Synopsis of Causation

Cancer of the Kidney

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Disclaimer

This synopsis has been completed by medical practitioners. It is based on a literature search at the standard of a textbook of medicine and generalist review articles. It is not intended to be a meta-analysis of the literature on the condition specified.

Every effort has been taken to ensure that the information contained in the synopsis is accurate and consistent with current knowledge and practice and to do this the synopsis has been subject to an external validation process by consultants in a relevant specialty nominated by the Royal Society of Medicine.

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1. **Definition**

1.1. "**Cancer of the kidney**" is a broad term which covers several malignant neoplasms involving renal tissues:

- renal cell carcinoma (RCC); (*hypernephroma* is a synonymous term although it is no longer favoured by all)
- transitional cell carcinoma
- renal sarcoma
- renal medullary carcinoma
- collecting duct tumour
- renal lymphoma and renal leukaemic infiltration
- metastatic tumour of the kidney
- Wilm’s Tumour (nephroblastoma)
- oncocytooma

1.2. **RCC** accounts for about 85% of all primary renal cancers.

1.2.1. It arises in the renal tubule epithelium and accounts for about 3% of all adult malignancies.

1.2.2. In Western populations there are approximately 8 new cases per 100,000 per year, in the ratio male:female of approximately 3:2.

1.2.3. It is diagnosed mainly in adults in their fifties, sixties or seventies and is familial in about 4% of cases.

1.2.4. It is rare in children and adolescents.\(^1\)^\(^2\)

1.2.5. **Classification** In the past, RCC has been classified by cell type, (employing labels such as clear, granular, spindle, and oncycytic) or by pattern of growth (employing labels such as acinar, papillary, and sarcomatoid). More recently, however, classification takes into account several sets of defining factors: *histochemistry, morphology* and *cytogenetic* characteristics. Five types have been defined in this way:

- clear cell
- chromophlic (papillary)
- chromophobic
- oncocytoic
1.2.5.1. The clear cell type accounts for over 75% of RCCs and typically has a specific chromosome abnormality (3p).

1.2.5.2. The chromophilic (papillary) type accounts for about 15% of RCCs, may be multifocal and bilateral, is often small and typically may have multiple chromosome abnormalities (including 7, 17, 16 and Y but not 3p).\textsuperscript{3,4}

1.2.5.3. The chromophobic type accounts for about 4% of RCCs is usually well circumscribed and has a reduced chromosome number but no 3p abnormality.\textsuperscript{5,6,7}

1.2.5.4. The oncocytic type has been thought to account for about 3% of RCCs. It can grow to be quite large and has distinct histological characteristics but no consistent chromosomal abnormalities. However, distinction between an oncocytic RCC and an oncocytoma (benign) can be difficult, thus casting doubt on the reliability of diagnosis of malignancy within this subgroup. Indeed some regard it as distinct from RCC altogether.

1.2.5.5. The collecting duct (Bellini duct) type is rare, arises from medullary or pelvic tissue, and has a distinctive histological appearance but no consistent chromosomal abnormalities. It can be a very invasive tumour. There is still some uncertainty about whether all renal medullary carcinomas and collecting duct carcinomas should be considered as RCC subtypes or whether some may be separate entities.\textsuperscript{9,10,11,12}

1.3. Transitional cell carcinoma is the next most common at around 8%, but it arises in the renal pelvis so is not considered further here.

1.4. Renal sarcoma accounts for 1% to 2% of primary renal cancers.

1.4.1. The most common is fibrosarcoma which is a very aggressive tumour.

1.4.2. Rarer are leiomyosarcoma, liposarcoma, rhabdomyosarcoma, osteogenic sarcoma, carcinosarcoma, malignant fibrous histiocytoma, angiosarcoma and malignant hemangiopericytoma. All are very aggressive tumours.

1.5. Renal medullary carcinoma, considered by some to be distinct from RCC, is a rare tumour affecting patients with sickle cell trait or disease.\textsuperscript{9,10,13} It is a very aggressive tumour.

1.6. Collecting duct tumour may sometimes be distinct from RCC.\textsuperscript{14,8,12,11} It is a rare but very aggressive tumour.

1.7. Renal lymphoma and renal leukaemic infiltration occur in about one third of patients dying from the systemic disease and disseminate mainly via the blood stream. Primary renal lymphoma is rare.

1.8. Metastatic tumour involving the kidney is more common than primary renal cancer and occurs in over 10% of people dying from all cancers. The usual primary sources are:

- lung
• breast
• stomach
• bowel
• malignant melanoma.

1.9. **Wilm’s Tumour** is the commonest renal cancer in children.

1.9.1. It occurs in about 8 of a million children under the age of 15, being commonest between 2 and 5 years.

1.9.2. Rarely, RCC can occur in children too,\(^{15,1}\) as can other rare tumours, including rhabdoid tumour of the kidney, mesoblastic nephroma, and multilocular cystic nephroma.\(^{16}\)

1.9.3. Rarely, Wilm’s tumour can occur in adults.\(^{17,18}\)

1.9.4. Two forms of Wilm’s tumour can be identified histologically:

- **favourable** which is the most usual and has cell characteristics that do not include anaplasia

- **unfavourable** which has cell features including markedly enlarged and hyperchromatic nuclei and is more likely in older patients. One subtype of this form is clear cell sarcoma.

1.10. **Oncocytoma** is thought to be a benign tumour and is managed by nephrectomy. Recurrence and metastasis are extremely rare, so it is not considered further here.
2. Clinical features

Clinical Features vary with the tumour type.

2.1. RCC classically presents with a triad of symptoms:

- **haematuria** (frank or microscopic)
- loin pain
- swelling in the abdomen or loin

2.1.1. However, this triad occurs in only 10% of cases and symptomless renal cancer is more often found incidentally, during other investigative procedures such as computed tomography (CT) or magnetic resonance imaging (MRI).

2.1.2. Cases can present with sudden onset of scrotal varicocele due to venous obstruction within the abdomen, but this is very unusual.

2.1.3. Unfortunately, presentation can often be due to symptoms caused by metastases:

- **pathological fractures**
- cough
- **haemoptysis**
- dyspnoea related to pleural effusions
- **lymph node** enlargement

2.1.4. An RCC may secrete substances known as para-neoplastic factors that cause generalised symptoms such as weakness, weight loss, anaemia, fever, night sweats and malaise.

2.1.5. As the kidney is a major source of hormones involved in many homeostatic mechanisms, RCC can stimulate abnormal hormone production which can cause a variety of para-neoplastic syndromes. Features include:

- hypertension
- hyperglycemia
- hypercalcaemia
- polycythaemia
- eosinophilia
- clotting disorders
• leukaemia-like reactions
• hepatic dysfunction (Stauffer’s syndrome)
• Cushing’s syndrome
• feminisation or masculinisation
• galactorrhea
• neuromyopathy
• amyloidosis.

RCC, in summary, can present with a wide variety of clinical features, some very non-specific.

2.2. **Renal Sarcoma** can have a very similar presentation to RCC and may be very difficult to distinguish clinically from an RCC that shows sarcomatoid change. However, factors which can be useful include:

- position of origin within the kidney
- large size with no lymph node involvement
- occurrence of fat or bone tissue, suggestive of liposarcoma or osteosarcoma
- hypovascular pattern on angiography
- tendency to displace rather than invade the surrounding tissues

2.2.1. Leiomyosarcoma is particularly liable to grow very rapidly and metastasises readily.

2.2.2. Osteogenic sarcoma is often very hard due to extensive calcification.

2.3. **Renal medullary carcinoma** presents with haematuria, flank pain and a renal mass. It has often invaded local tissues and metastasised by the time of diagnosis.

2.4. **Collecting duct tumour** displays features that are very similar to those of renal medullary carcinoma.

2.5. **Renal lymphoma** and **renal leukaemic infiltration** usually occur late in the development of the systemic disease and may contribute comparatively little to the patient’s clinical state, although, exceptionally, renal failure can occur.

2.6. **Metastatic tumour of the kidney** is usually multifocal and almost always associated with metastatic lesions at other sites.

2.7. **Wilm’s Tumour** usually occurs in one kidney but can occasionally be bilateral. It most commonly presents as an abdominal mass, which may be symptomless.

2.7.1. However, it may cause pain and/or vomiting and haematuria may occasionally be
detected on examination.

2.7.2. It may also present with raised blood pressure.

2.7.3. It can occur in association with congenital abnormalities, usually of genitourinary type.

2.7.4. It tends to present later in adults than in children.\textsuperscript{18}

**Staging systems**, which are applied at the time of initial diagnosis, aid choice of therapy and assessment of prognosis. They vary slightly with tumour type.

2.8. In RCC a number of staging systems have been described.

2.8.1. The Robson system was formerly employed, allocating cases to Stages I – IV.

2.8.2. Since the late 1990’s the TNM (tumour, node, metastasis) system has been found preferable. In this system:

- local spread into surrounding tissues is allocated a T grade
- degree of metastasis into local lymph nodes is allocated an N grade
- presence or otherwise of detectable distant metastases is allocated an M grade

2.8.3. Alternative staging systems are employed by some, combining TNM with other grading methods.

2.9. In Renal sarcoma, TNM staging is employed for tumours in children.\textsuperscript{20}

2.9.1. In adults a variant that includes tumour size may be employed.\textsuperscript{21,22}

2.10. Renal medullary carcinoma and collecting duct tumour can be staged using the TNM method.\textsuperscript{19}

2.11. In renal lymphoma, renal leukaemic infiltration and metastatic tumour of the kidney staging will be applied to the primary disease.

2.12. In Wilm’s Tumour a 5 stage method based on clinical findings at diagnosis and at initial operation is usually employed in children and adults:

- Stage I - the tumour is confined to the kidney and is completely excised with the tumour capsule intact
- Stage II - the tumour is confined to the kidney but the capsule is penetrated or tumour is present in the peri-renal soft tissue
- Stage III - the tumour has inoperable local spread left after surgery. This is confined to the abdomen and may involve local lymph nodes
- Stage IV - the tumour is characterised by distant metastases, generally involving the lungs and occasionally the liver
• Stage V - the tumour occurs in both kidneys at the time of diagnosis
3. Aetiology

3.1. Some insight into the possible mechanisms of renal carcinogenesis can be gleaned from studies of von Hippel-Lindau (VHL) disease.

3.1.1. This is a rare familial disorder in which patients develop RCC and other tumours. It is typified by the mutation of a germline gene known as the VHL gene.\textsuperscript{23,24}

3.1.2. When normal tissues are deprived of oxygen for any reason, complex mechanisms stimulate cells into adaptive responses including new blood vessel formation and anaerobic mobilisation of cell energy sources.\textsuperscript{25,26} In healthy tissues this adaptive process is kept inactive by a series of gene-mediated factors\textsuperscript{27,28} in which the normal VHL gene features.\textsuperscript{23}

3.1.3. In VHL disease, however, the mutated VHL gene fails to function properly and the adaptive process is not held in check. Tissues which have a good oxygen supply may be stimulated inappropriately, perhaps encouraging malignant growth.\textsuperscript{29,30}

3.2. Assessment of risk can be studied by comparing the occurrence of disease in large groups exposed to the risk factor in question with unexposed control groups.

3.3. In considering the results of studies on risk factors, individual susceptibility has to be taken into account.

3.3.1. In one study the risk of developing RCC after exposure to an environmental risk factor was different in two groups defined by the presence of two different alleles of the same gene.\textsuperscript{31} One group was more susceptible than the other to the risk factor being studied.

3.3.2. Susceptibility of an individual to development of cancer is likely to involve the genetic pattern that defines that individual, and this may change as the individual ages.

3.4. The possibility of viruses being involved in human renal carcinogenesis has featured little in recent research and is thought to be unlikely as there is no apparent increase in incidence of renal cancers in groups most vulnerable to virus infections nor is there any suggestion of horizontal transmission in humans.

RCC risk factors

3.5. Inherited diseases

3.5.1. The commonest, but still relatively rare, is von Hippel-Lindau disease (described above) which is a multisystem familial cancer syndrome occurring in approximately 1 in 36,000 of the population. Development of clear cell RCC in later life is a common feature of this syndrome, typified by mutation of the germline VHL gene.\textsuperscript{23,32,33}

3.5.2. Another uncommon autosomal dominant disorder is tuberous sclerosis complex which is characterised by mental retardation, seizures and benign tumours of the heart, lung, skin, central nervous system and kidney. Sometimes malignancy can develop, especially in the kidney, the commonest being RCC. Non-VHL gene mutations have been described.\textsuperscript{34,35,36}
3.5.3. RCC has been thought by some to have links with the rare **autosomal dominant polycystic kidney disease** but these have **not** been convincingly demonstrated.\(^{37,38}\)

3.5.4. **Hereditary papillary cell renal carcinoma** is a rare inherited RCC thought to be genetically distinct from other inherited renal cancers.\(^{39,40}\)

3.5.5. Virtually all patients with the **clear cell** variant of RCC have a mutated VHL gene.

3.6. **Genetic factors**

3.6.1. People with a **family history** of cancer of the kidney in a first or second degree relative have been found to have a slightly increased risk of RCC.\(^{41,42}\)

3.6.2. A family history of other cancers does not seem to be associated with RCC risk.\(^{41}\)

3.6.3. A family history of cancer of the kidney does not seem to be associated with any additional increase in susceptibility to external risk factors.\(^{41}\)

3.7. **Chronic renal disease**

3.7.1. Studies have shown that the risk of RCC is very much much higher in patients who suffer from chronic renal failure, with or without acquired cystic kidney disease,\(^{43,44}\) estimates varying from 20 to 100 times more.\(^{45,46,47,48}\)

3.8. **Other risk factors**

3.8.1. A number of studies have been carried out to determine if certain other factors are associated with an increased risk of RCC. Most of these studies involve analysis of the occurrence of the risk factors in groups of RCC patients compared with the occurrence in other patient groups where RCC has not been diagnosed.

3.8.2. As RCC has a very low prevalence in the population, such studies are inevitably limited in the number of cases available for comparison with controls, particularly after the study groups are subdivided to account for several potentially **confounding** factors.

3.8.3. Most of the studies express results in the form of **relative risk** (RR) or the very similar **odds ratio** (OR). An RR of 2.0, for example, indicates that the associated risk is doubled while an RR of 0.5 indicates that the risk is halved. Very few of the studies produce an RR above 2.0 and the fairly wide **confidence interval** (CI) quoted in most of the studies limits the significance of the findings. This translates into at most only very slight association between the factor under study and the occurrence of RCC.

3.8.4. No standard definition of “prolonged exposure” is consistently used throughout the studies, but a period of over 10 years is regarded as prolonged in some.

3.8.5. Some of the studies reveal at most only very slight associated risk from **constitutional factors** which include:

- obesity \(^{41,42,49,50,51,52}\)
- hypertension \(^{53,54,55}\)
• oestrogenic hormones ⁵⁶,⁵⁷,⁵⁸

3.8.6. Others reveal at most only very slight associated risk from prolonged exposure to external factors which include:

- tobacco smoking ⁴²,⁵⁰,⁵⁹,⁶⁰,⁶¹,⁶²,⁶³,⁶⁴,⁶⁵
- industrial solvents including trichloroethylene ⁶⁶,⁶⁷,⁶⁸,⁶⁹,⁷⁰,⁷¹,⁷²
- cadmium ⁶⁸,⁷³
- lead ⁶⁸
- solder fumes ⁶⁸
- asbestos ⁶⁶
- copper sulphate ⁶⁹
- pesticides ³¹,⁶⁹
- paints ⁶⁸
- mineral oils ⁶⁸
- cutting fluids ⁶⁸
- benzene ⁶⁸
- polycyclic aromatic hydrocarbons ⁶⁸

3.8.7. Others reveal at most only very slight associated risk from prolonged work in certain industries which include those involving:

- dry cleaning ⁶⁶
- soldering ⁶⁸
- welding ⁶⁸
- milling ⁶⁸
- petrol station attending ⁷⁴

3.8.8. Others reveal at most only very slight associated risk from prolonged use of certain therapeutic drugs which include:

- paracetamol ⁷⁵,⁷⁶,⁷⁷
- aspirin ⁷⁶,⁷⁷
• phenacitin \textsuperscript{76,77}

• non-steroidal anti-inflammatory agents \textsuperscript{77}

• amphetamine \textsuperscript{55,56}

3.8.9. Others reveal at most only very slight associated risk from regular dietary factors which include:

• high energy diet \textsuperscript{51}

• fried meats \textsuperscript{51,78}

• low intake of vitamin E \textsuperscript{51}

• low intake of magnesium \textsuperscript{51}

3.8.10. There may well be additional factors that have not yet been researched.

3.8.11. The “other” risk factors listed above are associated with at most only very slight increase in RCC. But RCC occurs in an average of only 8 per 100,000 of the population per year in the western world, so the risk to an average individual is very small indeed and the risk to an individual exposed to any of these “other” factors only slightly greater.

3.8.12. Also, since these “other” risk factors involve constitution, habits, diet, drugs and work exposures, excluding the confounding effect of some of these factors on others under consideration is extremely difficult, even when studying large groups, and virtually impossible when considering the causes in an individual case.

3.8.13. Furthermore, in each group exposed to a risk factor under study there will be individuals of widely varying susceptibility to that factor. Assessing the risk associated with that factor in an individual is thus extremely difficult, as precise measures of individual susceptibility are not yet available.

3.8.14. These “other” risk factors, therefore, while contributing to research on mechanisms of renal carcinogenesis and to definition of health policy for populations, are of very little value in defining causes of RCC in individuals.

3.9. Exposure to radioactivity

3.9.1. After the Chernobyl accident in 1986, the rate of RCC occurrence per 100,000 people living in the contaminated area gradually increased from 4.7 in 1986 to 7.5 in 1998. Caesium 137, which is excreted mainly through the kidneys, was the main contaminant.\textsuperscript{79,80} However there are doubts about the reliability of the locally collected data and the significance of the findings is thus very limited.

3.9.2. In 1988, a cohort of over 22 thousand men who participated in the United Kingdom's atmospheric nuclear weapon tests and experimental programmes in Australia and the Pacific Ocean between 1952 and 1967 was studied and compared with a matched control cohort of servicemen.\textsuperscript{51} The study focussed on mortality from various causes, and on mortality and incidence for 27 types of cancer. No evidence was found of increased incidence of solid tumours in the test group compared with the controls. Further follow
up analyses of the cohorts, published in 1993 and 2004, produced the same conclusion.

3.9.3. A few cases of RCC occurring 25 to 30 years after radiotherapy in the 1950’s and 1960’s have been reported. In all cases the therapy was for other malignancies therefore the significance of any link between the radiotherapy itself and the later RCCs is unclear. Another factor to be considered is that radiotherapy doses were much higher then than now.

3.10. **Trauma**

3.10.1. There is no clear association between renal cancer with trauma except in one large international case-control study of renal-cell cancer where the authors concluded that the link they found was very unlikely to be significant because of unreliability of recall.

**Other renal tumour risk factors**

3.11. No studies of risk factors for renal sarcoma have been reported.

3.12. Studies of renal medullary carcinoma have found various characteristics suggesting they form a distinct group with gene patterns different from those in RCC and that tissue hypoxia associated with sickle cell trait may be involved in tumour development.

3.13. Genetic changes have been found in collecting duct tumour but their significance is not fully established.

3.14. The causes of renal lymphoma, renal leukaemic infiltration and metastatic tumour of the kidney are those of the primary disease.

3.15. **Wilm’s tumour** in children is associated with several genetic abnormalities and with several congenital abnormality syndromes. However, a family history of the tumour is very uncommon.

3.15.1. One study found that Wilm’s tumour occurred twice as often in the children of mothers who had a heavy smoking habit than in those of non-smokers. However, this was not confirmed in a subsequent study of habits of parents of 200 children with a history of Wilm’s tumour.

3.15.2. A recent study describes gene abnormality in a case of adult Wilm’s tumour.

3.15.3. Another study demonstrated a very weak association of Wilm’s tumour with high birth weight but no association with high parental age at birth, consumption of coffee and tea during pregnancy, or maternal exposure to pesticides.
4. Prognosis

4.1. Prognosis in cancer of the kidney varies with the type of tumour.

4.1.1. In RCC several factors have a bearing on prognosis.

4.1.2. The most important prognostic factor is the strong correlation between Robson or TNM staging, applied at initial diagnosis, and 5-year survival rates.\(^93,\text{94,95}\) With both, typical 5-year survival rates are:

- 70 – 95% where tumour is confined to the kidney; the smaller the tumour the better the prognosis
- 50 – 60% where tumour extends no further than the peri-renal fascia
- 40 – 50% where there is true venous invasion
- 25 – 30% where tumour is confined to the kidney and there is only a single metastasis in one regional node
- 15 – 20% where tumour extends no further than the peri-renal fascia and there is only a single metastasis in one regional node
- 10% where there is tumour extension beyond the peri-renal fascia or there are metastases in more than one regional node
- < 5% where there are distant metastases

4.1.3. Other factors which contribute to assessment of prognosis are:

- Fuhrman grading, a very useful classification which allocates microscopic changes within the nuclei of tumour cells to one of four grades.\(^93,\text{96,97,98}\) Some now feel that redefinition of this system to include only two grades would be preferable.

- variations in tumour cell subtype

- sarcomatoid growth pattern changes\(^99,\text{100,101}\) and collecting duct cell type both have a particularly poor prognosis

- chromophilic and chromophobic types have been thought to have a better prognosis than clear cell type\(^102\) but they can be less responsive to some therapies and may have a worse prognosis in advanced cases.

4.1.4. In RCC in the earlier stages, nephrectomy, radical or partial, is the usual treatment of choice and 5-year survival rates of over 60% are common.

4.1.4.1. Post-surgery radiotherapy offers no benefit and is not indicated.

4.1.5. In RCC in the later stages, factors that influence survival\(^103\) include:
- site and number of metastases
- the patient’s general state
- fever
- anorexia
- weight loss
- malaise
- substantially raised ESR
- anaemia
- hypercalcaemia\textsuperscript{104}
- hypoalbuminaemia\textsuperscript{103}
- liver dysfunction
- presence of chronic renal failure

4.1.6. Treatment in the later stages seldom includes chemotherapy or hormone therapy as both are usually ineffective. However, metastases can sometimes be excised with resulting improvement in 5-year survival rates.

4.1.7. Much more promising is immunotherapy with interferon or interleukin 2, sometimes together, or combined with other drugs.

4.1.8. With ever-increasing understanding of molecular processes underlying the condition, therapies aimed specifically at these processes are being explored.

4.1.9. However, overall, later stage prognosis remains poor.

4.2. Renal sarcoma generally has a poor prognosis unless it is diagnosed at an early stage.\textsuperscript{105,106,107}

4.3. Renal medullary carcinoma and collecting duct tumour generally have a very poor prognosis. However, significant response to therapy has been described recently.\textsuperscript{108}

4.4. The presence of renal lymphoma, renal leukaemic infiltration and metastatic tumour of the kidney indicates distant spread from the primary source, implying a poor prognosis, but more specific assessment will depend on the overall prognosis of the primary disease.

4.5. In Wilm’s tumour the main prognostic factors at diagnosis are size, stage and histological type (favourable or unfavourable).

4.5.1. With chemotherapy or radiotherapy after surgery, 4 year survival rates in children can be:
• over 90% for stages I and II with favourable histology
• 80 to 90% for stages III and IV with favourable histology
• well over 80% for stage I with unfavourable histology
• 50 to 60% for stages II to IV with unfavourable histology
• 60 to 85% for stage V (bilateral)#even with inoperable tumours, over 50% can be achieved

4.5.2. Similar figures for adults with Wilm’s tumour have been found\textsuperscript{109} although more of the adult tumours present at higher stages\textsuperscript{18} and thus, overall, have a less favourable prognosis.\textsuperscript{110}
5. Summary

5.1. Most cancers of the kidney are RCC although several other types occur.

5.2. They can present in many different ways and are increasingly detected at earlier stages during the course of investigations for other conditions.

5.3. Causes remain uncertain. Genetic, constitutional and environmental factors probably play a part in the aetiology of the condition but the exact mechanisms involved are complex.

5.4. Prognosis varies substantially with the type of tumour and its staging. Prognosis has improved in recent years due to earlier detection and advances in treatment. However, it remains poor for some of the tumours, especially if they are at an advanced stage at diagnosis.
6. Related Synopses

Cancer of the Lung
Cancer of the Stomach
Cancer of the Colon
Cancer of the Rectum
<table>
<thead>
<tr>
<th>Term</th>
<th>Definition</th>
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<tbody>
<tr>
<td>allele</td>
<td>Any one of a series of two or more different genes that occupy the same position on a chromosome.</td>
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<tr>
<td>amyloidosis</td>
<td>A disease process involving deposition of a glycoprotein substance between tissue cells.</td>
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<tr>
<td>anaerobic</td>
<td>Functioning in the absence of oxygen.</td>
</tr>
<tr>
<td>anaplasia</td>
<td>A cell characteristic which takes a primitive form typical of malignancy.</td>
</tr>
<tr>
<td>angiography</td>
<td>A X-ray technique which images blood vessels.</td>
</tr>
<tr>
<td>anorexia</td>
<td>Loss of appetite for food.</td>
</tr>
<tr>
<td>autosomal dominant</td>
<td>Requires that only one parent need have the trait (characteristic) in order to pass it to the offspring.</td>
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<tr>
<td>bilateral</td>
<td>Occurring on both sides.</td>
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<tr>
<td>calcification</td>
<td>Hardening of tissue by deposition of calcium salts.</td>
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<tr>
<td>carcinogenesis</td>
<td>Generation of cancer from normal cells.</td>
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<tr>
<td>case-control study</td>
<td>A study in which the risk factors of people with a disease are compared with those without the disease.</td>
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<tr>
<td>chromosome</td>
<td>The self-replicating genetic structures within cell nuclei, each chromosome having a linear array of genes.</td>
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<tr>
<td>chronic renal failure</td>
<td>Persistent and substantial decline in kidney function.</td>
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<tr>
<td>circumscribed</td>
<td>Well localised.</td>
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<tr>
<td>computed tomography</td>
<td>An investigation technique that uses a computer to assimilate multiple X-ray images into a two-dimensional cross-sectional image.</td>
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<tr>
<td>confidence interval</td>
<td>A statistical calculation which defines a range within which the true value of a variable being studied will fall with specified probability.</td>
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<tr>
<td>Term</td>
<td>Definition</td>
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<td>----------------------</td>
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<tr>
<td>confounding</td>
<td>Distortion of the apparent effect of an exposure on risk, brought about by the association with other factors that can influence the outcome.</td>
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<tr>
<td>congenital</td>
<td>Pertaining to conditions present at birth.</td>
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<tr>
<td>correlation</td>
<td>Statistical association.</td>
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<tr>
<td>Cushing’s syndrome</td>
<td>A disorder due to an excess of glucocorticoid hormone in the bloodstream, produced by a benign tumour of the adrenal gland.</td>
</tr>
<tr>
<td>cytogenetic</td>
<td>Relating to the origin and development of cells.</td>
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<tr>
<td>dyspnoea</td>
<td>Difficulty in breathing or laboured breathing – breathlessness.</td>
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<tr>
<td>eosinophil</td>
<td>A white blood cell that plays a part in allergic reactions and the body’s response to parasites and fungi. Hence eosinophilia; an excess of these cells above the normal.</td>
</tr>
<tr>
<td>ESR</td>
<td>A test which gives a non-specific index of inflammation.</td>
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<tr>
<td>galactorrhoea</td>
<td>The excessive, persistent or spontaneous flow of breast milk irrespective of nursing.</td>
</tr>
<tr>
<td>germline gene</td>
<td>A gene within cells which give rise to the reproductive cells.</td>
</tr>
<tr>
<td>gene</td>
<td>Unit of inheritance consisting of DNA and occupying a specific position on a chromosome.</td>
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<tr>
<td>genitourinary</td>
<td>Pertaining to the genital and urinary organs.</td>
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<tr>
<td>haematuria</td>
<td>Blood in the urine; (if easily visible it is described as <em>frank haematuria</em>).</td>
</tr>
<tr>
<td>haemoptysis</td>
<td>Coughing up blood or bloodstained sputum.</td>
</tr>
<tr>
<td>hepatic</td>
<td>Pertaining to the liver.</td>
</tr>
<tr>
<td>histochemistry</td>
<td>Study of the chemical composition of tissues by means of specific staining reactions.</td>
</tr>
<tr>
<td>histological</td>
<td>pertaining to the study of the microscopic structure of tissues.</td>
</tr>
<tr>
<td>homeostatic mechanism</td>
<td>A mechanism which maintains stability in the normal body state.</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
</tr>
<tr>
<td>-----------------------------</td>
<td>-----------------------------------------------------------------------------</td>
</tr>
<tr>
<td>horizontal transmission</td>
<td>Transfer of a disease from one individual to another generally within a population.</td>
</tr>
<tr>
<td>hypercalcaemia</td>
<td>Excessive levels of calcium compounds in the bloodstream.</td>
</tr>
<tr>
<td>hyperchromatic nuclei</td>
<td>Nuclei showing excessive staining. The cell nucleus holds the chromosomes.</td>
</tr>
<tr>
<td>hyperglycaemia</td>
<td>Excessive levels of glucose in the bloodstream.</td>
</tr>
<tr>
<td>hypertension</td>
<td>Increased blood pressure.</td>
</tr>
<tr>
<td>hypoalbuminaemia</td>
<td>An abnormally low concentration of albumin in the blood.</td>
</tr>
<tr>
<td>hypovascular</td>
<td>Having an abnormally low number of blood vessels.</td>
</tr>
<tr>
<td>hypoxia</td>
<td>Lack of oxygen.</td>
</tr>
<tr>
<td>immunotherapy</td>
<td>Treatment of disease by stimulating the body’s own immune system.</td>
</tr>
<tr>
<td>lymph nodes</td>
<td>Small bean-shaped organs located along the lymphatic system throughout the body.</td>
</tr>
<tr>
<td>magnetic resonance imaging</td>
<td>An investigation technique used to image internal structures of the body, particularly soft tissues.</td>
</tr>
<tr>
<td>malaise</td>
<td>A vague feeling of being unwell.</td>
</tr>
<tr>
<td>malignant melanoma</td>
<td>A malignant tumour of the skin.</td>
</tr>
<tr>
<td>medullary</td>
<td>Relating to the inner area (of the kidney).</td>
</tr>
<tr>
<td>menarche</td>
<td>The start of menstrual function.</td>
</tr>
<tr>
<td>metastatic</td>
<td>Referring to a deposit of a malignant tumour in a distant site in the body. Hence metastasis, metastasise.</td>
</tr>
<tr>
<td>molecular</td>
<td>Peratining to molecules, which result from two or more atoms combining by chemical bonding.</td>
</tr>
<tr>
<td>morphology</td>
<td>The study of the structure of an organism or cell.</td>
</tr>
<tr>
<td>mutation</td>
<td>A permanent change in genetic material that can be transmitted to future generations.</td>
</tr>
<tr>
<td><strong>neoplasm</strong></td>
<td>New growth, usually cancerous.</td>
</tr>
<tr>
<td><strong>nephrectomy</strong></td>
<td>Surgical removal of the kidney; (if radical nephrectomy, then nearby tissues and lymph nodes removed also).</td>
</tr>
<tr>
<td><strong>neuromyopathy</strong></td>
<td>A disorder of muscle due to or combined with disorder of its nerve supply.</td>
</tr>
<tr>
<td><strong>odds ratio</strong></td>
<td>A statistical calculation of the number of people with disease who were exposed to a risk factor over those with disease who were not exposed divided by the number of those without disease who were exposed over those without who were not exposed.</td>
</tr>
<tr>
<td><strong>oestrogenic hormones</strong></td>
<td>Chemical substances that produce effects that characterise female functions.</td>
</tr>
<tr>
<td><strong>pathological fractures</strong></td>
<td>Fractures occurring from minor injury due to abnormal weakness of the bone structure.</td>
</tr>
<tr>
<td><strong>pelvic</strong></td>
<td>Pertaining to the chamber between the kidney tissue and the ureter (renal pelvis), through which urine flows to the bladder.</td>
</tr>
<tr>
<td><strong>peri-renal</strong></td>
<td>Pertaining to tissues surrounding the kidney.</td>
</tr>
<tr>
<td><strong>pleural effusion</strong></td>
<td>Collection of fluid between the lung outer surface and the chest wall.</td>
</tr>
<tr>
<td><strong>polycythaemia</strong></td>
<td>An increase in the total mass of cells in the blood; primarily used to refer to an increase in the mass of red blood cells.</td>
</tr>
<tr>
<td><strong>primary</strong></td>
<td>Pertaining to the original site of a malignant tumour, from where metastases may occur.</td>
</tr>
<tr>
<td><strong>regional node</strong></td>
<td>A lymph node receiving drainage from nearby tissue.</td>
</tr>
<tr>
<td><strong>relative risk</strong></td>
<td>A statistical calculation of the proportion of diseased people amongst those exposed to the relevant risk factor divided by the proportion of diseased people amongst those not exposed to the risk factor.</td>
</tr>
<tr>
<td><strong>renal</strong></td>
<td>Pertaining to the kidney.</td>
</tr>
<tr>
<td><strong>sarcomatoid</strong></td>
<td>Having the appearance of tumour cells that arise in tissues such as bone, cartilage, fat or muscle.</td>
</tr>
<tr>
<td>Term</td>
<td>Definition</td>
</tr>
<tr>
<td>----------------------</td>
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</tr>
<tr>
<td>scrotal varicocele</td>
<td>Varicose veins in the scrotum.</td>
</tr>
<tr>
<td>sickle cell trait</td>
<td>A genetically determined tendency to develop sickle cell disease.</td>
</tr>
<tr>
<td>sickle cell disease</td>
<td>A type of anaemia developing in people with the trait.</td>
</tr>
<tr>
<td>syndrome</td>
<td>A set of signs or a series of events occurring together that point to a single disease or condition as the cause.</td>
</tr>
<tr>
<td>systemic</td>
<td>Affecting the body as a whole.</td>
</tr>
<tr>
<td>tubule epithelium</td>
<td>the lining tissue of the minute tubes within the kidney tissues.</td>
</tr>
</tbody>
</table>
8. References

26 Wenger RH, Gassmann M. Oxygen(es) and the hypoxia-inducible factor-1. Biol Chem 1997;378(7):609-16.
