SHORT CUTS

ALL YOU NEED TO READ IN THE OTHER GENERAL JOURNALS

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Fetal growth in the first trimester has far reaching implications

We already know that what happens to babies in the womb has implications way beyond birth. The first trimester seems particularly important, according to the latest analysis of data from an established cohort in the Netherlands. Researchers found a link between poor growth in the first trimester and adverse birth outcomes in 1631 pregnant women with reliable dates. They also recorded accelerated growth in infancy for these babies, who seemed to be "catching up" growth they had missed in the first trimester. Rapid growth in infancy is a well known risk factor for cardiovascular disease in adults. A poor intrauterine environment in early pregnancy may have lifelong implications, say the researchers.

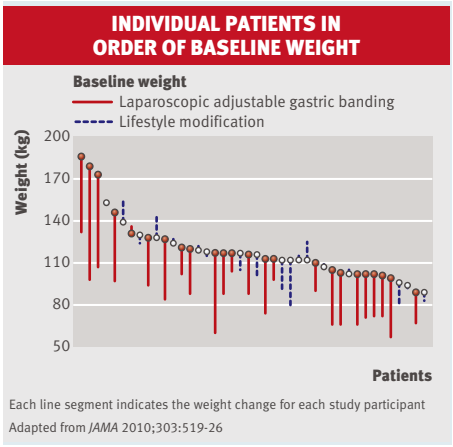
They used crown-rump length between the 10th and 13th week of pregnancy as a proxy for early fetal growth. Smoking and failing to take folic acid supplements were both independently associated with shorter crown-rump length in the first trimester. So were increases in diastolic blood pressure and maternal haematocrit. After multiple adjustments, babies with a crown-rump length in the bottom fifth had more than twice the odds of being born preterm (2.12, 95% CI 1.24 to 3.61), at low birth weight (2.42, 1.41 to 4.16), or small for gestational age (2.64, 1.64 to 4.25) compared with other babies.

JAMA 2010;303:527-34

Preliminary trial supports bariatric surgery for teenagers

Bariatric surgery is a controversial treatment for obese adolescents. Surgeons, parents, policy makers, and third party payers continue to argue over the evidence, which is generally poor. An Australian team recently added a much needed randomised trial to the mix. It was small (n=50) and compared adjustable gastric banding with a generous lifestyle intervention based on education, diet, and exercise. Surgery worked significantly better over two years of follow-up.

This trial is important, says an editorial (p 559), because it tells us that randomly allocating adolescents to surgical or medical options is at least feasible. These researchers managed



to recruit 50 well motivated adolescents with a mean body mass index (BMI) over 40. Exactly half had laparoscopic surgery. They lost 78.8% of their excess weight over two years (95% CI 66.6% to 91.0%; 12.7 BMI units, 11.3 to 14.2). The 25 controls lost a mean of 13.2% of excess body weight (2.6% to 21.0%; 1.3 BMI units, 0.4 to 2.9), although only 18 completed follow-up.

Markers of cardiovascular risk improved more after surgery. So did some measures of quality of life. The main trade off was a relatively high rate of revision procedures. In this trial, seven adolescents needed further surgery—mostly removal and replacement of the band after pouch dilation, heartburn, reflux, or vomiting.

JAMA 2010;303:519-26

One-off treatment for leishmaniasis worked well in India

The cost of treating visceral leishmaniasis came down recently after the manufacturers agreed to cut the price of a phial of liposomal amphotericin B from $200 (£128; €146) to $20 in endemic areas. The treatment is now affordable in places like Bihar in northeast India, which is home to an estimated 50% of all cases worldwide.

In a local trial, a single infusion of liposomal amphotericin B (10 mg/kg), lasting just one hour, cured all 304 patients, compared with a cure rate of 98% (106/108) for the control treatment—admission to hospital for 15 infusions of amphotericin B deoxycholate over 30 days. The trial was designed to test "non-inferiority" in adults and children with visceral leishmaniasis (kala-azar). Cure rates at six months were similar, and liposomal amphotericin B seemed to have fewer side effects, particularly rigors and fever (40% *v* 64%). The authors are confident the new treatment is no less safe and effective than the old one. It is certainly more convenient, and may even be cheaper, according to crude costings. Patients given liposomal amphotericin B had more relapses than those treated with amphotericin B deoxycholate (4.3% (13/304) *v* 1.9% (2/108)), although the difference wasn't significant.

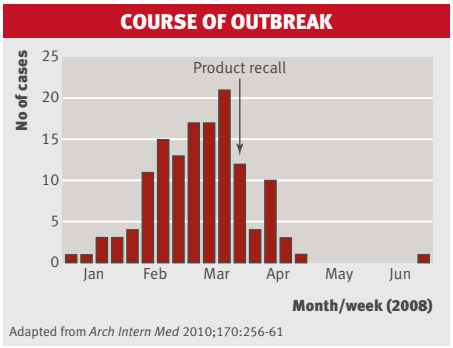
The patients in this trial had their liposomal amphotericin B during an overnight stay in hospital. If the safety profile is confirmed, others should be able to attend local health clinics instead, say the authors.

N Engl J Med 2010;362:504-12

Tighter regulation of supplements please

An outbreak of selenium poisoning from a misformulated supplement has prompted calls for an urgent re-evaluation of controversial US regulations governing the manufacture and sale of dietary supplements. At least 201 people aged between 4 and 92 were poisoned by a supplement containing 200 times the dose of selenium that was given on the product label. Most of the affected people reported diarrhoea, nausea, fatigue, hair loss, joint pain, and nail abnormalities. Symptoms persisted for more than 90 days in some cases. After a detailed nationwide investigation, the outbreak was eventually blamed on human error at one of the manufacturer's suppliers. People began to get ill in late January 2008. The product was recalled in late March.

One expert (p 261) says the current regulations, such as they are, fail to protect people



"Laparoscopic gastric banding for severely obese adolescents doesn't quite come into that category, but as remedies go, it smacks of desperation"
Richard Lehman's journal blog, doc2doc.bmj.com

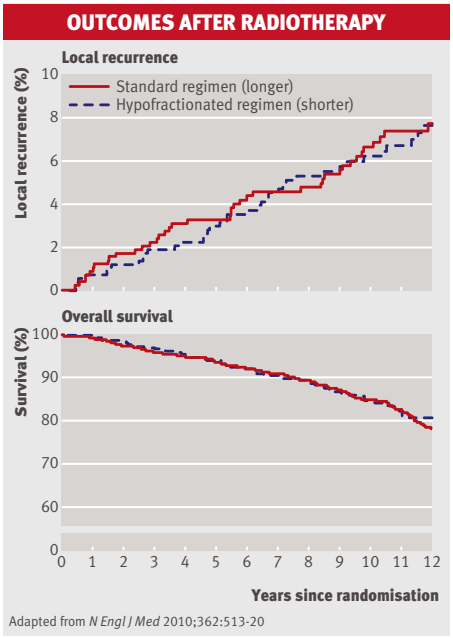
from the potential harms associated with untested products. But they do ensure healthy tax revenues from a booming supplements industry. The 70% of US adults who take supplements now have more than 75 000 to choose from. Total annual sales have grown from $4bn (£2.6bn; €2.9bn) to $25bn in 15 years, driven by aggressive advertising direct to consumers. It is time to redress the balance, he writes. Open access to supplements has failed to improve population health and sometimes does the opposite. The regulations are still full of holes, despite recent attempts to introduce good manufacturing practice. They must be tightened up, urgently.
Arch Intern Med 2010;170:256-61

MRI doesn't reduce reoperations after lumpectomy

Preoperative magnetic resonance imaging (MRI) helps surgeons assess the size and extent of breast cancers. But can this kind of imaging actually make a difference to women? One trial looked at the effect of routine MRI on reoperation rates for women having lumpectomies. It made no difference. Around one in 10 women in both groups (MRI or no MRI) needed further excisions within six months. Fewer needed mastectomies, but again preoperative imaging made no difference to the rates. Overall, nearly one in five women in both groups needed further surgery or had an avoidable initial mastectomy prompted by MRI findings (19% (153/816) *v* 19% (156/807); odds ratio 0.96, 95% CI 0.75 to 1.24). All the women had standard preoperative assessments with mammography, ultrasound, and either aspiration cytology or biopsy.

This was a pragmatic trial, conducted in 45 UK hospitals, and designed to reflect local practice, which includes a very generous surgical margin for lumpectomies. A commentator from the US (p 528) argues that MRI might have more of an effect in centres where surgeons take as little tissue as possible to start with and accept higher reoperation rates. MRI might not be for everyone, but it is still too early to abandon it completely, she writes. Not least because we still don't know the effects of imaging on important clinical outcomes, such as recurrence and survival.
Lancet 2010;375:563-71

Three weeks of radiotherapy works as well as five weeks for localised breast cancers



Adapted from *N Engl J Med* 2010;362:513-20

Radiotherapy for breast cancer is broken down into fractions of a total dose, given daily over several weeks. A schedule that gives higher daily doses of radiation for a shorter period is more convenient for women, and clinical trials suggest results are good up to five years after surgery for localised cancers. One trial, from Canada, has achieved 10 years of follow-up and again results looked promising, with matching mortality and recurrence rates for women given shorter or longer treatment schedules after a lumpectomy. The higher daily doses required for a shorter schedule seemed no more toxic in the long term, and cosmetic outcomes were similar for women in both groups.

This trial compared a traditional regimen of a total of 50.0 Gy in 25 fractions over five weeks with one of a total of 42.5 Gy given in 16 fractions over three weeks. All women had clear resection margins after a lumpectomy and no affected axillary lymph nodes. Few had chemotherapy. Survival to 10 years was almost identical in the two groups (84.4% *v* 84.6%). Cosmetic appearance after 10 years was good or excellent for 69.8% women treated with the shorter schedule and 71.3% of controls.

Women with high grade tumours had more local recurrences after the three week schedule in subgroup analyses (hazard ratio 3.08, 95% CI 1.22 to 7.76). But this result may be unreliable and should be confirmed, say the authors.
N Engl J Med 2010;362:513-20

Most quitters go it alone

Most people give up smoking on their own, without help from drugs, nicotine replacements, or psychological treatments. This silent majority is comprehensively ignored by the tobacco control community and by governments setting health policy, write two public health experts from Australia. They blame the medicalisation of smoking cessation, the influence of the drugs industry, and the prevailing interventionist view of tobacco control research that values randomised trials of medical treatments over observational research that asks successful quitters how they did it.

What little research there is suggests that most people either go "cold turkey" or cut down gradually. And they do it alone. Messages to the contrary are widespread and damaging—not least because whole populations lose the confidence to help themselves, which can lead to fatalism. As usual, these effects are felt most keenly in low and middle income countries where citizens cannot afford nicotine replacement, bupropion, or counselling, and cigarettes are so much cheaper, they write. Health authorities everywhere should emphasise that these props aren't necessary and focus on more equitable interventions such as taxation, hard hitting public health campaigns, pack warnings, and smoking bans.

In business, arts, and sport, successful people who reach their goals are a rich source of information for the rest of us. We study their motivation, profiles, environments, attitudes, and habits. We should do the same for successful quitters, they write. This kind of research would help restore some much needed balance. Among the 662 studies of smoking cessation indexed by Medline in 2007 and 2008, they found only 57 reporting data on doing it without help.
PLoS Med 2010; doi:10.1371/journal.pmed.1000216

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