SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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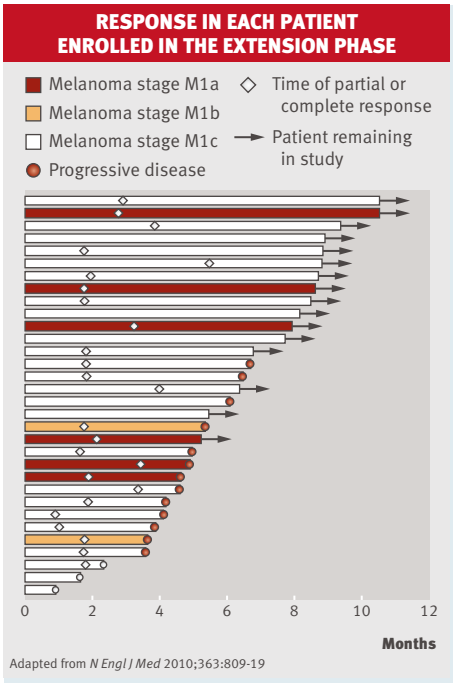
"When I become confused, I try to hide it. This is a skill honed by 35 years of clinical practice, and I expect it will stand me in good stead when I develop delirium at some point in the future"

Read Richard Lehman's journal blog at www.bmj.com/blogs

Eight out of 10 melanomas with V600E mutation respond to new drug



Adapted from *N Engl J Med* 2010;363:809-19

PLX4032 has been shown in animal studies to stop the growth of melanoma cells, but only when the target oncogene, which encodes the enzyme serine-threonine protein kinase B-RAF, has the V600E mutation (valine substituted for glutamic acid at amino acid 600). A phase I dose escalation trial has found the maximum dose at which side effects such as rash, fatigue, and joint pain occur in fewer than one in six people. Most participants had metastatic melanoma, three had papillary thyroid cancer, and three had other cancers, regardless of the V600E mutation. Tumours without the mutation did not respond to treatment but those with the mutation did, and the dose was set at 960 mg twice daily.

Thirty two more patients were then entered into the extension phase of the trial, all of whom had metastatic melanoma that was positive for the mutation. Melanoma disappeared in two of these participants and shrank in 24 of 32. Squamous cell carcinoma developed as an adverse event in 10 of 32. The study is ongoing, but median survival without progression of the disease has exceeded seven months.

Other research indicates that treatment could be harmful in people with melanomas that lack this mutation, and the editorialists warn that for now this should be avoided (p 876). Upcoming trials should elucidate how PLX4032 fits in with other drugs that show promise for melanoma—MEK (mitogen activated protein kinase kinase 1) inhibitors and ipilimumab.

N Engl J Med 2010;363:809-19

Antivirals against herpes seem safe in the first three months of pregnancy

Aciclovir, valaciclovir, and famciclovir—antiviral drugs used to treat infections with herpes simplex and herpes zoster—did not increase the odds of major birth anomalies in a population based registry study set in Denmark. Participants were 837 795 children born alive, and their mothers, between 1996 and 2008.

In total, 19 960 infants (2.4%) were diagnosed with a major birth anomaly. Of 1804 pregnancies in which mothers took the antivirals in the first trimester, 40 babies (2.2%) had a major birth defect. The corresponding figures were 19 920 (2.4%) in women who did not take antivirals (adjusted prevalence odds ratio 0.89, 95% CI 0.65 to 1.22).

There were 32 anomalies in babies born to the 1561 mothers who took aciclovir in the first trimester (2.0%). Valaciclovir was taken in 229 pregnancies, and seven of these babies were born with defects (3.1%). Only 26 women took famciclovir, and one baby born after such exposure had a major anomaly (3.8%); the authors say that there is insufficient evidence of safety for this drug.

The study was limited to anomalies diagnosed in hospital. The registry has previously been shown to be 90% complete and 88% accurate for birth anomalies. Finally, exposure to drugs was measured by filled prescriptions, so non-adherence could have diluted a possible effect among mothers who did take the drugs.

JAMA 2010;304:859-66

CBT tops relaxation plus education for adults with ADHD

A randomised trial, done in a single centre, investigated 86 adults, aged 43 years on average, with attention deficit/hyperactivity disorder (ADHD). All participants took drugs for the condition but still had clinically relevant symptoms related to inattention, hyperactivity, and impulsivity. Only three previous trials have tested psychosocial interventions for adults with ADHD, but they were small and did not use an active comparator.

Both cognitive behavioural therapy (CBT) and the control intervention—which included relaxation techniques, education about ADHD, and supportive psychotherapy—were delivered in 12 weekly sessions lasting 50 minutes. Outcomes were assessed in a blinded manner using the ADHD rating scale (assesses 18 symptoms of ADHD; a score of 0 indicates no condition, 3 indicates severe ADHD) and the clinical global impression scale for severity (a score of 1 indicates not ill, 7 indicates extremely ill). Patients also rated their symptoms on an 18 item scale.

Cognitive behavioural therapy topped the control by −4.631 points (95% CI −8.30 to −0.963) on the ADHD rating scale and by −0.0531 points (−1.01 to −0.05) on the global impression scale. Outcomes as assessed by patients also favoured cognitive behavioural therapy. The differences were maintained nine months after treatments ended.

JAMA 2010;304:875-80

Prevention of CVD: some approaches widen, some narrow, the inequality gap

Strategies aimed at preventing cardiovascular disease can decrease inequalities in populations if they are delivered to all people equally, such as through legislation or fiscal policies. Because poorer people experience a greater burden of cardiovascular disease, they can gain more from whole population approaches, which narrow the inequality gap. This applies to approaches such as smoking bans, salt reduction in processed foods, and bans on industrial *trans*-fats.

Approaches that rely on the behaviours of individuals, however, such as health promotion campaigns and behaviour change programmes, work better for more affluent people and less well for poorer people, thus increasing inequality. Such approaches include smoking cessation services, dietary interventions, as well as diagnosis and prescription of drugs for high blood lipids or hypertension.

Currently, only Sweden has successfully combined whole population and high risk approaches to reduce mortality from cardiovascular diseases and narrow the inequality gap.

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