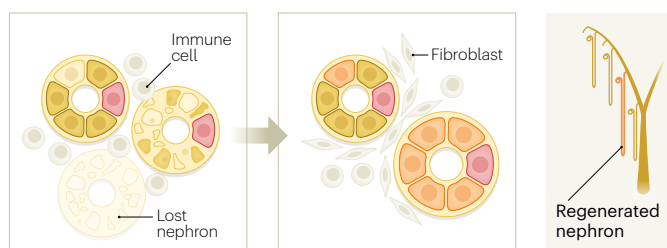
## INJURY AND RESILIENCE

Acute kidney injury (AKI) describes a range of conditions in which nephrons are damaged, impairing their function and reducing the efficiency of filtration through the glomerulus.

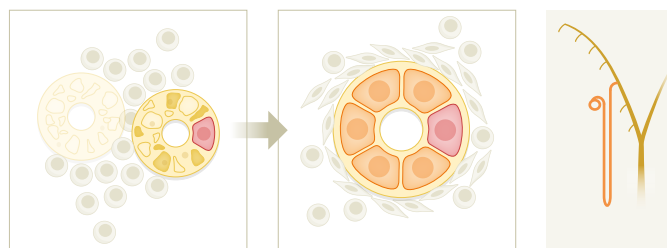
**1.** Modest damage to the nephron tubules can be repaired by stem cells, which can restore any temporary loss of function.



**2.** More-significant damage can cause some cells to die off and obstruct tubules, leading to the loss of some nephrons, which are replaced with fibrous tissue.



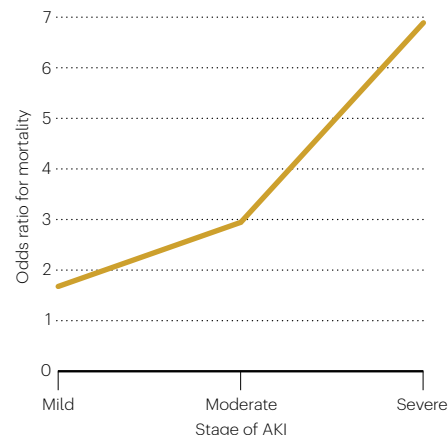
**3.** In the most advanced cases, several nephrons are lost and the rate at which blood is filtered falls considerably. The few remaining nephrons significantly increase in size.



### Mortality risk

AKI is classified as mild, moderate or severe on the basis of the contents and quantity of urine that a person produces.

Even mild AKI might increase the risk of death for people in hospital. In the most severe cases, the odds of death have been estimated to be around six-times higher<sup>2</sup>. AKI also increases the chance of stroke and heart attack.

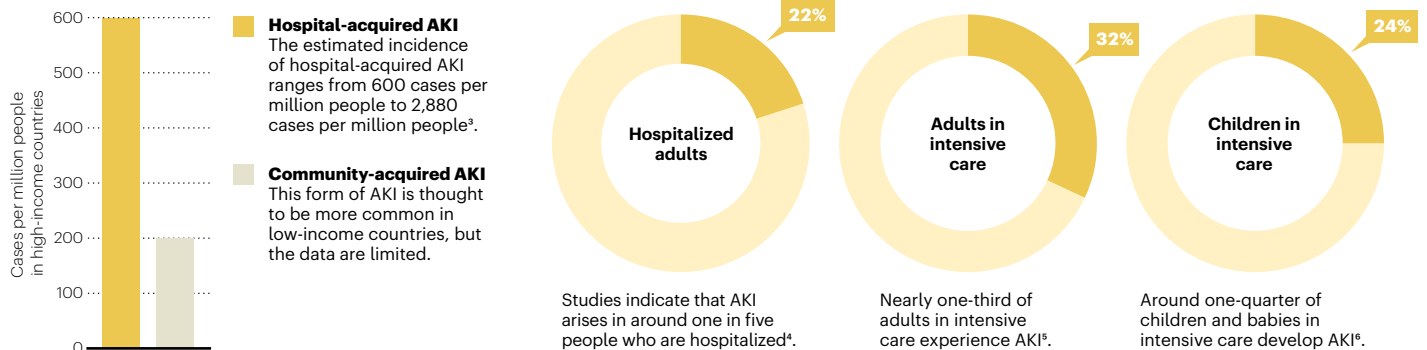




Watch an animation at [nature.com/collections/acute-kidney-injury-outline](https://nature.com/collections/acute-kidney-injury-outline)

## AN UNWANTED GIFT

AKI can be community acquired — as a complication of existing health problems, for instance — but in high-income countries it is thought to occur most commonly in hospitals as a consequence of factors such as surgery or sepsis.

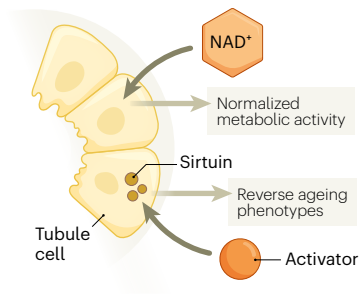


## A HELPING HAND

Currently, the only way to treat AKI is renal replacement therapy, which usually involves dialysis. This is generally effective, but it is costly and onerous for patients and is typically reserved for people who are severely ill. A number of clinical trials are now exploring alternative approaches for treatment and prevention.

### Metabolic pathways

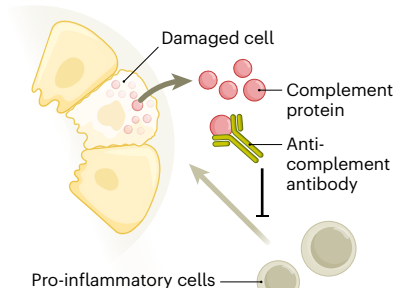
Interventions that strengthen the metabolic function of tubule cells could insulate against AKI damage. These include drugs that replenish nicotinamide adenine dinucleotide (NAD<sup>+</sup>) — a metabolite that is depleted in cells affected by AKI — and agents that delay aspects of cellular ageing through the sirtuin pathway, which is involved in metabolic regulation.



### Inflammation

AKI activates parts of an immune signalling cascade known as the complement pathway, provoking a damaging inflammatory response.

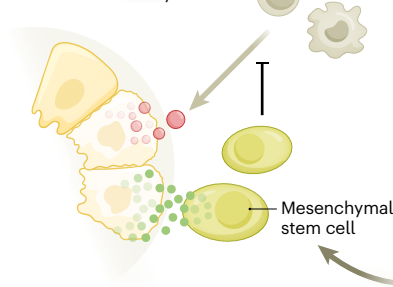
Treatments, such as antibodies, that interfere with the proteins involved in this pathway could limit inflammation and cell death.



### Regeneration

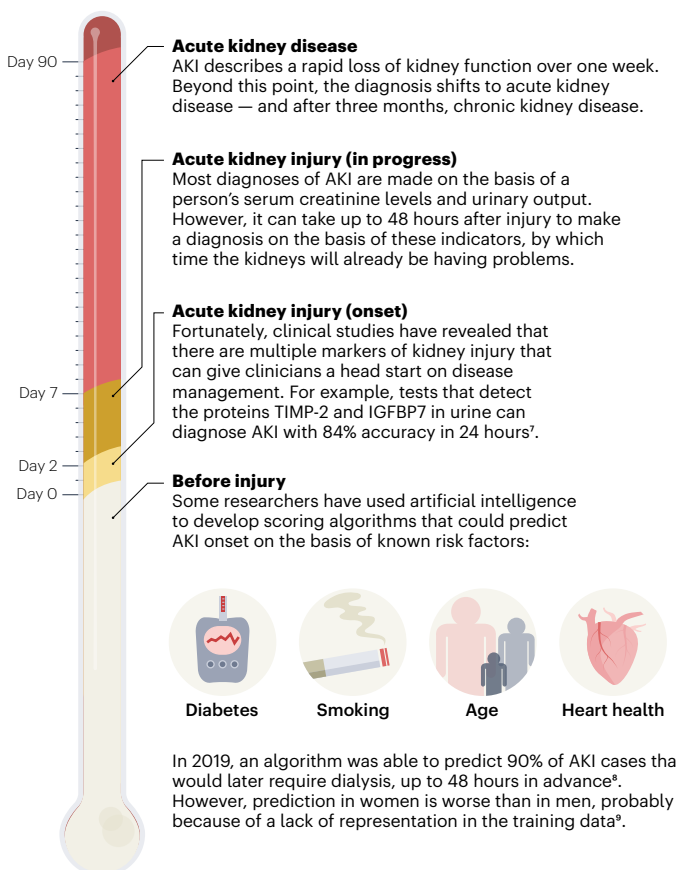
Infusions of mesenchymal stem cells derived from bone marrow or adipose tissue might be able to quell inflammation.

These cells might also secrete molecules that stimulate tissue regeneration.



## AN EARLIER START

Without intervention, AKI can give rise to chronic kidney disease (see [go.nature.com/3s83am6](https://go.nature.com/3s83am6)). Measures such as fluid management, blood-pressure monitoring and changes in medication can avert this crisis, but many cases of AKI are identified too late. Diagnostic tools that are currently in development could make a difference.



## REFERENCES

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