Factsheet
Acute kidney injury

CPPE
CENTRE FOR PHARMACY POSTGRADUATE EDUCATION

Contents

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Introduction

Acute kidney injury (AKI) is a term used to cover a spectrum of injury to the kidneys.[1] This term replaced acute renal failure (ARF), because 'AKI' betters conveys the fact that kidney injury can occur before failure.

- AKI is common
- AKI is associated with significant harm
- AKI produces significant costs

It is important to recognise that the development of AKI is often preventable, and the course of AKI is modifiable with good recognition, management and follow-up. However, there have been concerns that suboptimal care has contributed to the development of AKI. [1],[2]

In response to the scale of the problem, in 2012 the NHS launched a major campaign to reduce avoidable harm and death to patients with AKI known as Think Kidneys, an NHS program initially led by NHS England in partnership with the UK Renal Registry (UKRR). The UKRR collates and analyses data from UK renal centres and hospital laboratories, reporting on approximately 67,000 people on renal replacement therapy (RRT) (ie, with a kidney transplant or on dialysis) and on about 500,000 people with an AKI each year.

Alongside setting several examples of good practice guidance, Think Kidneys facilitated the development of the NHS England-funded AKI warning test score, now mandated by the NHS patient safety directorate and described later in the factsheet.[1, 3]

Think Kidneys Disclaimer: As a result of the significant contribution and considerable work of the Think Kidneys program, you will see several references to it throughout this factsheet. The NICE Clinical Knowledge Summary (CKS) for AKI, reviewed as recently as July 2023, also continues to include best practice guidelines developed as part of the Think Kidneys program as the basis of several of its recommendations. However, we have noticed that a number of the guidance documents on the Think Kidneys website that are referenced here, in the NICE CKS and also in the 2018 UK Kidney Association (UKKA) Clinical Practice Guidelines for AKI are overdue their respective review dates. We would therefore advise caution in the use of these Think Kidneys sources as sole references for clinical information. As always, please refer to up-to-date UKKA or NICE CKS/CG sources where appropriate.

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Definition

AKI is characterised by a decline in renal function over hours or days that can result in failure to maintain fluid, electrolyte and acid-base homeostasis.[1] The sudden deterioration of kidney function might be caused by – for example – dehydration, sepsis or heart attack.

NICE guideline Acute kidney injury: prevention, detection and management [NG148] recommends defining acute kidney injury by any of the following criteria:

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- *'a rise in serum creatinine of 26 micromol/litre or greater within 48 hours*
- *a 50 percent or greater rise in serum creatinine known or presumed to have occurred within the past seven days*
- *a fall in urine output to less than 0.5 mL/kg/hour for more than six hours in adults and more than eight hours in children and young people*
- *a 25 percent or greater fall in eGFR in children and young people within the past seven days'.*[(2)]

AKI can be staged based on severity. Increasing severity of AKI correlates with higher risk of worse outcomes.[(3)] In 2012, the organization Kidney Disease: Improving Global Outcomes (KDIGO[a]) produced a Clinical practice guideline for acute kidney injury[b] which includes AKI staging information. The information in Table 1 is taken from this KDIGO guideline.[(4)] More recently, in 2018-19, the Renal Association (now incorporated into the UKKA) Clinical Practice Guideline for AKI, endorsed the continued use of this KDIGO system for the diagnosis and staging of AKI.[(5)]

Table 1. Staging of AKI [(4)]

Stage	Serum creatinine	Urine output
1	1.5 to 1.9 times baseline OR greater than or equal to 0.3 mg/dL (greater than or equal to 26.5 micromol/litre) increase	less than 0.5 mL/kg/h for 6 to 12 hours
2	2.0 to 2.9 times baseline	less than 0.5 mL/kg/h for greater than or equal to 12 hours
3	3.0 times baseline OR increase in serum creatinine to greater than or equal to 4.0 mg/dL (greater than or equal 353.6 micromol/litre) OR initiation of renal replacement therapy OR, in patients less than 18 years, decrease in eGFR to less than 35 mL/min/1.73 m^2	less than 0.3 mL/kg/h for greater than or equal 24 hours OR anuria (absence of urine production) for greater than or equal 12 hours

In the following video, Richard Fluck, the former national clinical director for renal disease for NHS England, speaks about AKI. The video was recorded at the start of the original Think Kidneys campaign from 2012.

[a] KDIGO is a global organisation developing and implementing evidence-based clinical practice guidelines in kidney disease.
[b] The KDIGO website (*accessed July 2023*) indicates that this guideline is in the process of being updated.

Some statistics may have changed, but the importance of understanding and acting on AKI to prevent avoidable harm remains relevant today.

Think Kidneys video

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Prevalence and incidence

Kidney Care UK[6] reports that:

- AKI affects 1 in 5 people admitted to hospital as an emergency and may be more deadly than a heart attack.
- In the UK, around 100,000 deaths each year are associated with AKI; that's equivalent to ten people every hour. Research shows that 30 percent of these could be prevented with the right care and treatment.
- The costs to the NHS of AKI are estimated to be between £434 million and £620 million per year, which is more than the costs associated with breast cancer, or lung and skin cancer combined.

AKI is commonly associated with acute illness. It is reported that more than 15 percent of those admitted to hospital in an emergency develop Stage 1 AKI.[1] Incidence of AKI is also increasing in the UK, possibly as a result of an ageing population with increasing comorbidities. Better detection methods may also play a part in the increase in reported incidence of AKI.[1]

Signs and symptoms

In the early stages, AKI may be symptomless. Some people may produce less urine than usual but this isn't always the case. The following symptoms can develop rapidly if someone with AKI deteriorates:

- nausea and vomiting or diarrhoea; evidence of dehydration
- reduced urine output or changes to urine colour
- new or worsening confusion, fatigue and drowsiness.[1]

For a personal story about AKI, read *Michael's story – a patient's experience of acute kidney injury* on the Think Kidneys website.

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Causes/risk factors

The causes of AKI can be divided into three categories, although more than one cause is often present.[1]

Pre-renal
Pre-renal causes are the most common type of AKI. A pre-renal AKI is a result of reduced blood flow to the kidneys. Reduced blood flow can be caused by hypovolaemia (low blood volume), reduced cardiac output, or hypotension. Medicines may cause a pre-renal AKI by reducing blood pressure, circulating blood volume (eg, loop diuretics), or by affecting renal blood flow (eg, angiotensin-converting enzyme (ACE) inhibitors, angiotensin receptor blockers (ARBs) and non-steroidal anti-inflammatory drugs (NSAIDs)).[1] A pre-renal AKI can also be caused by systemic vasodilation, for example in sepsis.[1, 7]

Intrinsic renal (or intrarenal)
Intrinsic causes are due to structural damage to the kidney tissues, and may be a result of persistent pre- or post-renal causes. Damage may also be caused by medicines such as antibiotics, X-ray contrast media or chemotherapy. Types of structural damage may be categorised as vascular, glomerular, tubular or interstitial, depending on which area of the kidneys is affected.[1]

Post-renal
This is the least common cause of AKI (accounting for around 10 percent of cases) and is due to obstruction of the flow of urine out of the kidneys. This can be caused by renal stones, blocked catheters, an enlarged prostate or genitourinary masses.[1]

Risk factors for AKI include:

- aged over 65 years
- history of AKI
- chronic kidney disease
- symptoms or history of urological obstruction
- chronic conditions such as heart failure, liver disease and diabetes mellitus
- neurological or cognitive impairment or disability (which may limit fluid intake because of reliance on a carer)
- sepsis
- hypovolaemia (low blood volume)
- oliguria (urine output less than 0.5 mL/kg/hour)
- use of medicines that negatively impact on the kidneys within the last week (especially if hypovolaemic), for example NSAIDs, ACE inhibitors, ARBs and diuretics
- exposure to iodinated contrast agents (used in radiography) within the past week
- cancer and cancer therapy (risk will depend on the type of cancer, proposed treatment and premorbid risk factors)
- immunodeficiency, for example human immunodeficiency virus (HIV) infection
- toxins such as some herbal remedies, poisonous plants and animals. [1, 8]

On the Think Kidneys website you will also find the resource *Communities at risk of developing acute kidney injury*, which gives detailed information about patient groups who are at risk of AKI in both secondary and primary care. This document can be found on the Pharmacists page, where you will also find examples of patient leaflets, including an easy-read version.

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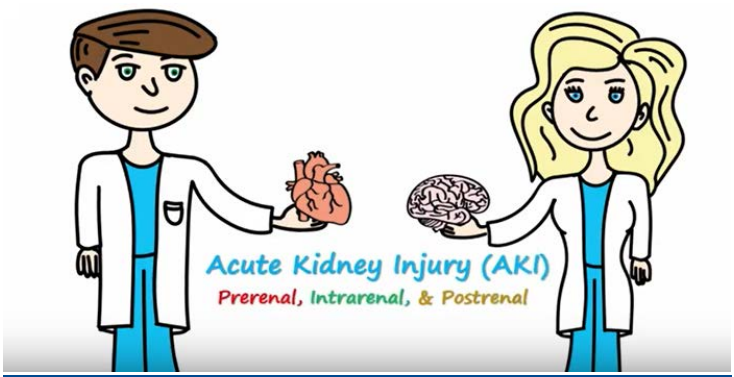
Pathophysiology (mechanism of disease)

Watch the following video for an introduction to the pathology of pre-renal, post-renal and intrarenal AKI.

PhysioPathoPharmaco – Acute Kidney Injury (AKI): Prerenal, Intrarenal, Postrenal



Please note that in this video the term 'nephrotoxic' is used. Think Kidneys and UKKA recommend that:

> 'the term "nephrotoxic" should be used with caution. Few medications truly have direct toxic effects on the kidneys, but several have the potential to impair renal function if used under certain circumstances, such as where the patient has a degree of chronic kidney disease in conjunction with hypovolaemia and acute illness. Under these circumstances, continued use of these medications may further exacerbate an episode of AKI.' (9)

For additional interest, and more detailed information on the pathophysiology of AKI, access the following *Comprehensive Physiology* article: Pathophysiology of acute kidney injury.

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Prognosis and complications

Kidney Disease Improving Global Outcomes (KDIGO) guidance states that 'the kidney is a fairly robust organ that can tolerate exposure to several insults without suffering significant structural or functional change. For this reason, any acute change in kidney function often indicates severe systemic derangement and predicts a poor prognosis'.(4)

The prognosis of AKI varies depending on clinical setting, the underlying cause and any comorbidities, but early detection is likely to improve prognosis.[1]

Complications of AKI can be serious and include electrolyte imbalances (including potentially serious hyperkalaemia), metabolic acidosis, volume overload, uraemia (raised urea and other nitrogenous waste), chronic kidney disease and end-stage renal disease.[1] For more information about these complications, visit the NICE CKS section Acute kidney injury - Complications.

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Diagnosis/detection

AKI is detected based on clinical assessment of signs and symptoms, risk factors, urine output and serum creatinine levels. Early detection and treatment of AKI may improve outcomes.[4, 10] Given that approximately two thirds of AKI cases begin in the community,[10] those working in primary care have a crucial role to play in prevention, early detection and management, as well as in post-AKI care.[3]

AKI warning stage test result

The Acute kidney injury (AKI) algorithm endorsed by NHS England is used by laboratories to identify potential cases of AKI based on creatinine levels. A biochemistry laboratory will communicate an AKI warning stage test result directly to general practice clinical systems, which enables the primary care team to take action based on their clinical judgement. [3, 11] These early warning alerts are intended less as a diagnostic label, and more as a trigger to prompt a response when AKI is detected.[1] To learn more about AKI warning stage test results, see the NICE CKS section *How should I respond to AKI warning stage test results?*[1]

Based on consensus expert opinion, Think Kidneys produced *Acute kidney injury best practice guidance: Responding to AKI warning stage test results for adults in primary care*, on which the NICE information above is based. Think Kidneys' resource includes the following quick guides:

- Table 1. Acute kidney injury: recommended response times to AKI warning stage test results for adults in primary care
- Table 2: Recognising and responding to acute kidney injury for adults in primary care

The Royal College of General Practitioners (RCGP) has also produced the *Acute kidney injury toolkit* which complements the Think Kidneys and NICE guidance, and includes information on recognising and responding to AKI warning stage test results for adults in primary care under the heading *Recognition and Response*.[10]

NICE guidance on prevention, detection and management

NICE guideline *Acute kidney injury: prevention, detection and management [NG148]* outlines:

- recommendations for assessment of risk of AKI (*Section 1.1 Assessing risk of acute kidney injury*)
- detection of AKI (*Section 1.3 Detecting acute kidney injury*)
- identifying causes of AKI (*Section 1.4 Identifying the cause(s) of acute kidney injury*).

Interpreting biochemistry information
To work through a biochemistry case study which looks at a person who experiences AKI, visit CPPE's Biochemistry learning gateway page. Further information on interpretation of biochemistry data can also be found in the *Further reading* section of this same learning gateway page.

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Prevention

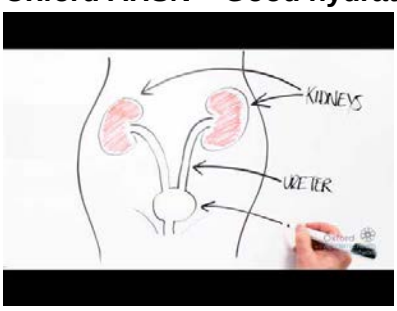
Prevention of AKI remains a national priority. The NICE CKS Acute kidney injury – Scenario: Prevention of acute kidney injury covers prevention of AKI.

The Think Kidneys website provides information for the public on how to keep their kidneys healthy. They offer an educational video, written information and a series of posters which can be found on their campaign page.

Prevention in older people and those living in care homes
Think Kidneys also developed practical resources to raise awareness and help with the prevention, detection and management of AKI in care homes on their Care homes webpage. This includes the learning guide *Care homes: Acute kidney injury and hydration guide*, which contains example care plans in Appendix 3 (page 20).

In 2018, the Oxford Academic Health Science Network (Oxford AHSN) produced a video series about the importance of good hydration in keeping care home residents happy and healthy. The link to the first video is below; the subsequent videos in the series will play after it ends.

Oxford AHSN – Good hydration! – improving hydration for care home residents



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Treatment

Management of AKI is dependent on the staging and presence of complicating factors. Read *Section 1.5 Managing acute kidney injury* of *Acute kidney injury: prevention, detection and management [NG148]* for information about the management of those who develop AKI.

All persons who develop AKI should have a thorough review of their medicines to eliminate the potential cause or contributory factor for AKI, and ensure all medicines are clinically appropriate. In March 2023, NICE updated the Quality Standard for AKI, including the requirement that adults discharged from hospital after acute kidney injury should have a clinical review within 3 months, or sooner if they are at higher risk of poor outcomes. [12]

To support this medication review process, see Section 5 of the UKKA Guidance on AKI (starting on page 70), including Table 4 on page 74 which lists specific higher-risk medicines and some suggested actions in AKI. This updates the high risk medicines table in the *Think Kidneys* *Guidelines for medicines optimisation in patients with acute kidney injury* which are now some years out of review date. Despite this, you may find the generic introduction to medicines optimisation (pages 1-4 of this *Think Kidneys* guidance) helpful as a basis for your understanding of review in AKI.

In many cases of AKI, it may be necessary to withhold medicines used to treat cardiac conditions such as ACE inhibitors, ARBs and diuretics. As a pharmacy professional you can help to ensure that medicines get reintroduced and re-titrated as appropriate following AKI. In patients with heart failure with left ventricular systolic dysfunction, it may be necessary to refer to the specialist heart failure team for advice.

More information about managing these types of medicines can be found in the following Think Kidneys documents (again, be mindful of their review dates):

- Changes in kidney function and serum potassium during ACEI/ARB/diuretic treatment in primary care
- When or if to re-start ACEI, ARB, diuretics and other antihypertensive drugs after an episode of acute kidney injury

Primary care professionals also need to be mindful of the recommendation in the NICE Guideline [NG203] for chronic kidney disease to 'monitor individuals for the development or progression of chronic kidney disease for at least 3 years after acute kidney injury (longer for people with acute kidney injury stage 3) even if eGFR has returned to baseline'.[13]

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Patient support

You can find information to support patients on websites for the UKKA, Think Kidneys and Kidney Care UK. Here is a link to a patient leaflet specific to AKI. Think Kidneys has an Information for the public page with links to support organisations. Pages on this and UKKA also offer supportive resources for health professionals including pharmacists and care homes and general advice for those working in primary care and secondary care.

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Further resources

CPPE's *Fundamentals of renal therapeutics* e-course aims to develop pharmacy professionals' knowledge and skills in renal therapeutics. This includes an e-unit on AKI and another on CKD.

In addition to the recently reviewed NICE CKS already referenced above, the *KDIGO Clinical practice guideline for acute kidney injury* [4] aims to assist practitioners caring for adults and children at risk for or with AKI and also contains chapters on definition, risk assessment, evaluation, prevention and treatment.

The UKKA has also been producing clinical practice guidance on the management of patients with kidney disease since 1995. They are accredited by NICE, and you can find links to their work on the Guidelines and Commentaries page of their website.

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External websites

CPPE is not responsible for the content of any non-CPPE websites referred to on this page or for the accuracy of any information found there.

All web links were accessed on 14 November 2023.

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Last review: August 2023
Next review due: August 2024