MANAGEMENT ISSUES IN RENAL MEDICINE

M. King, Specialist Registrar in Renal Medicine, Renal Medicine Unit, Royal Infirmary of Edinburgh

SESSION 1

RECOMBINANT HORMONES IN RENAL DISEASE

Chaired by Professor Andrew Rees, Regius Professor of Medicine, University of Aberdeen

Erythropoietin

Dr Donald Richardson, Consultant Nephrologist, York District Hospital

In the UK at present most recombinant erythropoietin is used in those with established end-stage renal failure (ESRF), defined by the World Health Organisation (WHO) criteria as a creatinine clearance of less than 60 mls/min. Most patients in this category will never reach ESRF, and most will never see a nephrologist, yet these patients have an increased morbidity and mortality associated with their renal disease, and renal-related anaemia is just one of their problems. The haemoglobin level may start to fall when the glomerular filtration rate (GFR) is less than 40 mls/min. Earlier intervention and treatment of this group of patients may delay progression to ESRF. The question raised was whether physicians should try and attend to these patients sooner, both to treat complications (anaemia being one of these) and to attempt to delay the progression to ESRF.

The need for earlier intervention is highlighted by current practice. Haemoglobin takes a long time to rise after initiation of erythropoietin therapy, and most patients continue to be exposed to long periods of anaemia when eventually commenced on dialysis. Epidemiologically, a low haemoglobin level is associated with increased risk from cardiovascular death. The presence of left ventricular hypertrophy (LVH) increases the risk of death by a factor of 2·7.

Only 16% of patients have a normal echocardiogram (ECG) at the start of dialysis.[1] Left ventricular hypertrophy occurs early in chronic kidney disease and deteriorates rapidly with progressive cardiac dilatation and hypertrophy, occurring especially within the first year on dialysis. Although left ventricular dilatation may be irreversible, LVH is more likely to stabilise, or even regress, if the haemoglobin level is normalised. In addition, large studies now support the proposed target of erythropoietin therapy of 11 g/dl (haematocrit 33%), with mortality being lowest in those who have reached this target.[2]

The evidence base for the use of erythropoietin and its cost-effectiveness is ever-increasing. As well as the positive physiological effects discussed earlier, models have shown that erythropoietin usage may reduce overall costs, with less hospitalisation.[3] In addition, Valderrabano *et al.* reported an improved physical and psychological quality of life,[4] whilst Revicki *et al.* reported improved levels of physical function and improved ability to cope at home.[5]

In conclusion, although studies of haemoglobin normalisation are ongoing, anaemia in chronic kidney disease is probably under-treated. Cardiovascular disease is the most common cause of death in renal patients, and there are strong epidemiological links between cardiovascular disease, anaemia and death in patients with chronic kidney disease. To improve outcome, and reduce treatment and maintenance costs, physicians may need to concentrate more on treatment at the time of presentation.

Growth hormone in chronic renal failure

Dr Heather Maxwell, Consultant Paediatric Nephrologist, Royal Hospital for Sick Children, Glasgow

Short stature and poor growth are common features in children with chronic renal disease, and they pose a significant problem. The important outcome measurement is 'final height', but a useful measure to assess height in children is the mean height standard deviation score, i.e. how many standard deviations away from the mean is a height measurement.

Children with renal disease are short for a number of reasons, and in each individual stunted growth is likely to be multi-factorial. Important factors include nutrition/anorexia/vomiting; anaemia; salt and water loss; acidosis; renal osteodystrophy; and growth hormone (GH) resistance.

The current percentages of children in the UK on GH are 2–3% of renal transplant patients, 19% of peritoneal dialysis patients and 11% of haemodialysis patients; indeed, there may be slight under-treatment, with the percentages of children with height in the normal range being 70%, 60%, and 55% for transplant, peritoneal dialysis and haemodialysis patients, respectively.

The best chance of achieving final height for a child receiving renal replacement therapy is transplantation. Even catch-up growth can occur after transplantation. Final height is improved with good graft function, younger age at the time of transplantation, better height standard deviation score at time of transplantation and lower

steroid dosage.

The use of recombinant growth hormone (rhGH) for short stature in renal disease is evidence-based. Fine *et al.* showed that GH significantly improved height velocity in children with a GFR <50 mls/min over a two-year period.[6] Studies of GH in transplanted patients found that height standard deviation scores improved with rhGH. Berard *et al.* has shown significant improvement in height velocity for children already on dialysis.[7]

Although these studies show benefit in height velocity and height standard deviation score measurements for the periods of childhood and early adolescence, the evidence is less conclusive for the effect GH has on final adult height. However, the evidence that does exist would suggest a positive outcome with the use of GH.[8]

Treatment with GH raises other problems. It is an expensive treatment and requires daily injections. In addition, a number of side-effects and concerns regarding treatment are recognised. Possible effects of GH include glucose intolerance, renal bone disease, benign intra-cranial hypertension, malignancy and increased risk of acute rejection in transplant patients. Perhaps another possibly detrimental effect on renal function is based on the observation that acromegalic patients can suffer from hyper-filtration injury. This fear is probably largely unjustified, and available evidence suggests that GFR is not reduced more rapidly by treatment with rhGH.

Growth hormone is a mitogen and, as such, it is not surprising that there could be an association of its use with malignancy. The evidence for this is weak at present, and is limited to case reports associating its use to renal cell carcinoma.[9] Most clinical trials have shown no increase in malignancy.

In summary, growth retardation is an important problem in children with renal disease. The aim should be to promote growth at an early stage, preferably before ESRF ensues, since growth on dialysis is often poor. The best method of obtaining a good height in those who have reached ESRF is transplantation. Growth hormone has a significant role and should be used in those who do not improve with conservative measures (such as a better diet); there is substantial evidence that its use will increase growth and probably result in an improved final height.

Abuse of erythropoietin and growth hormone

Professor Michael Greaves, Professor of Haematology, University of Aberdeen

We have all come across the television and newspaper reports relating to the abuse of these substances by sportspeople. Professor Greaves provided some insight into what goes on behind the headlines with a most interesting lecture.

In sports medicine, and particularly for an endurance athlete in an 'aerobic sport', one of the key factors that has a bearing on performance is VO2max, which is defined as the highest rate at which oxygen can be taken up and utilised during severe exercise. Endurance training, for example, should improve the VO2max, but actual VO2max is determined by a number of factors that are mainly physiological and relate to the cardio-respiratory system. VO2max increases with training due to the effect of exercise on the heart, with an increase in stroke volume; there is also an additional but small effect due to an increase in muscle mass.

There are a number of illicit ways of increasing your VO2max. Athletes have previously used blood auto-transfusion as a means of increasing performance. Blood would be collected prior to competition, stored and then it would be re-transfused immediately before the event. Evidence exists to show that such auto-transfusion increases haemoglobin levels and increases VO2max.[10] Equally, there is evidence that erythropoietin enhances performance. Birkland *et al.* showed that recombinant human erythropoietin (rhEPO) at 5,000 units three times a week for one month would enhance VO2max.[11] The downside is that, in excess, erythropoietin can be detrimental to performance since high blood viscosity may impair perfusion and increase cardiac work. Thus, rhEPO may be dangerous to health: there have been 18 reported deaths of cyclists relating to erythropoietin usage and associated high haematocrits.

The main problem with substance abuse in sport is that of detection. In particular, the problem of out-of-competition use is hard to discover. Serum erythropoietin levels are usually normal within 72 hours of administration, and therefore tests would only indicate recent use. Lasne and de Ceaurriz have devised a method of detection based on chemiluminescent immunodetection of erythropoietin in urine after isoelectric focusing.[12] Despite this being a reliable test, its use is limited again by the fact that detection can only occur during present usage, due to the short half-life of this polypeptide. Others have used complicated models for detecting erythropoietin abuse. Such models are based on commonly found characteristics of erythropoietin abusers such as a high haematocrit, the presence of reticulocytosis, the levels of serum transferring receptor and the percentage of macrocytic hypochromic cells, as well as an absolute erythropoietin level itself.[13] Although such models may well be more powerful predictors of those abusing erythropoietin, they are not yet validated so they would not stand up to serating in a court of law; therefore they are unlikely to become of practical use.

Perhaps less in the eye of the media is the abuse of GH, which is more attractive to sprinters and strength athletes, given that it increases muscle bulk. At present, there is no reliable method for exogenous GH detection, but a

relative deficiency of a 2010 Dalton protein (the size of endogenous GH following post-translational modifications) and excess of 2200 Dalton protein (the size of the recombinant protein) might suggest exogenous administration of the recombinant protein.

A wider issue open for discussion is whether doping control is appropriate at all. When samples have to be collected, there is the issue of infringement of civil liberties. There are certainly inconsistencies in the application of testing and detecting methods and punishments at present. It can also be argued that no matter how sophisticated our detection methods become, athletes and their mentors will always be one step ahead of the game, especially when there remains so much at stake.

SESSION 2

FLUID BALANCE AND BLOOD PRESSURE

Chaired by Professor Andrew Rees, Regius Professor of Medicine, University of Aberdeen

Diuretics

Dr William D. Plant, Consultant Renal Physician, Cork University Hospital

The thrust of this lecture was that doctors currently use diuretics in a way that is both misguided and without aim or objectives. 'What is it that we seek?' is the question we are told to ask ourselves before we embark on diuretic treatment. The answer might be that we desire fluid loss, but perhaps what we should be aiming for is natriuresis without electrolyte problems or metabolic problems, sufficient to restore a normal, steady state situation. A wealth of information exists about diuretics, and recently there has been a greater understanding of their actions and, in particular, their molecular sites of action on ion transporters.[15]

Frequently, when patients appear not to be responding to prescribed diuretics the term 'diuretic resistance' is applied to them. In fact, in such cases it is frequently the way that the diuretics are being prescribed that is at fault. In the words of Shakespeare's Julius Caesar, 'the fault, dear Brutus, lies not in our stars but with ourselves'.[14]

The tubule can be divided into sections that have characteristic functions, with characteristic transporters at various sites. A journey down the nephron starts at the proximal convoluted tubule (PCT), down the thick ascending loop of Henle (TALH), to the distal convoluted tubule (DCT) and finally to the cortical collecting duct (CCD). Sodium is filtered freely but less than 1% of it is excreted normally because most of it is reabsorbed (PCT (53%), TALH (37%), DCT (7%) and CCD (3%)). The various sections of the nephron do not act in isolation and respond to events that occur 'up-stream'. The reabsorption of sodium is under the influence of a number of external regulatory factors, in particular the action of angiotensin II, noradrenaline and dopamine.

Most sodium is reabsorbed in the PCT. The basolateral Na/K ATPase creates a 'hunger' in the cells for sodium. In fact, all tubular cells have their own transporter creating this 'sodium hunger'. In the PCT, this hunger is satisfied by the reabsorption of sodium utilising the Na/H antiporter. In the TALH, sodium reabsorption is by the NKCC2 co-transporter. On the luminal surface of the DCT there are a number of transporters, the most important of these being the NCCT transporter, which brings sodium and chloride into the cells. The CCD is a site of further sodium reabsoption, this time via epithelial sodium channels.

So the question is, 'what is really happening in cases of so-called diuretic resistance?'. A further question that should be asked is whether there is adequate natriuresis; the only way of knowing if this is being achieved is to measure the urinary sodium. In those who are achieving target (>100 mmol/day), there may be no net effect, unless the natriuresis is combined with adequate dietary salt restriction of <100 mmol/day.

The next problem may be one of diuretic delivery. In cases where diuretics appear not to be working, various pharmacokinetic and pharmacodynamic circumstances can be affecting diuretic achievement. Most diuretics are organic anions or cations that are highly protein-bound. They act on the tubular surface of the lumen but rather than being filtered, most are secreted in the PCT by exchangers and excretors. Pharmacokinetic considerations largely relate to bioavailability and drug delivery to the kidney. Hypoalbuminemia may decrease delivery, whilst coexisting liver or renal disease may produce other ions that compete for excretion. Pharmacokinetic effects may give rise to true diuretic resistance.

Pharmacodynamic circumstances may cause diuretic blunting. This occurs when there is tubular adaptation to diuretics. With prolonged diuretic therapy a new steady state is frequently obtained and the initially high state of natriuresis may fall. The new rate of natriuresis may be acceptable, but frequently one may want to go even further and perhaps by switching from bolus therapy to an infusion or by adding in further diuretic agents to perform sequential nephron blockade.

SYDNEY WATSON SMITH LECTURE

Chaired by Dr Niall D.C. Finlayson, President of the Royal College of Physicans of Edinburgh

Salt and water: a fine balance

Dr Burton D. Rose, Editor-in-Chief, UpToDate and Clinical Professor of Medicine, Harvard Medical School, Boston

The lecture emphasised the difference between salt and water regulation. An important fact to remember is that there is no predictable relationship between plasma sodium and extra-cellular fluid (ECF) volume. The way

the body regulates an increase in ECF volume is to increase urinary sodium excretion, and since volume is the major determinant of urinary sodium, there is no direct relationship between plasma sodium and sodium excretion. A state of too much water is termed hyponatraemia, and a state of too little water we call hypernatraemia.

However, plasma sodium is related to intra-cellular fluid volume. This is particularly important for the brain, since in hypernatraemia cells may shrink whilst in hyponatraemia water may move into the cells, which will swell. The symptoms of both hyponatraemia and hypernatraemia relate almost entirely to changes in brain volume, which in turn are related to the rate and the severity at which serum sodium concentration changes.

There are two basic protectors in water balance: the release of anti-diuretic hormone (ADH) and thirst. Hypernatraemia is commonly caused by water loss in excess of salt (as in diabetes insipidus or excessive insensible losses) or by sodium retention. Although ADH protects on a day-to-day basis against hypernatraemia, the ultimate protector is thirst. This is demonstrated by the fact that hypernatraemia is rare, even in cases of diabetes insipidus, since thirst always 'kicks in' as plasma osmolality increases. When water is available freely, the situation in which hypernatraemia can still occur is when thirst fails to produce an effect, as in adults with an impaired mental state.

Hyponatraemia is not the exact opposite of hypernatraemia. For social or habitual reasons we all continue to drink, even when not actually thirsty; thus, the ability to 'switch off' thirst is not readily available to us as a protective mechanism against the development of hyponatraemia. Most cases of hyponatraemia are therefore caused by states where there is inability to excrete enough water; they include primary polydipsia (including the use of ecstasy), hypovolaemic states and advanced chronic renal failure. Other rarer causes include hypoadrenalism, hypothyroidism and the syndrome of inappropriate anti-diuretic hormone (SIADH), such as in cancers. Of these, the most common are hypovolaemic states – which can be subdivided into true volume depletion, use of diuretics or heart failure – and hepatic cirrhosis.

Plasma sodium concentration is controlled by regulating water. Plasma osmolality is sensed by hypothalamic osmoreceptors that affect ADH and thirst, which, in turn, affect water intake and excretion. Disorders of plasma sodium are therefore caused by disorders in water balance and have nothing to do with disorders of sodium balance. Too much sodium we call oedema and too little sodium we call volume depletion or hypovolaemia. Volume is sensed in a different way to osmotic regulation, by effective tissue perfusion in the afferent arteriole regulating the rennin/angiotensin/aldosterone system, by the atrial regulating natriuretic peptide and by the carotid sinus regulating the sympathetic nervous system.

Plasma sodium concentration is important because hyponatraemia has a potential effect on brain water and may cause neurological symptoms. Studies have shown that the rate of change of the sodium concentration is the important factor. Slow reduction in plasma sodium to moderate levels is associated with very few symptoms, whilst rapid reduction to even moderate levels may cause death. This is because the brain can adapt and reduce cellular swelling by excreting solutes, but only over a relatively long period of time. With more rapid changes, the brain is exposed to potential osmotic damage.

Over-rapid correction of chronic asymptomatic hyponatraemia may result in osmotic axion demyelination and irreversible neurological damage, coma or death. Correction of plasma sodium at a rate of greater than 0·5 mEq/l per hour is associated with possible neurological damage.[16] However, animal studies suggest that the correction rate over 24 hours, and not the rate per hour, is important. Correction rate should not exceed 12 mmol/l per day. There is less in the literature regarding the correction of hypernatraemia. But too rapid correction of hypernatraemia in infants may be associated with seizures.[17]

An important physiological principle relevant to salt and water balance is that of steady state. The body adapts to changes and reaches a new steady state. For example, when starting the patient on diuretics, the best response is seen with the first dose. The sodium lost in the first few days before adaptation remains low, and therefore the plasma volume is lower but will not decrease any more. The important implication of this is that if diuretic dose is constant, then the fluid and electrolyte disturbances that will occur (such as hyponatraemia or worsening of renal function) will all happen within the first few weeks of therapy only.

SESSION 3

URINARY TRACT INFECTION AND RENAL SCARRING

Chaired by Dr Robin Winney, Consultant Nephrologist, Royal Infirmary of Edinburgh

The investigation and management of dysuria

Mr Lawrence Stewart, Consultant Urologist, Western General Hospital, Edinburgh

A definition of dysuria is difficult to find. Taking it literally from Greek and Latin sources, the word means 'bad urine'. Medical textbooks give either no explanation of the word or a brief definition such as 'painful micturition' or 'difficulty or pain on passing urine'. These definitions fail to describe the location or nature of the pain.

Dysuria is most commonly caused by urinary tract

infection (UTI). Urinary infections may be subdivided into those that are simple or isolated, those that are recurrent and those that are complicated. Recurrent urinary infections can be subdivided further into unresolved infections (inadequately treated) and true re-infections (either with the same organism or a new organism). Complicated UTIs are those associated with underlying pathology, such as an immunocompromised state, a dysfunctional urinary tract or anatomical defects.

Females are particularly prone to UTI, with a 10:1 ratio of infections in adulthood of females to males. Single isolated infections in females are easily treated, but recurrent infections need more thought. As a general rule it is recommended that a female patient with three or more proven urinary infections or a male patient with a single infection should be investigated further. Investigations include ultrasound and KUB X-ray or intravenous urography (IVU) routinely and urodynamic studies, and pressure flow testing and cystoscopy as more select tests.

A large number of possible anatomical defects can present with UTI. Examples include urinary stones, urinary obstruction, strictures, urethral diverticula, prostatic enlargement and space-occupying lesions.

It should be remembered that dysuria need not be infective in origin. Some examples of non-infective conditions that can present with dysuria are lichen scleroses of the male genitalia, foreign body, Reiter's syndrome and bladder/urethral stones. The term urethral syndrome has been used to describe the presence of sterile dysuria in females. This term has no strict definition but is generally used to describe the presence of symptoms suggestive of UTI but with no organisms on culture. The confusion comes from the fact that up to 80% of such cases will be associated with some evidence of infection if one looks hard enough, such as the presence of pyuria or a non-significant number of organisms. Many doubt if urethral syndrome exists at all as a definitive syndrome. The definition of what is a significant number of organisms in the urine is up for debate in itself and the presence of just 100 organisms per ml along with pyuria is probably significant enough to suggest infection.

Current perspectives on reflux and renal scarring

Dr Alan Watson, Consultant Paediatric Nephrologist, City Hospital, Nottingham and Special Senior Lecturer, University of Nottingham

A difficult balance has to be struck in the investigation of children with urinary infection, since the tests are lengthy and distressing and should not be undertaken lightly. Of the children presently investigated, only about 5% have an abnormality detected. However, the investigation of urinary infection in children is often of vital importance, not only for the relief and prevention of symptoms but also for the possible detection of underlying congenital abnormalities and for the prevention of long-term morbidity associated with hypertension and chronic renal failure. In particular, vesicoureteric reflux (VUR) is thought to be present in 30% of children with urinary tract infection. The Royal College of Physicians of London has stated that every urinary tract infection in a child should be investigated.[18]

Reflux nephropathy can present at any age. Often there is no history of infection, and presentation with end-stage renal disease, malignant hypertension or even blindness is not unheard of. Most cases remain silent, with hypertension occurring in less than 5% of cases during childhood. Vesicoureteric reflux can have a hereditary component, and 30% of case siblings may also have reflux disease. Although no single gene has been found responsible, there is linkage to chromosome 1.[19]

Vesicoureteric reflux can be assessed by imaging with DMSA scanning, but the presence of reflux bears no direct relationship to renal function. Acute parenchymal defects are seen on DMSA scanning during episodes of pyelonephritis, but these often resolve within 3–6 months. So not all demonstrated defects scar in the long term.[20] Cases show that kidney scars can occur without demonstrated reflux; equally, in cases with demonstrated reflux, scarring may in fact be a rare occurrence. There is probably a group of infants with dysfunctional voiding who fail to empty their bladders that may get scarring without reflux.

The term reflux nephropathy was created by Bailey in 1972.[21] The condition describes the presence of small, contracted, irregularly scarred kidneys. Perhaps a better terminology might be the 'reflux associated damage', which can be subdivided into four subtypes: Type1 congenital (with no obstruction or infection); Type 2 acquired obstructive; Type 3 acquired infective; and Type 4 dsyfunctional voiding. The final common pathway is reduced nephron mass, glomerulosclerosis and chronic renal failure.

Debate remains in connection with the management and treatment of VUR. Medical treatment involves the successful communication of information to the child and their carers and education, as well as the use of prophylactic antibiotics. The surgical option is reimplantation of ureters or sting procedure involving the injection of material to 'bulk up the ureters'. The Birmingham reflux study group showed no difference in the incidence of UTIs, progression of scars, the development of new scars or renal function between medically and surgically treated groups.[22] Smellie *et al.* looked at children with severe VUR and showed a slightly higher incidence of urinary infections in the medical group but no difference in GFR rates.[23] The evidence available supports the view that damage occurs early in the natural history of reflux disease and that therefore surgical

intervention has little outcome on renal function. However, surgical reimplantation of ureters can be useful in cases of recurrent infection where the use of prophylactic antibiotics has failed.

SESSION 4

INTERACTIVE DEBATE – DIALYSIS: IS IT FOR EVERYONE?

Chaired by Dr William D. Plant, Consultant Renal Physician, Cork University Hospital

The number of patients being presented to nephrologists to treat and the demand for renal services is increasing. Should all these patients be offered dialysis and are we not dialysing enough patients at the moment?

Digital voting was used in this session, and before any arguments were heard the audience voted as to whether they agreed with the statement that 'at present we do not dialyse enough people in the UK'. Fifty-five per cent said 'yes' while 21% voted 'no' and 24% 'don't know'. After hearing the arguments, voting at the end of the session in response to the same question gave an increased number thinking that more people should be dialysed (62%), with 21% saying 'no' and 17% 'don't know'. Thirty per cent of people stated that they had changed their opinion, suggesting movement towards both points of view!

We don't dialysis enough

Professor Dimitrios G. Oreopoulos, Director, Periotneal Dialysis Program, Division of Nephrology, University Health Network and Department of Medicine, University of Toronto

In the UK, 148 new patients per million develop ESRF per year, but it is estimated that only 54% are referred to a nephrologist and that of these only 65% get dialysis.[24] In 1988, the UK took 20 patients per million population onto dialysis compared with a rate of 44 per million in Germany. At this time, it was argued that the UK was not taking on all the patients it could, but some argued even at this stage that too many were already being dialysed. Today, the UK dialyses 90 new patients per million and the same arguments are still being debated. This figure is still lower than those of most other 'developed' countries.

The dialysis of more elderly patients is potentially high-risk and must be weighed up against the patients' quality of life. Most measurements of quality of life are based on questionnaires, but these are of questionable reliability and have their own problems. Quality of life measurements can fluctuate with the patients' emotional state and level of social support, and therefore basing treatment decisions on quality of life measurements requires extreme caution. At present, most studies are using a standardised questionnaire of 36 questions called the SF36 score, which gives measures of both physical and mental function.[25] Studies have shown that the elderly on dialysis have lower physical functioning scores but have higher mental functioning scores than the young. It appears that the older patients are more satisfied with life on dialysis than the young. Even comparison of elderly people on dialysis with those not on dialysis has shown that physical health may well be poorer but again index of well-being may be higher.[26]

Technical advances now make it possible to dialyse most patients. However, studies have suggested that referral may still be based on old knowledge of what dialysis is like.[27] General practitioners may still act as gate-keepers and decide which elderly patients to refer on for consideration of dialysis.

Caution is needed when patients are refused entry onto the dialysis programme for the apparent reason of futility. It is possible that this may be rationing under the cloak of futility where in reality we are rationing because of economic constraints.

In conclusion, Professor Oreopoulos stated that in his opinion age-based rationing of dialysis was still occurring in the UK despite significant improvement in the last ten years. Nephrologists have an obligation to convince the government to improve funding and to educate referring physicians regarding the advantages of dialysis in elderly people. It should not be forgotten that the physician's primary responsibility should be the patient.

More dialysis is not the answer

Dr James Tattersall, Consultant Nephrologist, Basildon General Hospital

Overall healthcare spending as a percentage of gross domestic product (GDP) is low in the UK – in fact probably half that of the US and the worst of any Western European country. However, this is partly offset by the fact that spending on renal replacement therapies as a multiple of per capita healthcare spending is actually much higher in the UK than in the US and Germany (i.e. a larger proportion of budget is spent on renal services). We therefore cannot push for a greater renal budget for dialysis in the UK without a total increase in healthcare spending.

Over one million people are on dialysis in the world, but it is estimated that probably half of this total number come from the US and Japan. Despite this, the US still expects an exponential growth in dialysis numbers with no flattening off of demand.[28] However, the evidence is that such growth is not sustainable. Predictions show that by 2040, overall healthcare budgets will have exceeded GDP in all developed countries.

Traditionally, the nephrologist spends a large proportion of their time looking after dialysis patients. An argument was made for more emphasis on pre-dialysis patients and more care in attempts to delay progression of renal failure.

Early intervention may not only postpone the onset of dialysis but may also reduce the related co-morbidity. Still, a large number of patients are referred late to nephrology services.

The ramipril efficacy in nephropathy (REIN) study looked at the use of ACE inhibitors in patients with progressive renal disease and showed a dramatic prevention of decline in renal function, which was particularly pronounced in those started early with a relatively high GFR.[29] In diabetics, a high glycosylated haemoglobin concentration correlates with progressive renal disease, so there is scope to prevent diabetic renal disease.

Dr Tattersall concluded that the volume of chronic renal disease is preventable. This, however, requires identification of patients at an early stage and the provision of adequate information to patients. For those who already need dialysis, it should be remembered that a palliative option of conservative treatment alone is available as a choice.

This presentation was followed up by a digital vote that showed that 88% thought earlier intervention could have an impact on the number of patients going onto dialysis.

Ethical slant . . .

Dr Kenneth Boyd, Senior Lecturer in Medical Ethics, University of Edinburgh

The decisions relating to who gets dialysis may not now be restrained by rationing and may be based on clinical appropriateness.[30] Deciding what is clinically appropriate is based on clinical judgement; this is not totally objective and includes a degree of moral judgement that is always contestable.

Various clinical and ethical criteria are applied to situations to give them a more objective basis for decision making. Four examples of criteria are triage, ordinary and extraordinary means, futility and quality of life. Triage is the most ethical way of deciding whom to treat first in an emergency. However, triage criteria are less useful in a non-emergency setting and triage is culture-dependent. Ordinary and extraordinary means of treatment is a way of dividing treatments into those that have to be considered obligatory and those that are discretionary. However, if the need is great enough, then often there is little left in the discretionary group. Futility describes treatment that would no longer preserve biological life or treatment where the burdens would outweigh benefits. This concept is difficult to use because prognosis is often difficult to predict and because patients may lack decision-making capacity as to what is acceptable. Quality of life is a difficult concept, since it is value-laden and obviously involves subjectivity. The patients themselves may ultimately be the only people who can assess their quality of life, but they may not possess the knowledge about the planned treatment and how this may affect their own quality of life.

Therefore, all these criteria have their problems. A basic problem is that often neither the patient nor the clinician can be sure of how a treatment will affect quality of life. In such situations, 'narrative ethics' and 'casuistry' may be of value. In narrative ethics, the clinician and patient constantly retell 'the story' until a combined decision emerges – in other words it relies on good communication. Casuistry, in contrast, is important when the patient lacks decision-making ability and the clinician has to make a 'best-interests' decision taking into consideration the patient's known past wishes and those of the relatives. The decision here largely relies on the clinician comparing the case with similar ones seen previously.

Macro-allocation decisions are dependent on technical advances and resource availability. Such considerations may limit which patients are considered for dialysis, but when they reach this point narrative ethics and casuistry methods should help select individual patients.

There was lively discussion at the end of the session, with continued disagreement and debate as to whether the UK dialyses too many or too few patients. However, there was consensus opinion for the need for better prevention strategies.

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