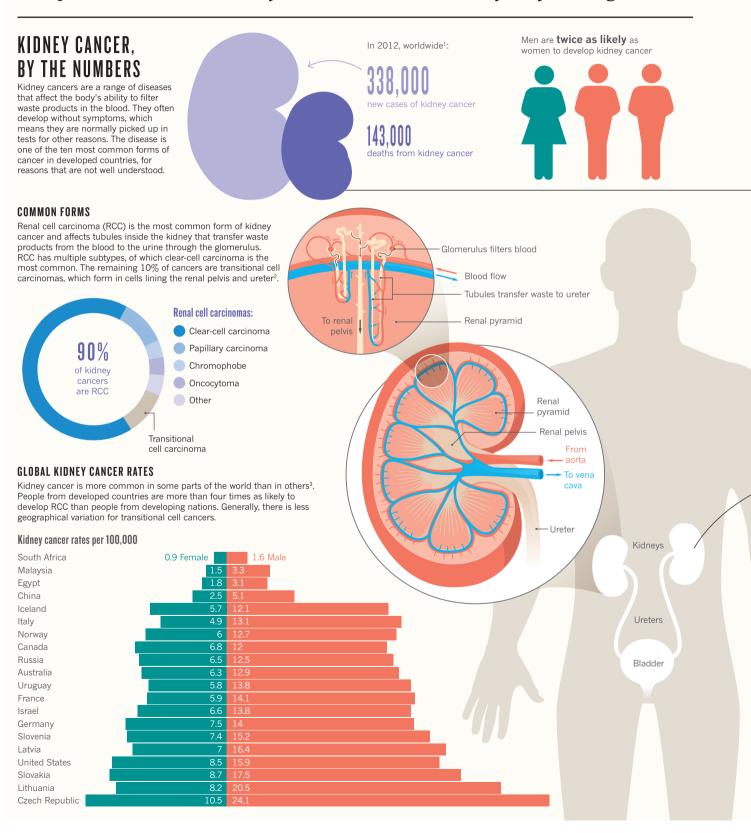
THE SILENT DISEASE

Kidney cancer is being detected earlier thanks to modern diagnostic techniques, meaning more patients receive treatment. By **Graham Shaw**; illustration by **Lucy Reading-Ikkanda**



TRIGGER WARNING

Smoking and obesity are the biggest risk factors for kidney cancer.

The falling popularity of smoking in developed countries could help to lower kidney-cancer incidence in these regions4.

Risk of kidney cancer

... increases by 20% for female smokers

... and by 50% for male smokers

Obesity

Every five-point increase in body mass index (BMI) increases risk by 24% for men and 34% for women. The rising level of obesity worldwide is likely to have contributed to increases in kidney cancer4.

40% in USA

Percentage of people with renal-cell cancers

30% in Europe

Development

of tumour

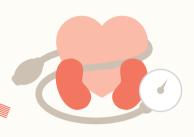
or cyst

Clear-cell renal carcinoma

cells

Hypertension

Risk of kidney cancer increases with rising blood pressure. Although obesity can increase blood pressure, the two risk factors are independent and the chance of developing the disease is higher among individuals with both conditions than for those who have one4.



DEVELOPING STORY

Loss-of-function mutations in the gene VHL are responsible for about 60% of clear-cell carcinomas². Around 2-3% of renal cell carcinomas run in families⁵. People with an inherited form of kidney cancer caused by von Hippel-Lindau syndrome (VHL) are born with a defect to an allele of VHL, and go on to acquire mutations that silence the gene. Most people with kidney cancer acquire VHL mutations during their lives as a result of environmental factors. A lack of symptoms can mean that some cancers can spread to other parts of the body before they are caught.

Gene Inherited mutation VHLor silencing, mutations Mutations, caused by risk factors, often to VHL, caused by silence VHL. When risk factors. other mutations occur (lighter cells), disease develops 0

Mutations lead to blood-vessel formation

The VHL protein is a tumour suppressor, but this protein is missing in mutated cells. When this happens, the transcription factor HIF- α accumulates in cancer cells, leading to the overexpression of proteins (such as VEGF and TGF- α) that are normally only produced in low-oxygen environments.

> The protein TGF-α acts on cancer cells to promote proliferation and survival.

> > PDGFB and VEGF (which play a part in blood-vessel formation and growth) and TGF-β (involved in tissue regeneration and cell differentiation) cause new blood vessels to grow, providing nutrients and oxygen to help the tumours to spread.

Spread of cancer to organs such as the lymph nodes

Spread of cancer to vena cava

Overexpression of proteins

2 New blood vessels

transport nutrients and oxygen to the tumour

Sources: 1. Znaor, A. et al. Eur. Urol. 67, 519-530 (2015). 2. Cohen, H. T. et al. N. Engl. J. Med. 353, 2477-2490 (2005). 3. Ferlay, J. et al. GLOBOCAN 2012 v1.0, Cancer Incidence and Mortality Worldwide: IARC CancerBase No. 11. (IARC, 2012). 4. Chow, W.-H. et al. Nature Rev. Urol. 7, 245-257 (2010). 5. Rini, B. I. et al. Lancet 373, 1119-1132 (2009).

TGF-α