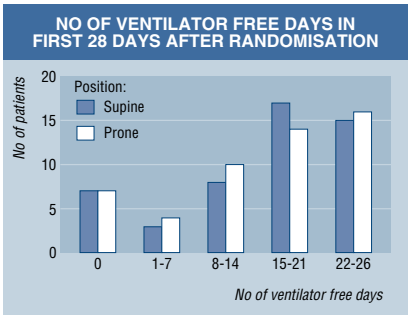
Short cuts

What's new in the other general journals

Prone positioning may not help children with ARDS



Children being ventilated because of acute respiratory distress syndrome should be nursed on their backs, not their stomachs, say a research team from the United States. Their trial in 102 infants and children found that prone positioning, which is common practice and is thought to improve ventilation and lung mechanics, did not reduce the time children spend on a ventilator or improve their chances of survival, despite improved oxygenation.

Children in the trial spent a mean of just under 16 days being ventilated, whether they were nursed prone or supine during the acute phase of their illness (adjusted mean difference 0.3 days, 95% confidence interval -3.0 to 3.5; P = 0.87). Children who were nursed prone for at least 20 hours a day did not recover any faster than those nursed supine and were no less likely to have neurological deficits or other health problems afterwards.

The authors were so convinced by their interim analysis that they stopped the trial early, but a linked editorial (pp 248-50) urges paediatric intensivists not to abandon prone positioning just yet: this trial is limited by, among other things, small size, atypical patients, and a primary outcome (ventilator-free days) that may not be clinically relevant.

JAMA 2005;294:229-37

Symptoms rebound after HRT

Women with menopausal symptoms who want hormone replacement therapy are advised to take the smallest effective dose for the shortest possible time. But what happens to their symptoms when they stop?

After one landmark randomised trial of HRT, 55.5% of the 503 women who had had vasomotor symptoms before taking HRT developed moderate or severe symptoms when they stopped taking it. Almost as many (54.7% of 1396) reported a return of pain and stiffness. Women who had had symptoms at the start of the trial and who took placebo pills were less likely to develop either vasomotor symptoms or joint pain after the end of the trial (21.3% of 447, 38.3% of 1445), as were women who took HRT but who did not have menopausal symptoms at the start (6.4% of 1114, 27.5% of 2688).

The women took oestrogen plus medroxyprogesterone or placebo for a mean of 5.6 years during the women's health initiative study, and then stopped abruptly when the study ended earlier than planned. Researchers asked them about symptoms 8-12 months later. This latest analysis included only half of the women in the original study, but it should give women and their doctors some insight into what to expect when they stop HRT. Overall, 63.3% of the women who had taken HRT reported at least one withdrawal symptom.

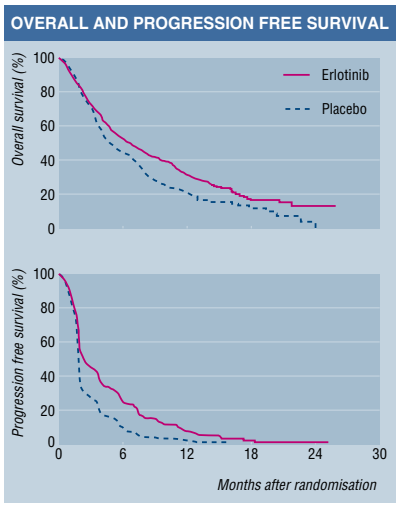
JAMA 2005;294:183-93

Erlotinib prolongs survival for some people with advanced lung cancer

Erlotinib is a tyrosine kinase inhibitor that targets epidermal growth factor receptors in non-small cell lung cancers. It's currently being evaluated as a third line chemotherapy treatment for people with advanced cancers; and, in the first trial to look at survival, patients who had erlotinib lived two months longer than patients who had placebo (6.7 *v* 4.7 months; hazard ratio 0.7; P < 0.001). They also survived longer without deteriorating cough, breathlessness, or pain. Rash and diarrhoea were among the commonest side effects, but only 26/485 (5%) of patients had to stop treatment because of toxicity.

In this large trial, which was sponsored by the manufacturers of erlotinib, almost all the 731 patients had tried platinum based chemotherapy and half still had worsening disease despite two attempts at cytotoxic chemotherapy. Erlotinib improved their chances of surviving for a year from 22% to 31%, a difference the authors say is clinically worthwhile as well as statistically significant.

Even so, only 8.9% of patients given erlotinib had a measurable response to treatment. The ongoing challenge is to find the molecular characteristics that predict a response, so erlotinib can be offered only to those most likely to benefit. Ideally, this work should be completed before clinical trials begin, says a linked editorial (pp 200-2). The molecular results from this trial were inconclusive (pp 133-44).



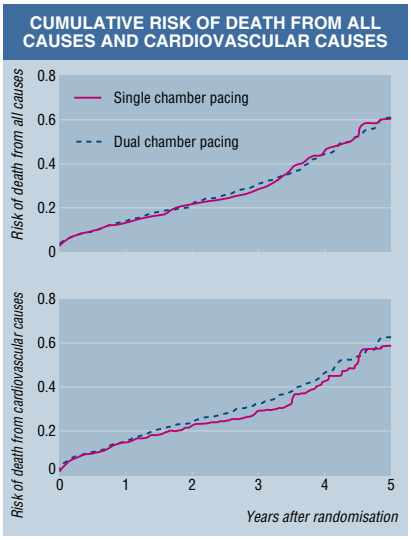
New England Journal of Medicine 2005;353:123-32

Single chamber pacing works as well as dual chamber pacing in elderly people with heart block

For people with heart block, pacing both atrial and ventricular chambers—dual chamber pacing—is a more physiological approach than single chamber pacing, but better haemodynamics do not translate to a longer or healthier life, according to a large head to head trial comparing the two pacing methods in elderly patients.

During 4.6 years of follow-up, the annual death rate from all causes was just over 7% in both groups (hazard ratio for single *v* dual pacing 0.96, 95% confidence interval 0.83 to 1.11). Dual pacing did not reduce the incidence of atrial fibrillation, heart failure, or thromboembolic events including stroke, but it did cause more complications both during and after the procedure (7.8% *v* 3.5% (P < 0.001) and 10.4% *v* 6.1% (P < 0.001)).

Over 2000 people took part in this UK trial, which researchers confined to people aged 70 or older because they suspected that previous studies favouring dual pacing were biased by preferential selection of young and relatively fit patients. These findings suggest they were right. Pacing



both atrial and ventricular chambers should work better, and it's still unclear why it didn't. The only difference between the treatment groups in this trial was a slightly higher risk of stroke, transient ischaemic attack, or thromboembolism among the 502 patients treated with fixed rate single chamber pacing compared with the dual chamber group (2.5% *v* 1.7%), a finding the authors say could have been due to chance.

New England Journal of Medicine 2005;353:145-55

Better communication improves access to hospice care for residents in nursing homes

There's some evidence that residents in nursing homes get better care if staff refer them to hospice services during their final illness. Only the lucky minority are offered the chance in the US, although researchers recently reported that better access to hospices and a better death could be a simple matter of identifying residents who might benefit and then letting their doctor know.

In a randomised trial, researchers interviewed 205 residents of three nursing homes or their relatives using a structured interview lasting only 5-10 minutes. They identified 84 residents who needed and wanted hospice care. In the intervention group, results of each interview were faxed to the resident's primary care doctor, who was asked to reply by fax indicating whether he or she would like the nursing home to arrange a hospice visit. Residents and relatives in the control group were simply told that they could learn more about hospice care from their doctor.

Residents in the intervention group were more likely to get hospice care than those in the control group (21/107 (20%) *v* 1/98 (1%); P < 0.001), as well as spending less time in hospital (mean number of days 1.2 *v* 3.0; P = 0.03) and having a better end of life experience (mean satisfaction rating (on a scale of 1-5) 4.1 *v* 2.5; P = 0.04). Quality of care at the end of life was rated by relatives two months after each death.

The authors say their intervention is quick and easy to administer, and therefore relatively cheap. They also think it's exportable to most long term care settings, with the caveat that all the nursing homes in their study had a good relationship with a local community hospice.

JAMA 2005;294:211-7

Hydroxycarbamide is preferable to anagrelide for patients with essential thrombocythaemia

Essential thrombocythaemia is a relatively benign chronic myeloproliferative disease. The challenge of treatment is to prevent thrombosis or bleeding without increasing the risk of transformation into something less benign such as myelofibrosis or acute myeloid leukaemia. Hydroxycarbamide is the mainstay of treatment, but fears that it might be leukaemogenic led researchers to test other treatments including the antiplatelet drug anagrelide. Thanks to a large randomised trial, it's now fairly clear that hydroxycarbamide is the better, safer treatment.

The trial included 809 patients with essential thrombocythaemia and a high risk of thrombosis. They all took low dose aspirin and either anagrelide or hydroxycarbamide for a median of 39 months. Both treatments controlled patients' platelet counts without increasing the risk of leukaemia, but anagrelide was associated with a significantly increased risk of arterial thrombosis (odds ratio 2.16, 95% confidence interval 1.27 to 3.69, P = 0.004), bleeding (2.61, 1.27 to 5.33, P = 0.008), and transformation to myelofibrosis (2.92, 1.24 to 6.86, P = 0.01). Patients taking anagrelide reported more side effects than those taking hydroxycarbamide, and they were more likely withdraw from treatment (148/405 *v* 79/404, P < 0.001).

These emphatic results, which stopped the trial earlier than planned, mean that hydroxycarbamide plus low dose aspirin should remain the treatment of choice for people with essential thrombocythaemia and a high risk of thrombosis.

New England Journal of Medicine 2005;353:33-45

Prayers don't help cardiac patients having catheterisation

Faithful congregations have always prayed for the sick. Much more recently, researchers have started applying rigorous trial methods to see if it works. Four previous trials have failed to secure an answer either way, partly because there's no consensus about who should do the praying, how long they should pray for, and what outcomes should be assessed. In the most recent trial, researchers asked whole congregations from various faiths to pray for patients admitted for cardiac catheterisation or percutaneous coronary intervention. The congregations prayed for between five and 30 days, and in the final year of the trial an extra 12 prayer groups were recruited to pray for the praying congregations (two tier praying)

Neither strategy made any difference to the 748 US patients in the trial, who were equally likely to have had a cardiovascular event, been readmitted to hospital, or died by six months after randomisation with or without prayer (hazard ratio 0.97, 95% confidence interval 0.77 to 1.24 for single tier praying; 0.83, 0.5 to 1.4, for two tier praying). A more "hands on" healing therapy at the bedside involving touch, image therapy, and music was equally ineffective against the composite primary end point, but did seem to reduce six month mortality in a small secondary analysis (7/374 (2%) *v* 20/374 (6%); hazard ratio 0.35, 0.15 to 0.82).

The authors were disappointed by their negative result, which probably means that intercessory prayer does not save lives. Of course, it's also possible that prayer does work but that the trial failed to detect it; nearly 90% of the patients in the "no prayer" group had someone praying for them somewhere, a protocol violation that could have seriously reduced any difference in outcome between the groups.

Lancet 2005;366;211-7

Handwashing with soap prevents diarrhoea, pneumonia, and impetigo in squatter communities in Pakistan

Families in Pakistan can dramatically reduce their children's risk of diarrhoea or pneumonia simply by washing their hands more often with soap. In a randomised trial in Karachi, weekly encouragement of handwashing and bathing and a free supply of soap reduced the incidence of pneumonia in children aged < 5 years by 50% (2.2 *v* 4.4 cases/100 person weeks) and the incidence of diarrhoea in children aged ≤ 15 by 53% (1.9 *v* 4.06). Bathing with soap also reduced the incidence of impetigo by a third compared with the incidence in control neighbourhoods, where researchers visited households but did not discuss hygiene.

Researchers randomised 36 poor neighbourhoods in Karachi, including 906 households with a mean of nearly 10 residents each. The intervention was fairly intensive, with field workers holding community meetings, showing videos, and visiting households once a week for a year. The hard work and free soap (from the sponsors Procter and Gamble) paid off, but the authors think their intervention may be too expensive to roll out to all poor communities in the developing world. They have shown once again that handwashing protects against common and lethal infectious diseases. The challenge now is to find a cheap way to promote it.

Lancet 2005;366:225-33