- obstruction to urine outflow is the most common cause of functional renal impairment in the community but is uncommon in the ICU involves humoral and mechanical factors post-renal - typical causes include bladder neck obstruction from an enlarged prostate, ureteric obstruction from pelvic tumours or retroperitoneal fibrosis, papillary necrosis or large calculi clinical presentation:
- clinical presentation may be acute or acute on chronic in patients with long standing calculi. It may not always be associated with oliquria. this is used to define a syndrome where the principle source of damage is within the kidney and where typical structural changes can be seen on microscopy
- pathogenesis of parenchymal renal failure is generally immunological and varies from vasculitis to interstitial nephropathy Glomerulonephritis Interstitial nephritis Malignant hypertension aetiology - more than 1/3rd of patients who develop ARF in ICUs have chronic renal dysfunction due to factors such as age related changes, long-standing changes, long-standing Bilateral cortical necrosis hypertension, diabetes or renal vascular disease Amyloidosis Nephrotoxins Non-steroidal anti-Inflammatory drugs: is lactain ambliotics (interstitial nephropathy) drug-induced renal failure
- many cases of drug-induced renal failure improve rapidly on removal of the offending agent and accordingly a drug history is important in all cases of renal failure parenchymal renal failure henatorenal failure (i) general:
- a form of ARF that occurs in the setting of severe liver dysfunction in the absence of other known causes of ARF. Typically, it presents as progressive oliquria with a very low urinary pathogenesis is not well understood but it is thought to involve severe vasoconstriction (ii) differential diagnosis:
- other causes of acute renal failure are more common than hepatorenal syndrome in severe liver disease. They include sepsis, paracentesis-induced hypovolaemia, alcoholic cardiomyopathy Chronic or acute liver disease with advanced hepatic failure and or any combination of these (iii) prevention and treatment:

- the use of albumin in patients with SBP has been shown to reduce renal failure in an RCT Low GFR defined by serum creatinine > 130 mmobil or creatistudies suggest vasopressin derivatives (terlipressin) may improve GFR rhabdomyolysis-associated ARF Absence of shock, bacterial infection and recent creatment with - accounts for 5-10% of cases of ARF in ICU depending on the setting - pathogenesis involves pre-renal, renal and post renal factors 30/12/07 No sustained improvement of renal function after expansion - typically seen following major trauma, drug overdose & vascular embolism
 - treatment principles are based on retrospective data and include aggressive fluid resuscitation, elimination of causative agents, correction of compartment syndromes, alkalinisation of urine Proteinuria <0.5 g/day, and no ultrasonographic evidence of (pH>6.5), and maintenance of polyuria the fundamental principle of acute renal failure is to treat its cause. - if pre-renal factors contribute these must be identified and haemodynamic resuscitation quickly instituted - intravascular volume must be maintained or rapidly restored & oxygenation must - mid-avascular volume flust be maintained or a body genation must be maintained; an adequate haemoglobin concentration should be maintained - once intravascular volume has been restored, some patients remain hypotensive in these patients autoregulation of renal blood flow may be lost & increasing MAP \* The additional criteria relate to factors that are commonly present, but with vasopressors may increase GFR; the role of additional fluid in a patient with normal blood pressure and cardiac output is questionable - despite the above measures pre-renal renal failure may develop if cardiac output

is inadequate nephroprotective drugs:

- evidence of efficacy or safety is lacking; however, this agent is a tubular diuretic and occasionally increases urine output --randomised controlled trial evidence in critically ill patients shows that low-dose dopamine is no more effective than placebo in prevention of renal dysfunction; however,

in patients with low cardiac output dopamine may increase cardiac output, renal blood flow and GFR (as would dobutamine or milrinone)

animal experiments offer some encouraging findings; however, no human data exist to

these agents may protect the loop of Henle from ischaemic from decreasing its transport related workload; however, there are no double blind randomised controlled trials proving that these agents reduce the incidence of renal failure

- several studies support the view that loop diuretics may decrease the need for dialysis in patients developing acute renal failure. They appear to achieve this by inducing polyuria which results in the prevention or easier contorl of volume overload, acidosis & hyperkalaemia

- because avoiding dialysis simplifies treatment and reduces the cost of care, loop diuretics

ITU with ARF, or who subsequently develop ARF, remains high at 23-80%.

- if the cause of ARF has been removed and he patient has become physiologically stable slow recovery

occurs over 4-5 days to 3-4 weeks; in some cases the urine output can be above normal for several days

- Renal replacement therapy (RRT) is now a routine element of organ support in the intensive therapy unit (ITU). Yet despite great improvements in the recognition and management of ARF, including RRT, the mortality of patients who are admitted to

- other experimental agents include theophylline, urodilatin and anaritide (a synthetic atrial

(i) 'low dose' dopamine

Vasculitis

Malignancy

Radiocontrast agents

Aminoglycosides Amphotericin

Solphorocoides

Methotrexate

Cyclospann A

FK-506 (Tacrolimus)

Avriour

diagnostic criteria for hepatorenal syndrome

nine clearance < 40 mil/min

phrotoxic drugs

with 1.5 l'isotonic saline

Urine volume <500 ml/day

Series sodium < 130 romol/l

Urine osmolality > plasma osmolality
Urine red blood cell count <50 per high power field

Urine sodium < 10 mmot/

renal tract disea

Additional criteria!

ute rena failure [created by Paul Young failure

prevention

prognosis

(iii) resustration.

- Should reversible elements be corrected before the definition is applied? For example, is the correction of mean arterial pressure and filling pressures to normal physiological values necessary before ARF can be diagnosed? (iv) Nephrotoxic drugs: - what are the implications of nephrotoxic drugs, e.g. gentamicin or non-steroidal anti-inflammatory drugs, for the definition and the aetiology? (v) Pathophysiology: The underlying pathophysiological process is thought to be important to outcome.

Should this be included if it is known or should it be categorized according to aetiology? - Causes of postrenal ARF often have a very different natural history and outcome: if this is identified, should they be excluded? (vii) Confounding factors: - does an upper gastrointestinal haemorrhage or rhabdomyolysis need to be ruled out? - Acute renal failure (ARF) is a common problem in intensive care. It is said to have an incidence of 10-25%. The diagnosis of ARF is not difficult, although the term ARF encompasses a broad range of definitions with no universally accepted definition The combined published results for ARF, its incidence and outcome are: o An incidence of 10-25%.

o Patients who are admitted with or develop ARF on the ITU have an overall mortality of 23-80% o Patients with ARF not requiring RRT have a mortality of 10-55% o Patients with ARF indirequing RRT have a mortality of 10-93% or Patients who develop ARF that requires RRT have a higher mortality of 57-80% o Of those patients with ARF who receive RRT and survive, only 5-30% require longer-term dialysis. The mortality of patients who are admitted to ITU with ARF, or who go on to develop ARF, remains high. This wide variation in published results (up to six-fold) is due in part to the following problems that are not specifically addressed in the majority of studies:

(i) Inclusion criteria vary between studies because the definition of what constitutes ARF is so variable (ii) There is significant heterogeneity of the population in terms of severity of illness and demographics. (iii) Many different disease processes can cause ARF, so one may not be comparing like with like Is it the incidence of ARF that varies or the incidence of the disease process in different centres? (iv) Different disease processes have different incidences of renal damage and mortality. (v) Some centres are moving to the early initiation of RRT, often prior to the development of 'criteria' to define ARF. Should this group be considered separately? (vi) Outcome analysis varies: 14-day, 15-day, 28-day and 30-day mortality have all been used as endpoints. Alternatively, ICU, in-hospital or 1-year mortality figures have been used. general investigations include: (i) examination of urinary sediment and exclusion of a urinary tract infection (most if not all patients) (ii) careful exclusion of nephrotoxins (all patients) (iii) exclusion of obstruction (some patients) special investigations may include: (i) CK and myoglobin (for rhabdomyolysis) (ii) chest x-ray, blood film
(iii) specific antibodies (anti-GBM, antidsDNA, anti-smooth muscle etc) (iv) LDH haptoglobin unconjugated bilirubin (v) cryoglobulins (vi) Bence Jones Proteins (vii) renal biopsy Pre-rena Acute tubular Laboratory test failure necrosis investigation > 500 Urine osmolality; < 400 mOsm.ka<sup>-1</sup> Urine sodium < 20 > 40 mmol.l-1 Urine : plasma > 40 < 20 creatinine ratio Normal, occasionally Renal tubular Urinary sediment hyaline or finely epithelial cells. granular and muddy granular casts brown granular casts differentiation of prerenal and renal failure has limited clinical implication because they are part of the same continuum and treatment is the same - this form of ARF is the most common in ICUs - indicates that the kidney malfunctions predominantly because of the systemic factors which diminish renal blood flow and decrease GFR or by alteration of intraglomerular haemodynamics pathophysiology: - renal blood flow is decreased by: (i) decreased cardiac output (iii) hypotension
(iii) raised intraabdominal pressure (decompression should be considered when the intrabdominal pressure is greater than 25-30mmHg above the pubis) in septic patients with hyperdynamic circulations there may be adequate global blood flow to the kidney but intrarenal shunting away from the medullar causing medullary ischaemia or efferent arteriolar dilation thus decreasing GFR - if the systemic cause of renal failure is rapidly removed renal function improves relatively rapidly - several mechanisms are involved in the development of renal injury in pre-renal failure:

(i) ischaemia of the outer medulla with activation of tubuloglomerular feedback (ii) tubular obstruction from casts of exfoliated cells (iii) interstitial oedema secondary to back diffusion of fluid (iv) humorally mediated afferent arteriolar renal vasoconstriction (v) inflammatory response to cell injury and local release of mediators (vi) disruption of normal cellular adhesion to the basement membrane (vii) radical oxygen species induced apoptosis (viii) mitogen-activated protein kinases-induced renal injury

- Numerous papers highlight the lack of a universal definition for ARF in ICU. One review of the subject found 26 different definitions of postoperative ARF in 26 studies - Even a consensus conference of intensivists and nephrologists on the subject in 2000 could not provide an adequate, universal definition. This makes it difficult to draw

- A specific definition of disease with tight exclusion criteria is essential in the design of

- Is the absolute increase or the rate of increase of serum creatinine and urea important for the definition? Are acid-base imbalance, serum potassium level and urine output

(ii) Chronic renal impairment:

- How is this incorporated into the definition and what impact does it have on diagnosis

conclusions from all the individual trials that are published.

clinical studies of a heterogeneous syndrome

(i) Biochemistry:

definition

significant in the diagnosis?

management and outcome? (iii) Resuscitation