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of the key points of these studies is that nephrectomy should be offered only to patients with a good performance status. A major concern is that if nephrectomy is adopted as the standard for all patients with metastatic disease, many elderly or infirm and dying patients will be subject to inappropriate surgery.

These two trials, which show the value of a combined surgical and biological approach to metastatic renal cancer, will deservedly be recognised as classic studies. They will also serve as the basis for further studies of new biological and mechanistic agents that are active against this difficult and challenging disease. For future studies of metastatic renal cancer, adjunctive radical nephrectomy should be viewed as the standard of care.

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New developments in impulsivity

Impulsivity, a dimension of personality, is the failure to resist an impulse, drive, or temptation that is harmful to oneself or others. It is a measurable feature of the inability to delay or inhibit acting on impulse, and an inability to calculate odds of negative risk or outcome. Aspects of impulsivity are core symptoms of several of frontal-lobe syndromes, and frontal-lobe hypofunction has been observed in impulsive individuals. And metabolic abnormalities have been observed in the orbital frontal, adjacent ventral medial, and cingulate cortex in patients with impulsive-aggressive disorders. Thus, the orbitofrontal, nucleus accumbens, and amygdala regions seem to play an important role in mediating aspects of impulsivity.

The impulsive disorders are modulated by various neurotransmitter systems. Serotonergic dysregulation and a presynaptic deficit of available serotonin have been observed in human beings with various impulsive disorders, as well as animal models of impulsivity and aggression. Knockout mice lacking the serotonin receptor 5HT1B display increased impulsive aggression and a liking for cocaine and alcohol, and polymorphisms of tryptophan hydroxylase (the rate-limiting enzyme for serotonin synthesis) have been associated with impulsive-aggressive behaviours.

Specific impulse-control disorders, such as pathological gambling, probably involve abnormalities of dopamine receptors and reward pathways, as well as noradrenergic and serotonergic dysfunction. Dopamine function, particularly within the mesocorticolimbic pathways, is critical in the mediation of reward and reinforcement behaviours. Association studies of genes related to dopamine receptors have supported a genetic influence in impulsive behaviours, and µ-opioid receptors are involved in the regulation of these pathways. Peptides such as vasopressin have also been implicated in aggressive behaviours. Nevertheless, a better understanding of the role of neurotransmitters...
modulating relevant neurocircuitry (ie, ventromedial cortex and AcbC) is needed to develop specific treatments for pathological impulsivity across various disorders.

Therapeutic approaches involving pharmacological manipulation of neurotransmitters have been undertaken in an attempt to ameliorate pathological impulsivity in several psychiatric disorders. Much research to date has focused on modulation of serotonin transmission. Selective serotonin-reuptake inhibitors and other enhancers of serotoninergic transmission have reduced impulsive behaviours in a wide range of different disorders, including pathological gambling, borderline personality disorder, sexual addictions, and disorders in the obsessive-compulsive spectrum.14–15

Another pharmacological group of drugs that affect various neurotransmitter systems, including γ-aminobutyric acid, that has been reported to improve impulsive and aggressive behaviour in disorders as diverse as borderline personality disorder and autism are the anticonvulsant mood stabilisers, such as valproic acid.16 Although serotonin dysregulation and hypofunction seem to play a central role in these disorders, impulsivity is probably influenced to differing degrees by the highly interconnected serotonergic, noradrenergic, dopaminergic, opioid, and γ-aminobutyric-acid systems. It is impossible to manipulate the effect of one neurotransmitter system on a set of neurons to the exclusion of surrounding neurons.

Lesion studies to better identify the neurocircuitry of specific impulsive behaviours may be helpful, and Cardinal and colleagues’ tentative localisation of the neuroanatomical basis for delayed reinforcement may eventually lead to new diagnostic imaging or therapeutic procedures. Pharmacological manipulation of neurotransmitter or peptide systems specifically targeted at the AcbC and its relevant afferent pathways may moderate pathological impulsivity more specifically than do current treatments for pathological impulsivity across various psychiatric disorders.

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Health economics without tears

See page 993

It was once thought that expenditure on Britain’s National Health Service might even diminish with time as a backlog of ill-health was cleared. Nobody believes that today, not for the NHS or for any other method of delivering health care, and clinicians have been forced to come to terms with economics. So has The Lancet; time and again research papers would arrive at the office carrying the throwaway line that adoption of such-and-such a seemingly expensive drug, operation, or test would actually save money in the long run. To sift the valid claims from the wishful thinking, the journal now uses specialist health-economics reviewers and has been fortunate to have the services of a panel set up by Martin Meltzer at the US Centers for Disease Control and Prevention. This week, beginning with Dr Meltzer’s introduction to this important but not, I hope, arcane subject, The Lancet embarks on a five-part series on health economics. Those general principles, such as expenditure on one service means not funding something else and the fact that “value for money” will depend on the perspective from which the service is viewed, will be illustrated in the subsequent articles on surgery, drug treatment, diagnostic tests, and prevention.

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New Developments in Human Neurocognition: Clinical, Genetic, and Brain Imaging Correlates of Impulsivity and Compulsivity. CNS Spectrums, 19, 69-89. http://dx.doi.org/10.1017/S1092852913000801. [6].
Impulsivity is not simply rudeness or lack of self-discipline. It is a function of the interior signaling system of the brain. Learn more here! Impulsivity, a primary symptom of ADHD, may impair your ability to stop and think about the consequences before speaking or acting. How? In this video, learn about the brainâ€™s â€œresponse inhibitionâ€ center, and why it doesnâ€™t work as well for people with ADHD. Impulsivity, Explained. Impulsivity: a tendency to act or speak on a whim. An impulsive child may blurt out an answer before raising her hand. OR.