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JAMA

1)The Role of Laryngoscopy in the Diagnosis of Spasmodic Dysphonia

--- Laryngoscopy serves an important role in the diagnosis of SD (痉挛性发声困难) by excluding other pathologic causes and identifying vocal tremor.

2)Gabapentin treatment for alcohol dependence: a randomized clinical trial.

--- Gabapentin (particularly the 1800-mg dosage)
effective
relapse-related symptoms of insomnia, dysphoria, and craving, with a favorable safety profile.

3)Association Between Preoperative 25-Hydroxyvitamin D Level and Hospital-Acquired Infections Following Roux-en-Y Gastric Bypass Surgery(胃旁路手术)

---a significant inverse association was observed between preoperative 25(OH)D levels and the risk for HAIs.

4）Vitamin D as an Early Predictor of Multiple Sclerosis Activity and Progression.

----a strong risk factor for long-term MS activity and progression.

5）Effect of Communication Skills Training for Residents and Nurse Practitioners on Quality of Communication With Patients With Serious Illness.A Randomized Trial

----simulation-based communication training compared with usual education did not improve quality of communication about end-of-life care or quality of end-of-life care but was associated with a small increase in patients' depressive symptoms.

6）Calcium-channel blocker-clarithromycin drug interactions and acute kidney injury

----Among older adults taking a calcium-channel blocker, concurrent use of clarithromycin compared with azithromycin was associated with a small but statistically significant greater 30-day risk of hospitalization with acute kidney injury. These findings support current safety warnings regarding concurrent use of CYP3A4 inhibitors and calcium-channel blockers

Sex differences in acute coronary syndrome symptom presentation in young patients.

- **IMPORTANCE:**
- Little is known about whether sex differences in acute coronary syndrome (ACS) presentation exist in young patients and what factors determine absence of chest pain in ACS presentation.
- **OBJECTIVES:**
- To evaluate sex differences in ACS presentation and to estimate associations between sex, sociodemographic, gender identity, psychosocial and clinical factors, markers of coronary disease severity, and absence of chest pain in young patients with ACS.
- **DESIGN, SETTING, PARTICIPANTS:**
- We conducted a prospective cohort study of 1015 patients (30% women) 55 years or younger, hospitalized for ACS and enrolled in the GENESIS PRAXY (Gender and Sex Determinants of Cardiovascular Disease: From Bench to Beyond Premature Acute Coronary Syndrome) study (January 2009-September 2012).
- **MAIN OUTCOMES AND MEASURES:**
- The McSweeney Acute and Prodromal Myocardial Infarction Symptom Survey was administered during hospitalization.

- **RESULTS:**
- The median age for both sexes was 49 years. Women were more likely to have non-ST-segment elevation myocardial infarction (37.5 vs 30.7; P = .03) and present without chest pain compared with men (19.0% vs 13.7%; P = .03). Patients without chest pain reported fewer symptoms overall and no discernable pattern of non-chest pain symptoms was found. In the multivariate model, being a woman (odds ratio [OR], 1.95 [95% CI, 1.23-3.11]; P = .005) and tachycardia (OR, 2.07 [95% CI, 1.20-3.56]; P = .009) were independently associated with ACS presentation without chest pain. Patients without chest pain did not differ significantly from those with chest pain in terms of ACS type, troponin level elevation, or coronary stenosis.
- **CONCLUSIONS AND RELEVANCE:**
- Chest pain was the most common ACS symptom in both sexes. Although women were more likely to present without chest pain than men, absence of chest pain was not associated with markers of coronary disease severity. Strategies that explicitly incorporate assessment of common non-chest pain symptoms need to be evaluated.

Management of inadvertent carotid artery sheath insertion during central venous catheter placement.

- **IMPORTANCE:**
- Inadvertent(不经意) carotid sheath insertion during central venous catheter placement could lead to serious complications.
- **OBJECTIVE:**
- To describe management of inadvertent carotid artery sheath insertion placed intraoperatively during attempted jugular venous cannulation for pulmonary artery catheter placement.
- **DESIGN, SETTING, AND PARTICIPANTS:**
- In a retrospective medical record review of patients from hospitals affiliated with Baylor College of Medicine, Houston, Texas, a total of 12 patients over 11 years who sustained intraoperative carotid artery introducer sheath placement during attempted jugular vein cannulation were identified. Six patients underwent immediate carotid artery exploration with sheath removal and primary repair. The remaining 6 patients underwent percutaneous closure using a suture-mediated closure device. Treatment outcomes of these 2 groups were analyzed.
- **MAIN OUTCOMES AND MEASURES:**
- Technical success, duration of treatment, stroke, return to the operating room, and long-term outcomes.

- **RESULTS:**
- Technical success was achieved in all patients in both groups. The intended operations were aborted in all patients following catheter removal and carotid artery closure. The mean (SD) durations of treatment for the operative and endovascular groups were 32 (12) minutes and 6 (3) minutes, respectively (P = .03). No neurological deficit occurred in either group. The intended operations were all subsequently performed, and the mean delays of operation in the operative and endovascular groups were 5 and 3 days, respectively (P = .20). Follow-up carotid duplex showed no injury of the repaired artery in either group. During a mean follow-up of 42 months, no complications or neurological deficits were noted in either patient cohort.
- **CONCLUSIONS AND RELEVANCE:**
- Inadvertent carotid artery sheath placement during attempted central venous cannulation for pulmonary artery catheter insertion mandates catheter removal and repair of the carotid artery puncture site. The closure device permits percutaneous repair of the carotid artery expeditiously. Our experience showed this treatment modality to be as safe and effective as operative repair.

Low-dose dopamine or low-dose nesiritide in acute heart failure with renal dysfunction: the ROSE acute heart failure randomized trial

- **IMPORTANCE:**
- Small studies suggest that low-dose dopamine or low-dose nesiritide(奈西利肽) may enhance decongestion and preserve renal function in patients with acute heart failure and renal dysfunction; however, neither strategy has been rigorously tested.
- **OBJECTIVE:**
- To test the 2 independent hypotheses that, compared with placebo, addition of low-dose dopamine (2 μg/kg/min) or low-dose nesiritide (0.005 μg/kg/min without bolus) to diuretic therapy will enhance decongestion and preserve renal function in patients with acute heart failure and renal dysfunction.
- **DESIGN, SETTING, AND PARTICIPANTS:**
- Multicenter, double-blind, placebo-controlled clinical trial (Renal Optimization Strategies Evaluation [ROSE]) of 360 hospitalized patients with acute heart failure and renal dysfunction (estimated glomerular filtration rate of 15-60 mL/min/1.73 m2), randomized within 24 hours of admission. Enrollment occurred from September 2010 to March 2013 across 26 sites in North America.

- **INTERVENTIONS:**
- Participants were randomized in an open, 1:1 allocation ratio to the dopamine or nesiritide strategy. Within each strategy, participants were randomized in a double-blind, 2:1 ratio to active treatment or placebo. The dopamine (n = 122) and nesiritide (n = 119) groups were independently compared with the pooled placebo group (n = 119).
- **MAIN OUTCOMES AND MEASURES:**
- Coprimary end points included 72-hour cumulative urine volume (decongestion end point) and the change in serum cystatin C from enrollment to 72 hours (renal function end point).

- **RESULTS:**
- Compared with placebo, low-dose dopamine had no significant effect on 72-hour cumulative urine volume (dopamine, 8524 mL; 95% CI, 7917-9131 vs placebo, 8296 mL; 95% CI, 7762-8830 ; difference, 229 mL; 95% CI, -714 to 1171 mL; P = .59) or on the change in cystatin C level (dopamine, 0.12 mg/L; 95% CI, 0.06-0.18 vs placebo, 0.11 mg/L; 95% CI, 0.06-0.16; difference, 0.01; 95% CI, -0.08 to 0.10; P = .72).
- Similarly, low-dose nesiritide had no significant effect on 72-hour cumulative urine volume (nesiritide, 8574 mL; 95% CI, 8014-9134 vs placebo, 8296 mL; 95% CI, 7762-8830; difference, 279 mL; 95% CI, -618 to 1176 mL; P = .49) or on the change in cystatin C level (nesiritide, 0.07 mg/L; 95% CI, 0.01-0.13 vs placebo, 0.11 mg/L; 95% CI, 0.06-0.16; difference, -0.04; 95% CI, -0.13 to 0.05; P = .36). Compared with placebo, there was no effect of low-dose dopamine or nesiritide on secondary end points reflective of decongestion, renal function, or clinical outcomes.

- **CONCLUSION AND RELEVANCE:**
- In participants with acute heart failure and renal dysfunction, neither low-dose dopamine nor low-dose nesiritide enhanced decongestion or improved renal function when added to diuretic therapy.

Rates of cardiopulmonary resuscitation training in the United States.

- **IMPORTANCE** Prompt bystander cardiopulmonary resuscitation (CPR) improves the likelihood of surviving an out-of-hospital cardiac arrest. Large regional variations in survival after an out-of-hospital cardiac arrest have been noted.
- **OBJECTIVES** To determine whether regional variations in county-level rates of CPR training exist across the United States and the factors associated with low rates in US counties.
- **DESIGN, SETTING, AND PARTICIPANTS** We used a cross-sectional ecologic study design to analyze county-level rates of CPR training in all US counties from July 1, 2010, through June 30, 2011. We used CPR training data from the American Heart Association, the American Red Cross, and the Health & Safety Institute. Using multivariable logistic regression models, we examined the association of annual rates of adult CPR training of citizens by these 3 organizations (categorized as tertiles) with a county's geographic, population, and health care characteristics. EXPOSURE Completion of CPR training.
- **MAIN OUTCOME AND MEASURES** Rate of CPR training measured as CPR course completion cards distributed and CPR training products sold by the American Heart Association, persons trained in CPR by the American Red Cross, and product sales data from the Health & Safety Institute.

- **RESULTS** During the study period, 13.1 million persons in 3143 US counties received CPR training. Rates of county training ranged from 0.00% to less than 1.29% (median, 0.51%) in the lower tertile, 1.29% to 4.07% (median, 2.39%) in the middle tertile, and greater than 4.07% or greater (median, 6.81%) in the upper tertile. Counties with rates of CPR training in the lower tertile were more likely to have a higher proportion of rural areas (adjusted odds ratio, 1.12 [95% CI, 1.10-1.15] per 5-percentage point [PP] change), higher proportions of black (1.09 [1.06-1.13] per 5-PP change) and Hispanic (1.06 [1.02-1.11] per 5-PP change) residents, a lower median household income (1.18 [1.04-1.34] per $10 000 decrease), and a higher median age (1.28 [1.04-1.58] per 10-year change). Counties in the South, Midwest, and West were more likely to have rates of CPR training in the lower tertile compared with the Northeast (adjusted odds ratios, 7.78 [95% CI, 3.66-16.53], 5.56 [2.63-11.75], and 5.39 [2.48-11.72], respectively).
- **CONCLUSIONS AND RELEVANCE** Annual rates of US CPR training are low and vary widely across communities. Counties located in the South, those with higher proportions of rural areas and of black and Hispanic residents, and those with lower median household incomes have lower rates of CPR training than their counterparts. These data contribute to known geographic disparities in survival of cardiac arrest and offer opportunities for future community interventions.

Effect of CPAP on blood pressure in patients with obstructive sleep apnea and resistant hypertension: the HIPARCO randomized clinical trial.

- **IMPORTANCE:**
- More than 70% of patients with resistant hypertension have obstructive sleep apnea (OSA). However, there is little evidence about the effect of continuous positive airway pressure (CPAP) treatment on blood pressure in patients with resistant hypertension.
- **OBJECTIVE:**
- To assess the effect of CPAP treatment on blood pressure values and nocturnal (夜间)blood pressure patterns in patients with resistant hypertension and OSA.
- **DESIGN, SETTING, AND PARTICIPANTS:**
- Open-label, randomized, multicenter clinical trial of parallel groups with blinded end point design conducted in 24 teaching hospitals in Spain involving 194 patients with resistant hypertension and an apnea-hypopnea index (AHI) of 15 or higher. Data were collected from June 2009 to October 2011.
- **INTERVENTIONS:**
- CPAP or no therapy while maintaining usual blood pressure control medication.
- **MAIN OUTCOMES AND MEASURES:**
- The primary end point was the change in 24-hour mean blood pressure after 12 weeks. Secondary end points included changes in other blood pressure values and changes in nocturnal blood pressure patterns. Both intention-to-treat (ITT) and per-protocol analyses were performed.

- **RESULTS:**
- A total of 194 patients were randomly assigned to receive CPAP (n = 98) or no CPAP (control; n = 96). The mean AHI was 40.4 (SD, 18.9) and an average of 3.8 antihypertensive drugs were taken per patient.
- Baseline 24-hour mean blood pressure was 103.4 mm Hg; systolic blood pressure (SBP), 144.2 mm Hg; and diastolic blood pressure (DBP), 83 mm Hg. At baseline, 25.8% of patients displayed a dipper pattern (a decrease of at least 10% in the average nighttime blood pressure compared with the average daytime blood pressure). The percentage of patients using CPAP for 4 or more hours per day was 72.4%. When the changes in blood pressure over the study period were compared between groups by ITT, the CPAP group achieved a greater decrease in 24-hour mean blood pressure (3.1 mm Hg [95% CI, 0.6 to 5.6]; P = .02) and 24-hour DBP (3.2 mm Hg [95% CI, 1.0 to 5.4]; P = .005), but not in 24-hour SBP (3.1 mm Hg [95% CI, -0.6 to 6.7]; P = .10) compared with the control group.
- Moreover, the percentage of patients displaying a nocturnal blood pressure dipper pattern at the 12-week follow-up was greater in the CPAP group than in the control group (35.9% vs 21.6%; adjusted odds ratio [OR], 2.4 [95% CI, 1.2 to 5.1]; P = .02). There was a significant positive correlation between hours of CPAP use and the decrease in 24-hour mean blood pressure (r = 0.29, P = .006), SBP (r = 0.25; P = .02), and DBP (r = 0.30, P = .005).

- **CONCLUSIONS AND RELEVANCE:**
- Among patients with OSA and resistant hypertension, CPAP treatment for 12 weeks compared with control resulted in a decrease in 24-hour mean and diastolic blood pressure and an improvement in the nocturnal blood pressure pattern. Further research is warranted to assess longer-term health outcomes.

- **Blood Pressure Trajectories in Early Adulthood and Subclinical Atherosclerosis in Middle Age**

- **Importance** Single measures of blood pressure (BP) levels are associated with the development of atherosclerosis; however, long-term patterns in BP and their effect on cardiovascular disease risk are poorly characterized.
- **Objectives** To identify common BP trajectories throughout early adulthood and to determine their association with presence of coronary artery calcification (CAC) during middle age.
- **Design, Setting, and Participants** Prospective cohort data from 4681 participants in the CARDIA study, who were black and white men and women aged 18 to 30 years at baseline in 1985-1986 at 4 urban US sites, collected through 25 years of follow-up (2010-2011). We examined systolic BP, diastolic BP, and mid-BP at baseline and years 2, 5, 7, 10, 15, 20, and 25. Latent mixture modeling was used to identify trajectories in systolic, diastolic, and mid-BP over time.
- **Main Outcomes and Measures** Coronary artery calcification greater than or equal to Agatston score of 100 Hounsfield units (HU) at year 25.

- **Results** We identified 5 distinct mid-BP trajectories: low-stable (21.8%; 95% CI, 19.9%-23.7%; n=987), moderate-stable (42.3%; 40.3%-44.3%; n=2085), moderate-increasing (12.2%; 10.4%-14.0%; n=489), elevated-stable (19.0%; 17.1%-20.0%; n=903), and elevated-increasing (4.8%; 4.0%-5.5%; n=217). Compared with the low-stable group, trajectories with elevated BP levels had greater odds of having a CAC score of 100 HU or greater. Adjusted odds ratios were 1.44 (95% CI, 0.83-2.49) for moderate-stable, 1.86 (95% CI, 0.91-3.82) for moderate-increasing, 2.28 (95% CI, 1.24-4.18), for elevated-stable, and 3.70 (95% CI, 1.66-8.20) for elevated-increasing groups. The adjusted prevalence of a CAC score of 100 HU or higher was 5.8% in the low-stable group. These odds ratios represent an absolute increase of 2.7%, 5%, 6.3%, and 12.9% for the prevalence of a CAC score of 100 HU or higher for the moderate-stable, moderate-increasing, elevated-stable and elevated-increasing groups, respectively, compared with the low-stable group. Associations were not altered after adjustment for baseline and year 25 BP. Findings were similar for trajectories of isolated systolic BP trajectories but were attenuated for diastolic BP trajectories.
- **Conclusions and Relevance** Blood pressure trajectories throughout young adulthood vary, and higher BP trajectories were associated with an increased risk of CAC in middle age. Long-term trajectories in BP may assist in more accurate identification of individuals with subclinical atherosclerosis.

Hospital Variation in the Use of Noninvasive Cardiac Imaging and Its Association With Downstream Testing, Interventions, and Outcomes

Importance Current guidelines allow substantial discretion in use of noninvasive cardiac imaging for patients without acute myocardial infarction (AMI) who are being evaluated for ischemia. Imaging use may affect downstream testing and outcomes.

Objective To characterize hospital variation in use of noninvasive cardiac imaging and the association of imaging use with downstream testing, interventions, and outcomes.

Design, Setting, and Participants Cross-sectional study of hospitals using 2010 administrative data from Premier, Inc, including patients with suspected ischemia on initial evaluation who were seen in the emergency department, observation unit, or inpatient ward; received at least 1 cardiac biomarker test on day 0 or 1; and had a principal discharge diagnosis for a common cause of chest discomfort, a sign or symptom of cardiac ischemia, and/or a comorbidity associated with coronary disease. We excluded patients with AMI.

Main Outcomes and Measures At each hospital, the proportion of patients who received noninvasive imaging to identify cardiac ischemia and the subsequent rates of admission, coronary angiography, and revascularization procedures.

- **Results** We identified 549 078 patients at 224 hospitals. The median (interquartile range) hospital noninvasive imaging rate was 19.8% (10.9%-27.7%); range, 0.2% to 55.7%. Median hospital imaging rates by quartile were Q1, 6.0%; Q2, 15.9%; Q3, 23.5%; Q4, 34.8%. Compared with Q1, Q4 hospitals had higher rates of admission (Q1, 32.1% vs Q4, 40.0%), downstream coronary angiogram (Q1, 1.2% vs Q4, 4.9%), and revascularization procedures (Q1, 0.5% vs Q4, 1.9%). Hospitals in Q4 had a lower yield of revascularization for noninvasive imaging (Q1, 7.6% vs Q4, 5.4%) and for angiograms (Q1, 41.2% vs Q4, 38.8%). *P* <.001 for all comparisons. Readmission rates to the same hospital for AMI within 2 months were not different by quartiles (*P* = .51). Approximately 23% of variation in imaging use was attributable to the behavior of individual hospitals.
- **Conclusions and Relevance** Hospitals vary in their use of noninvasive cardiac imaging in patients with suspected ischemia who do not have AMI. Hospitals with higher imaging rates did not have substantially different rates of therapeutic interventions or lower readmission rates for AMI but were more likely to admit patients and perform angiography.

N Engl J Med.

Deficiency of innate and acquired immunity caused by an IKBKB mutation

- **BACKGROUND:**
- Severe combined immunodeficiency (SCID) comprises a heterogeneous group of heritable deficiencies of humoral and cell-mediated immunity. Many patients with SCID have lymphocyte-activation defects that remain uncharacterized.
- **METHODS:**
- We performed genetic studies in four patients, from four families of Northern Cree ancestry, who had clinical characteristics of SCID, including early onset of severe viral, bacterial, and fungal infections despite normal B-cell and T-cell counts. Genomewide homozygosity mapping was used to identify a candidate region, which was found on chromosome 8; all genes within this interval were sequenced. Immune-cell populations, signal transduction on activation, and effector functions were studied.

- **RESULTS:**
- The patients had hypogammaglobulinemia or agammaglobulinemia, (低丙种球蛋白或缺乏) and their peripheral-blood B cells and T cells were almost exclusively of naive phenotype. Regulatory T cells and γδ T cells were absent. All patients carried a homozygous duplication--c.1292dupG in exon 13 of IKBKB, which encodes IκB kinase 2 (IKK2, also known as IKKβ)--leading to loss of expression of IKK2, a component of the IKK-nuclear factor κB (NF-κB) pathway.
- Immune cells from the patients had impaired responses to stimulation through T-cell receptors, B-cell receptors, toll-like receptors, inflammatory cytokine receptors, and mitogens.
- **CONCLUSIONS:**
- A form of human SCID is characterized by normal lymphocyte development despite a loss of IKK2 function. IKK2 deficiency results in an impaired response to activation stimuli in a variety of immune cells, leading to clinically relevant impairment of adaptive and innate immunity.

A randomized trial of genotype-guided dosing of warfarin.

- **BACKGROUND:**
- The level of anticoagulation in response to a fixed-dose regimen of warfarin is difficult to predict during the initiation of therapy. We prospectively compared the effect of genotype-guided dosing with that of standard dosing on anticoagulation control in patients starting warfarin therapy.
- **METHODS:**
- We conducted a multicenter, randomized, controlled trial involving patients with atrial fibrillation or venous thromboembolism. Genotyping for CYP2C9*2, CYP2C9*3, and VKORC1 (-1639G→A) was performed with the use of a point-of-care test. For patients assigned to the genotype-guided group, warfarin doses were prescribed according to pharmacogenetic-based algorithms for the first 5 days. Patients in the control (standard dosing) group received a 3-day loading-dose regimen. After the initiation period, the treatment of all patients was managed according to routine clinical practice. The primary outcome measure was the percentage of time in the therapeutic range of 2.0 to 3.0 for the international normalized ratio (INR) during the first 12 weeks after warfarin initiation.

- **RESULTS:**
- A total of 455 patients were recruited, with 227 randomly assigned to the genotype-guided group and 228 assigned to the control group. The mean percentage of time in the therapeutic range was 67.4% in the genotype-guided group as compared with 60.3% in the control group (adjusted difference, 7.0 percentage points; 95% confidence interval, 3.3 to 10.6; P<0.001). There were significantly fewer incidences of excessive anticoagulation (INR ≥4.0) in the genotype-guided group. The median time to reach a therapeutic INR was 21 days in the genotype-guided group as compared with 29 days in the control group (P<0.001).
- **CONCLUSIONS:**
- Pharmacogenetic-based dosing was associated with a higher percentage of time in the therapeutic INR range than was standard dosing during the initiation of warfarin therapy.

Targeted temperature management at 33°C versus 36°C after cardiac arrest

- **BACKGROUND:**
- Unconscious survivors of out-of-hospital cardiac arrest have a high risk of death or poor neurologic function. Therapeutic hypothermia is recommended by international guidelines, but the supporting evidence is limited, and the target temperature associated with the best outcome is unknown. Our objective was to compare two target temperatures, both intended to prevent fever.
- **METHODS:**
- In an international trial, we randomly assigned 950 unconscious adults after out-of-hospital cardiac arrest of presumed cardiac cause to targeted temperature management at either 33°C or 36°C. The primary outcome was all-cause mortality through the end of the trial. Secondary outcomes included a composite of poor neurologic function or death at 180 days, as evaluated with the Cerebral Performance Category (CPC) scale and the modified Rankin scale.

- **RESULTS:**
- In total, 939 patients were included in the primary analysis. At the end of the trial, 50% of the patients in the 33° C group (235 of 473 patients) had died, as compared with 48% of the patients in the 36° C group (225 of 466 patients) (hazard ratio with a temperature of 33° C, 1.06; 95% confidence interval [CI], 0.89 to 1.28; P=0.51). At the 180-day follow-up, 54% of the patients in the 33° C group had died or had poor neurologic function according to the CPC, as compared with 52% of patients in the 36° C group (risk ratio, 1.02; 95% CI, 0.88 to 1.16; P=0.78). In the analysis using the modified Rankin scale, the comparable rate was 52% in both groups (risk ratio, 1.01; 95% CI, 0.89 to 1.14; P=0.87). The results of analyses adjusted for known prognostic factors were similar.
- **CONCLUSIONS:**
- In unconscious survivors of out-of-hospital cardiac arrest of presumed cardiac cause, hypothermia at a targeted temperature of 33° C did not confer a benefit as compared with a targeted temperature of 36° C.

Risk of a Thrombotic Event after the 6-Week Postpartum Period

- **Background** The postpartum(产后)state is associated with a substantially increased risk of thrombosis. It is uncertain to what extent this heightened risk persists beyond the conventionally defined 6-week postpartum period.
- **Methods** Using claims data on all discharges from nonfederal emergency departments and acute care hospitals in California, we identified women who were hospitalized for labor and delivery between January 1, 2005, and June 30, 2010. We used validated diagnosis codes to identify a composite primary outcome of ischemic stroke, acute myocardial infarction, or venous thromboembolism. We then used conditional logistic regression to assess each patient's likelihood of a first thrombotic event during sequential 6-week periods after delivery, as compared with the corresponding 6-week period 1 year later.

- **Results** Among the 1,687,930 women with a first recorded delivery, 1015 had a thrombotic event (248 cases of stroke, 47 cases of myocardial infarction, and 720 cases of venous thromboembolism) in the period of 1 year plus up to 24 weeks after delivery. The risk of primary thrombotic events was markedly higher within 6 weeks after delivery than in the same period 1 year later, with 411 events versus 38 events, for an absolute risk difference of 22.1 events (95% confidence interval [CI], 19.6 to 24.6) per 100,000 deliveries and an odds ratio of 10.8 (95% CI, 7.8 to 15.1). There was also a modest but significant increase in risk during the period of 7 to 12 weeks after delivery as compared with the same period 1 year later, with 95 versus 44 events, for an absolute risk difference of 3.0 events (95% CI, 1.6 to 4.5) per 100,000 deliveries and an odds ratio of 2.2 (95% CI, 1.5 to 3.1). Risks of thrombotic events were not significantly increased beyond the first 12 weeks after delivery.
- **Conclusions** Among patients in our study, an elevated risk of thrombosis persisted until at least 12 weeks after delivery. However, the absolute increase in risk beyond 6 weeks after delivery was low.

Genetic PTX3 deficiency and aspergillosis in stem-cell transplantation

- **BACKGROUND:**
- The soluble pattern-recognition receptor known as long pentraxin 3 (穿透素3 PTX3) has a nonredundant role in antifungal immunity. The contribution of single-nucleotide polymorphisms (SNPs) in PTX3 to the development of invasive aspergillosis 曲霉 is unknown.
- **METHODS:**
- We screened an initial cohort of 268 patients undergoing hematopoietic stem-cell transplantation (HSCT) and their donors for PTX3 SNPs modifying the risk of invasive aspergillosis. The analysis was also performed in a multicenter study involving 107 patients with invasive aspergillosis and 223 matched controls. The functional consequences of PTX3 SNPs were investigated in vitro and in lung specimens from transplant recipients.

- **RESULTS:**
- Receipt of a transplant from a donor with a homozygous haplotype (h2/h2) in PTX3 was associated with an increased risk of infection, in both the discovery study (cumulative incidence, 37% vs. 15%; adjusted hazard ratio, 3.08; P=0.003) and the confirmation study (adjusted odds ratio, 2.78; P=0.03), as well as with defective expression of PTX3. Functionally, PTX3 deficiency in h2/h2 neutrophils, presumably due to messenger RNA instability, led to impaired phagocytosis and clearance of the fungus.
- **CONCLUSIONS:**
- Genetic deficiency of PTX3 affects the antifungal capacity of neutrophils and may contribute to the risk of invasive aspergillosis in patients treated with HSCT. (造血干细胞移植).

Upper-airway stimulation for obstructive sleep apnea

- **BACKGROUND:**
- Obstructive sleep apnea is associated with considerable health risks. Although continuous positive airway pressure (CPAP) can mitigate these risks, effectiveness can be reduced by inadequate adherence to treatment. We evaluated the clinical safety and effectiveness of upper-airway stimulation at 12 months for the treatment of moderate-to-severe obstructive sleep apnea.
- **METHODS:**
- Using a multicenter, prospective, single-group, cohort design, we surgically implanted an upper-airway stimulation device in patients with obstructive sleep apnea who had difficulty either accepting or adhering to CPAP therapy. The primary outcome measures were the apnea-hypopnea index (AHI; the number of apnea or hypopnea events per hour, with a score of ≥15 indicating moderate-to-severe apnea) and the oxygen desaturation index (ODI; the number of times per hour of sleep that the blood oxygen level drops by ≥4 percentage points from baseline). Secondary outcome measures were the Epworth Sleepiness Scale, the Functional Outcomes of Sleep Questionnaire (FOSQ), and the percentage of sleep time with the oxygen saturation less than 90%. Consecutive participants with a response were included in a randomized, controlled therapy-withdrawal trial.

- **RESULTS:**
- The study included 126 participants; 83% were men. The mean age was 54.5 years, and the mean body-mass index (the weight in kilograms divided by the square of the height in meters) was 28.4. The median AHI score at 12 months decreased 68%, from 29.3 events per hour to 9.0 events per hour (P<0.001); the ODI score decreased 70%, from 25.4 events per hour to 7.4 events per hour (P<0.001). Secondary outcome measures showed a reduction in the effects of sleep apnea and improved quality of life. In the randomized phase, the mean AHI score did not differ significantly from the 12-month score in the nonrandomized phase among the 23 participants in the therapy-maintenance group (8.9 and 7.2 events per hour, respectively); the AHI score was significantly higher (indicating more severe apnea) among the 23 participants in the therapy-withdrawal group (25.8 vs. 7.6 events per hour, P<0.001). The ODI results followed a similar pattern. The rate of procedure-related serious adverse events was less than 2%.
- **CONCLUSIONS:**
- In this uncontrolled cohort study, upper-airway stimulation led to significant improvements in objective and subjective measurements of the severity of obstructive sleep apnea.

A randomized trial of hyperglycemic control in pediatric intensive care.

- **BACKGROUND:**
- Whether an insulin infusion should be used for tight control of hyperglycemia in critically ill children remains unclear.
- **METHODS:**
- We randomly assigned children (≤16 years of age) who were admitted to the pediatric intensive care unit (ICU) and were expected to require mechanical ventilation and vasoactive drugs for at least 12 hours to either tight glycemic control, with a target blood glucose range of 72 to 126 mg per deciliter (4.0 to 7.0 mmol per liter), or conventional glycemic control, with a target level below 216 mg per deciliter (12.0 mmol per liter). The primary outcome was the number of days alive and free from mechanical ventilation at 30 days after randomization. The main prespecified subgroup analysis compared children who had undergone cardiac surgery with those who had not. We also assessed costs of hospital and community health services.

- **RESULTS:**
- A total of 1369 patients at 13 centers in England underwent randomization: 694 to tight glycemic control and 675 to conventional glycemic control; 60% had undergone cardiac surgery. The mean between-group difference in the number of days alive and free from mechanical ventilation at 30 days was 0.36 days (95% confidence interval [CI], -0.42 to 1.14); the effects did not differ according to subgroup. Severe hypoglycemia (blood glucose, <36 mg per deciliter [2.0 mmol per liter]) occurred in a higher proportion of children in the tight-glycemic-control group than in the conventional-glycemic-control group (7.3% vs. 1.5%, P<0.001). Overall, the mean 12-month costs were lower in the tight-glycemic-control group than in the conventional-glycemic-control group. The mean 12-month costs were similar in the two groups in the cardiac-surgery subgroup, but in the subgroup that had not undergone cardiac surgery, the mean cost was significantly lower in the tight-glycemic-control group than in the conventional-glycemic-control group: -$13,120 (95% CI, -$24,682 to -$1,559).
- **CONCLUSIONS:**
- This multicenter, randomized trial showed that tight glycemic control in critically ill children had no significant effect on major clinical outcomes, although the incidence of hypoglycemia was higher with tight glucose control than with conventional glucose control.

Unexpected abrupt increase in left ventricular assist device thrombosis

- **BACKGROUND:**
- We observed an apparent increase in the rate of device thrombosis among patients who received the HeartMate II left ventricular assist device, as compared with preapproval clinical-trial results and initial experience. We investigated the occurrence of pump thrombosis and elevated lactate dehydrogenase (LDH) levels, LDH levels presaging thrombosis (and associated hemolysis), and outcomes of different management strategies in a multi-institutional study.
- **METHODS:**
- We obtained data from 837 patients at three institutions, where 895 devices were implanted from 2004 through mid-2013; the mean (±SD) age of the patients was 55±14 years. The primary end point was confirmed pump thrombosis. Secondary end points were confirmed and suspected thrombosis, longitudinal LDH levels, and outcomes after pump thrombosis.

- **RESULTS:**
- A total of 72 pump thromboses were confirmed in 66 patients; an additional 36 thromboses in unique devices were suspected. Starting in approximately March 2011, the occurrence of confirmed pump thrombosis at 3 months after implantation increased from 2.2% (95% confidence interval [CI], 1.5 to 3.4) to 8.4% (95% CI, 5.0 to 13.9) by January 1, 2013. Before March 1, 2011, the median time from implantation to thrombosis was 18.6 months (95% CI, 0.5 to 52.7), and from March 2011 onward, it was 2.7 months (95% CI, 0.0 to 18.6). The occurrence of elevated LDH levels within 3 months after implantation mirrored that of thrombosis. Thrombosis was presaged by LDH levels that more than doubled, from 540 IU per liter to 1490 IU per liter, within the weeks before diagnosis. Thrombosis was managed by heart transplantation in 11 patients (1 patient died 31 days after transplantation) and by pump replacement in 21, with mortality equivalent to that among patients without thrombosis; among 40 thromboses in 40 patients who did not undergo transplantation or pump replacement, actuarial mortality was 48.2% (95% CI, 31.6 to 65.2) in the ensuing 6 months after pump thrombosis.
- **CONCLUSIONS:**
- The rate of pump thrombosis related to the use of the HeartMate II has been increasing at our centers and is associated with substantial morbidity and mortality.

Epidemiology of human infections with avian influenza A(H7N9) virus in China

- **BACKGROUND:**
- The first identified cases of avian influenza A(H7N9) virus infection in humans occurred in China during February and March 2013. We analyzed data obtained from field investigations to describe the epidemiologic characteristics of H7N9 cases in China identified as of December 1, 2013.
- **METHODS:**
- Field investigations were conducted for each confirmed case of H7N9 virus infection. A patient was considered to have a confirmed case if the presence of the H7N9 virus was verified by means of real-time reverse-transcriptase-polymerase-chain-reaction assay (RT-PCR), viral isolation, or serologic testing. Information on demographic characteristics, exposure history, and illness timelines was obtained from patients with confirmed cases. Close contacts were monitored for 7 days for symptoms of illness. Throat swabs were obtained from contacts in whom symptoms developed and were tested for the presence of the H7N9 virus by means of real-time RT-PCR.

- **RESULTS:**
- Among 139 persons with confirmed H7N9 virus infection, the median age was 61 years (range, 2 to 91), 71% were male, and 73% were urban residents. Confirmed cases occurred in 12 areas of China. Nine persons were poultry workers, and of 131 persons with available data, 82% had a history of exposure to live animals, including chickens (82%). A total of 137 persons (99%) were hospitalized, 125 (90%) had pneumonia or respiratory failure, and 65 of 103 with available data (63%) were admitted to an intensive care unit. A total of 47 persons (34%) died in the hospital after a median duration of illness of 21 days, 88 were discharged from the hospital, and 2 remain hospitalized in critical condition; 2 patients were not admitted to a hospital. In four family clusters, human-to-human transmission of H7N9 virus could not be ruled out. Excluding secondary cases in clusters, 2675 close contacts of case patients completed the monitoring period; respiratory symptoms developed in 28 of them (1%); all tested negative for H7N9 virus.
- **CONCLUSIONS:**
- Most persons with confirmed H7N9 virus infection had severe lower respiratory tract illness, were epidemiologically unrelated, and had a history of recent exposure to poultry. However, limited, nonsustained human-to-human H7N9 virus transmission could not be ruled out in four families.

LANCET

Association between change in daily ambulatory activity and cardiovascular events in people with impaired glucose tolerance (NAVIGATOR trial): a cohort analysis

- **BACKGROUND:**
- The extent to which change in physical activity can modify the risk of cardiovascular disease in individuals at high cardiovascular risk is uncertain. We investigated whether baseline and change in objectively-assessed ambulatory activity is associated with the risk of a cardiovascular event in individuals at high cardiovascular risk with impaired glucose tolerance.
- **METHODS:**
- We assessed prospective data from the NAVIGATOR trial involving 9306 individuals with impaired glucose tolerance who were recruited in 40 countries between January, 2002, and January, 2004. Participants also either had existing cardiovascular disease (if age ≥50 years) or at least one additional cardiovascular risk factor (if age ≥55 years). Participants were followed-up for cardiovascular events (defined as cardiovascular mortality, non-fatal stroke, or myocardial infarction) for 6 years on average and had ambulatory activity assessed by pedometer at baseline and 12 months. Adjusted Cox proportional hazard models quantified the association of baseline and change in ambulatory activity (from baseline to 12 months) with the risk of a subsequent cardiovascular event, after adjustment for each other and potential confounding variables. This study is registered with ClinicalTrials.govNCT00097786.

- **FINDINGS:**
- During 45 211 person-years follow-up, 531 cardiovascular events occurred. Baseline ambulatory activity (hazard ratio [HR] per 2000 steps per day 0·90, 95% CI 0·84-0·96) and change in ambulatory activity (0·92, 0·86-0·99) were inversely associated with the risk of a cardiovascular event. Results for change in ambulatory activity were unaffected when also adjusted for changes in body-mass index and other potential confounding variables at 12 months.
- **INTERPRETATION:**
- In individuals at high cardiovascular risk with impaired glucose tolerance, both baseline levels of daily ambulatory activity and change in ambulatory activity display a graded inverse association with the subsequent risk of a cardiovascular event.

Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: a meta-analysis of randomised trials

- **BACKGROUND:**
- Four new oral anticoagulants compare favourably with warfarin for stroke prevention in patients with atrial fibrillation; however, the balance between efficacy and safety in subgroups needs better definition. We aimed to assess the relative benefit of new oral anticoagulants in key subgroups, and the effects on important secondary outcomes.
- **METHODS:**
- We searched Medline from Jan 1, 2009, to Nov 19, 2013, limiting searches to phase 3, randomised trials of patients with atrial fibrillation who were randomised to receive new oral anticoagulants or warfarin, and trials in which both efficacy and safety outcomes were reported. We did a prespecified meta-analysis of all 71 683 participants included in the RE-LY, ROCKET AF, ARISTOTLE, and ENGAGE AF-TIMI 48 trials. The main outcomes were stroke and systemic embolic events, ischaemic stroke, haemorrhagic stroke, all-cause mortality, myocardial infarction, major bleeding, intracranial haemorrhage, and gastrointestinal bleeding. We calculated relative risks (RRs) and 95% CIs for each outcome. We did subgroup analyses to assess whether differences in patient and trial characteristics affected outcomes. We used a random-effects model to compare pooled outcomes and tested for heterogeneity.

- **FINDINGS:**
- 42 411 participants received a new oral anticoagulant and 29 272 participants received warfarin. New oral anticoagulants significantly reduced stroke or systemic embolic events by 19% compared with warfarin (RR 0·81, 95% CI 0·73-0·91; p<0·0001), mainly driven by a reduction in haemorrhagic stroke (0·49, 0·38-0·64; p<0·0001). New oral anticoagulants also significantly reduced all-cause mortality (0·90, 0·85-0·95; p=0·0003) and intracranial haemorrhage (0·48, 0·39-0·59; p<0·0001), but increased gastrointestinal bleeding (1·25, 1·01-1·55; p=0·04). We noted no heterogeneity for stroke or systemic embolic events in important subgroups, but there was a greater relative reduction in major bleeding with new oral anticoagulants when the centre-based time in therapeutic range was less than 66% than when it was 66% or more (0·69, 0·59-0·81 vs 0·93, 0·76-1·13; p for interaction 0·022). Low-dose new oral anticoagulant regimens showed similar overall reductions in stroke or systemic embolic events to warfarin (1·03, 0·84-1·27; p=0·74), and a more favourable bleeding profile (0·65, 0·43-1·00; p=0·05), but significantly more ischaemic strokes (1·28, 1·02-1·60; p=0·045).

- **INTERPRETATION:**
- This meta-analysis is the first to include data for all four new oral anticoagulants studied in the pivotal phase 3 clinical trials for stroke prevention or systemic embolic events in patients with atrial fibrillation. New oral anticoagulants had a favourable risk-benefit profile, with significant reductions in stroke, intracranial haemorrhage, and mortality, and with similar major bleeding as for warfarin, but increased gastrointestinal bleeding. The relative efficacy and safety of new oral anticoagulants was consistent across a wide range of patients. Our findings offer clinicians a more comprehensive picture of the new oral anticoagulants as a therapeutic option to reduce the risk of stroke in this patient population.

Compression stockings to prevent post-thrombotic syndrome: a randomised placebo-controlled trial

- **BACKGROUND:**
- Post-thrombotic syndrome (PTS) is a common and burdensome complication of deep venous thrombosis (DVT). Previous trials suggesting benefit of elastic compression stockings (ECS) to prevent PTS were small, single-centre studies without placebo control. We aimed to assess the efficacy of ECS, compared with placebo stockings, for the prevention of PTS.
- **METHODS:**
- We did a multicentre randomised placebo-controlled trial of active versus placebo ECS used for 2 years to prevent PTS after a first proximal DVT in centres in Canada and the USA. Patients were randomly assigned to study groups with a web-based randomisation system. Patients presenting with a first symptomatic, proximal DVT were potentially eligible to participate. They were excluded if the use of compression stockings was contraindicated, they had an expected lifespan of less than 6 months, geographical inaccessibility precluded return for follow-up visits, they were unable to apply stockings, or they received thrombolytic therapy for the initial treatment of acute DVT. The primary outcome was PTS diagnosed at 6 months or later using Ginsberg's criteria (leg pain and swelling of ≥1 month duration). We used a modified intention to treat Cox regression analysis, supplemented by a prespecified per-protocol analysis of patients who reported frequent use of their allocated treatment. This study is registered with ClinicalTrials.gov, number NCT00143598, and Current Controlled Trials, number ISRCTN71334751.

- **FINDINGS:**
- From 2004 to 2010, 410 patients were randomly assigned to receive active ECS and 396 placebo ECS. The cumulative incidence of PTS was 14·2% in active ECS versus 12·7% in placebo ECS (hazard ratio adjusted for centre 1·13, 95% CI 0·73-1·76; p=0·58). Results were similar in a prespecified per-protocol analysis of patients who reported frequent use of stockings.
- **INTERPRETATION:**
- ECS did not prevent PTS after a first proximal DVT, hence our findings do not support routine wearing of ECS after DVT.

- **Can closure of live poultry markets halt the spread of H7N9?**

----By contrast with LPM closure, a multisectoral approach leading to restructuring rather than destabilisation of the LPM system would be more likely to result in a sustainable reduction in the risk of disease spread while also protecting livelihoods and food security.

谢谢！！！