Thrombolysis benefits elderly stroke patients

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All patients with stroke, regardless of age, should receive thrombolysis according to findings from two studies.

In one, the third International Stroke Trial (IST-3), researchers determined whether all patients with stroke, irrespective of age, benefited from treatment with the thrombolytic agent alteplase, a recombinant plasminogen activator (rt-PA), when given up to 6 hours following stroke onset. [Lancet 2012;379:2352-2363]

This multicenter, randomized, open treatment trial assessed 3,035 patients (1,515 receiving alteplase and 1,520 in a control group) at 156 hospitals in 12 countries; of these 53 percent were older than 80 years. At 6 months, 554 (37 percent) patients in the alteplase group met the primary end point (ie, were alive and independent) compared with 534 (35 percent) of those in the control group (OR 1·13, 95% CI 0·95-1·35, P=0·181). For every 1,000 patients treated within 6 hours, 14 more were alive and independent.

The effect of alteplase on disability was, thus, not statistically significant. But the odds of surviving with less disability were 27 percent greater for patients treated with alteplase. Among the patients (about 80 percent of them aged >80 years) treated within 3 hours, the benefit was much greater—for every 1,000 treated, 80 more were alive and able to look after themselves at 6 months.

In terms of tolerability, fatal or non-fatal symptomatic hemorrhage within 7 days occurred in 104 (7 percent) of patients in the alteplase group versus 16 (1 percent) in the control group. More deaths occurred within 7 days in the alteplase group (163 [11 percent]) than in the control group (107 [7 percent]).

However, between 7 days and 6 months, there were fewer deaths in the alteplase group than in the control group, so that, by 6 months, similar numbers of patients had died in the two groups in aggregate (408 [27 percent] in the alteplase group vs. 407 [27 percent] in the control group).

“The data add weight to the policy of treating patients as soon as possible, and justify extending treatment to patients older than 80 years of age,” said co-author Professor Peter Sandercock of the University of Edinburgh and Western General Hospital, Edinburgh, UK.

“[The findings] do not support any restriction of treatment on the basis of stroke severity or the presence of early ischemic change on the baseline brain scan.”

The second paper reported an analysis of pooled data from 12 trials, including the IST-3
trial results, involving a total of 7,012 patients. [Lancet 2012;379:2364-2372]

This meta-analysis showed that for every 1,000 patients allocated to intravenous alteplase up to 6 hours after stroke, 42 more patients were alive and independent, and 55 more had the better outcome of being alive with a favorable outcome at the end of follow-up. This benefit occurred despite an increase in the number of early symptomatic intracranial hemorrhages and early deaths associated with thrombolysis.

Among the 1,711 patients older than 80 years, the absolute benefits from alteplase were at least as large as for the younger patients, especially with early treatment (for those over 80 treated within 3 hours, 96 patients more per 1,000 treated were alive and independent).

Although net benefit from thrombolysis clearly declines with increasing delay to treatment, the data suggest that the benefit probably extends beyond 4.5 hours, possibly as late as 6 hours in some patients, although the time probably varies with key individual or combined patients’ characteristics, which were not possible to identify from this analysis, said the authors.

“If small gains in functional ability by 3 months translate into greater long-term survival free of disability, this is likely to reduce health-care costs and increase quality of life and cost effectiveness.”

The key message of IST-3 and the updated meta-analysis is that many eligible patients from subgroups excluded by the European license should now be given alteplase, said Drs Didier Leys and Charlotte Cordonnier of the department of neurology (stroke unit) at the Roger Salengro Hospital in Lille, France, while commenting on the study findings’ clinical relevance. [Lancet 2012; DOI:10.1016/S0140-6736(12)60822-8]

When asked about their relevance for Asia, Professor Sandercock explained that as life expectancy increases in Asia, the proportion of very elderly people in the population, and hence the number of older stroke patients, will continue to rise over the coming decades.

“The finding that thrombolysis benefits the very elderly as much as younger patients is, therefore, very important,” he said.

In many Asian countries where traffic delays in reaching hospital quickly are a big problem, he said that thrombolysis with an expensive drug like rt-PA within 3 hours is only relevant to the very small number of wealthier individuals who can afford to pay for the treatment.

“The population health benefits will come from making sure all acute stroke patients are cared for in well-organized stroke units, not by thrombolysing the few.”

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Regulators affirm dabigatran efficacy, safety

Yen Yen Yip

The superiority of the direct thrombin inhibitor dabigatran (Pradaxa®, Boehringer Ingelheim) over warfarin in preventing ischemic and hemorrhagic strokes has now been affirmed by the US Food and Drug Administration.

This latest update, reflected in the prescribing information of dabigatran 150 mg twice daily, was based on results from the Randomized Evaluation of Long-Term Anticoagulation Therapy (RE-LY) trial, which established that dabigatran 150 mg reduced the risk of stroke and systemic embolism by 35 percent compared with well-controlled warfarin. In the study, investigators also showed that dabigatran 110 mg twice daily was as effective as warfarin in preventing stroke. [N Engl J Med 2009;361:1139-1151]

RE-LY was a prospective, randomized, open-label trial with blinded end point evaluation, conducted in more than 18,000 patients with non-valvular atrial fibrillation (NVAF).

Dabigatran also received a nod from a European regulatory agency for its safety profile. Concerns had previously been raised about bleeding events associated with use of the drug.

The European Medicines Agency (EMA) recently acknowledged that the frequency of reported fatal bleedings with dabigatran was significantly lower than levels reported in clinical trials. The EMA arrived at this conclusion following a review of available data from clinical trials and post-marketing surveillance reports on the risk of serious or fatal bleeding with dabigatran.

“The latest available data are consistent with the known risk of bleeding and that the risk profile of dabigatran is unchanged,” the EMA stated.

The EMA Committee for Medicinal Products for Human Use (CHMP) pointed out dabigatran’s importance as an alternative to other blood-thinning agents. However, given that the risk of bleeding is a common complication of all anticoagulants, CHMP has also recommended more specific guidance on patient management, when dabigatran should not be used, and how dabigatran’s anticoagulant effect can be reversed if bleeding occurs.
Finding a cure for HIV: The need for science, collaboration and advocacy

Excerpts from a plenary lecture delivered by Professor Sharon R. Lewin, director of the Infectious Diseases Unit, Alfred Hospital, and professor, Department of Infectious Diseases, Monash University, in Melbourne, Australia, during the 15th International Congress on Infectious Diseases held recently in Bangkok, Thailand.

Combination antiretroviral therapy (cART) has led to major reductions in HIV-related mortality and morbidity, but still HIV cannot be cured. Current paradigms of treatment are not sufficient. With increasing numbers of infected people, emerging new toxicities secondary to cART and the need for life-long treatment, there is now a real urgency to find a cure for HIV.

Currently, there are multiple barriers to curing HIV. The most significant is the establishment of a latent or “silent” infection in resting CD4+ T-cells as the virus is able to integrate into the host cell genome, but does not proceed to active replication. Reactivation of latently infected resting CD4+ T-cells can then re-establish infection once cART is stopped.

Other significant barriers to cure include residual viral replication in patients receiving cART. In addition, HIV can be sequestered in long-lived cells such as macrophages and astrocytes in anatomical reservoirs, such as the brain, gastrointestinal tract and lymphoid tissue. Achieving either a functional cure (long-term control of HIV in the absence of cART) or a sterilizing cure (elimination of all HIV-infected cells) remains a major challenge.

Several studies have demonstrated that treatment intensification with additional antiretrovirals (ARVs) appears to have little impact on latent reservoirs. One potential approach to eliminate latently infected cells is to promote viral production in these cells. If this is done in a patient in cART, subsequent rounds of viral replication will be inhibited and the infected cell will die. Drugs such as histone deacetylase inhibitors and methylation inhibitors, cytokines such as IL-7, or other activating agents including prostratin and anti-PD-1 show promising results in reversing latency in vitro when used alone or in combination.

In addition, gene therapy has been shown to effectively reduce expression of the HIV co-receptor CCR5 in both animal models and ex vivo human studies. Clinical trials using these approaches are underway. Recent new initiatives to fund collaborative private-public partnerships, enhance community engagement and define a scientific road map for cure research are also likely to significantly accelerate advances in the elusive path to finding a cure.

However, there are also a number of scientific challenges in HIV cure. We certainly need better in vitro and animal models to
evaluate new strategies, especially if we are to consider combination approaches to activating latent HIV, with or without boosting immunity. There should be standardized, non-invasive assays to quantify viral reservoirs in vivo particularly when we move into multi-site clinical trials. There is also a need for more drug development to increase specificity for latently infected cells and/or enhanced tissue delivery and finally, better understanding of the immune system in controlling low-level viremia and latent infection.

This area of endeavor also raises a whole range of ethical considerations. What are the acceptable risks and toxicities of interventions in a population doing quite well on stable cART? The perspective on this issue is very different amongst clinicians, patients and regulatory bodies and we therefore need far more open discussions about these issues. What surrogate markers of viral persistence will ultimately justify treatment interruptions as a clinical endpoint in subsequent clinical trials? We are now very well aware of the risk of treatment interruption, so when will we know that it will be safe to test whether an intervention has worked by stopping ART? Expectations of study participants in early “proof of concept” studies are also very important. Patients who participate in these studies are exposed to potential risks and will not get any benefit themselves but are contributing to future research. Finally, any work on HIV cure should never get in the way of universal access to ART for all patients infected with HIV.

In the last few years, we have seen a real increase in funding for research towards HIV cure, including some various significant investments in grant funding from both the National Institute of Health and the American Foundation for AIDS Research. Advocacy also remains a key component in achieving a cure. The International AIDS Society is leading this with the development of a global scientific strategy for HIV cure which will be launched in Washington in July.

In conclusion, there are multiple barriers to curing HIV. This will not be easy. A combination approach will almost certainly be needed. But we do know that sterilizing and functional cure is possible and we need to find a way to achieve this in more patients. There are multiple strategies being tested with most being early proof of concept, small and non-randomized studies – including activating latency, gene therapy and vaccination with or without intensification. Results from several of these studies should be available in the coming year. Engagement of the community, regulatory bodies and pharmaceutical companies will be very critical to advance the field, given the many ethical issues concerned.

Finally, the very significant and additional challenge to whatever we do is that some day we should identify a strategy for cure. This must ultimately be cheap, scalable and widely available to patients who need it.
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Indonesia sebagai negara tropis merupakan negara dengan keanekaragaman hayati terbesar kedua di dunia setelah Brazil. Indonesia memiliki sekitar 25.000-30.000 spesies tanaman yang merupakan 80% dari jenis tanaman di dunia dan 90% dari jenis tanaman di Asia. Hal ini menjadikan Indonesia sebagai salah satu negara terkaya di dunia dalam cadangan plasma nutfah tanaman obat.

Sekitar 940 spesies tanaman berpotensi menjadi tanaman obat dan baru sekitar 283 spesies yang sudah digunakan oleh industri obat tradisional. Kemajuan industri herbal ini didukung oleh pemerintah melalui berbagai implementasi berbagai pelayanan kesehatan formal obat tradisional dan 40 rumah sakit di seluruh Indonesia sudah mulai memberikan layanan kesehatan obat tradisional.


Perkembangan penggunaan jamu


Pemakaian jamu di Indonesia sesuai dengan Riskesdas 2010 mencapai angka 59,12%, pemakaian tertinggi di Kalimantan Selatan (80,71%) dan terendah di Sulawesi Utara (23,95%). Sedangkan frekuensi konsumsi jamu setiap hari mencapai 4,36% yang tertinggi di DKI Jakarta (7,75%) dan terendah di NTT (0,795).

Untuk pilihan tanaman obat yang dijadikan jamu buatan sendiri, terdiri dari temulan-wak (39,65%), jahe (50,36%), kencur (48,77%), meniran (48,77%), pace (11,17%) dan lainnya (72,51%). Bentuk jamu yang banyak menjadi pilihan adalah cair (55,3%), seduhan (44,1%), kapsul (11,6%) dan rebusan (20,3%). “Masih dari sumber yang sama (Riskesdas 2010), penduduk Indonesia yang merasakan manfaat ramuan tradisional yang digunakan sangat bermanfaat bagi kesehatan mencapai 95,6%,” tukas Direktur Bina Pelayanan Kesehatan Tradisional, Alternatif dan Komplementer Kementerian Kesehatan RI ini lebih lanjut.

Sesuai BPOM bahan baku yang telah ter-
standarisasi (uji pra-klinik) ada 38 dan yang terstandarisasi dengan uji klinik berjumlah 6 berupa fitofarmaka. Untuk rencana strategis 2009-2014, dr Abidinsyah melanjutkan, pencapaian target adalah 50% pusat layanan menyediakan pelayanan tradisional dan jumlah rumah sakit yang menyelenggarakan yankes trad yang aman dan bermanfaat sebagai pelayanan kesehatan alternatif dan komplementer mencapai 70. “Rumah sakit tradisional dan komplementer tahun 2011 telah mencapai 40 dengan menyediakan pengobatan herbal dan akupunktur, antara lain Jakarta, Surabaya, Yogyakarta, Makassar, Solo, Denpasar, Maluku, dll yang telah mendapat ijin pelayanan kesehatan obat tradisional dan dokter pun dilengkapi dengan pendidikan sertifikasi praktik pelayanan obat tradisional” lanjutnya.

Daftar masalah kesehatan yang dikomodir dalam formularium obat herbal asli Indonesia adalah dislipidemia, diabetes, hipertensi, hiperurikemia, demam, sakit gigi, obesitas, anoreksia, nefrolitiasis, dispepsia, mual muntah, paliatif dan suportif kanker, suportif penyakit jantung dan pembuluh darah, gastritis, artritis, konstipasi, batuk, gastroenteritis, insomnia, penyakit kulit, hepatoprotektor, disfungsi ereksi, imunomodulator, ISPA dan hemoroid.

Strategi pengembangan dan pemanfaatan obat tradisional Indonesia meliputi tiga segment yaitu jamu, sedian ekstrak terstandar dan sedian fitofarmaka. Selama tahun 2011 Sentra P3T melakukan berbagai penelitian, misalnya SP3T Sulawesi Utara meneliti ‘Pengaruh Aloe Vera terhadap Glukosa Darah Pasien DM Tipe 2’ (dr. Joudy Gessal), ‘Manfaat Kombinasi Ekstrak Temulawak, Jahe, Ke-

Uji pra-klinis


Dosis yang diberikan pada percobaan tersebut setara dengan dosis lazim pada manusia dan hasilnya menunjukkan adanya peningkatan aktivitas fagositosis makrofag, ketahanan fisik dan tidak menimbulkan gejala efek toksik.

Uji pra klinis tersebut terdiri dari 4 jenis, yaitu uji toksisitas akut (14 hari), uji toksisitas subkronik (90 hari), uji imunomodulator dan uji ketahanan fisik. “Uji pra klinis tersebut juga bertujuan untuk mengkaji keamanan pemakaian jangka pendek dan panjang,” lanjut Presiden Direktur PT Deltomed Laboratories ini.
Angka kejadian diare masih tinggi

Hardini Arivianti

Diare masih menempati posisi lima besar kematian di seluruh dunia, terutama di negara berkembang. Angka kematian mencapai 7,8/1000 per tahunnya. Hal ini diungkapkan oleh Dr. dr. Badriul Hegar, SpA(K).

Diare ada 2 jenis yaitu akut (berlangsung sampai dengan 7 hari) dan persisten (> 14 hari). Prevalensi tertinggi pada usia 6-11 bulan dan 12-23 bulan atau pada anak < 2 tahun. Di Indonesia, diare menjadi penyebab kematian pada anak tersering (15%) setelah problem neonatal yang lain seperti BBLR.


Bila disebabkan rotavirus, berdasarkan penelitian pada anak < 5 tahun yang dirawat gejala yang timbul adalah muntah, adanya mukus di feses, demam dan dehidrasi. Bila non-virus, gejala didominasi oleh darah pada feses. Diare yang diakibatkan rotavirus sebenarnya bisa sembuh dengan sendirinya dan biasanya berlangsung selama 4-8 hari

Penatalaksanaan diare

Dalam Program Lintas Diare ada lima langkah tatalaksana diare yang meliputi rehidrasi, dukungan nutrisi, suplementasi zink, antibiotik selektif dan edukasi.


Tanpa dehidrasi, pasien tidak perlu dirawat di rumah sakit, cukup dipantau dengan dan terus berikan oralit 5-10 cc/kgBB setiap diare cair. Oralit 75 ml x BB dapat diberikan pada pasien diare dengan dehidrasi ringan-sedang bisa dipantau di rumah sakit/klinik. Reevaluasi perlu dilakukan setelah 1-3 jam. Sedangkan untuk pasien diare dengan dehidrasi berat, perlu dirawat di rumah sakit.

Pada bayi yang mendapat ASI, pemberian ASI bisa dilanjutkan yang diselingi dengan pemberian oralit dan tidak dianjurkan mengganti dengan susu formula. Pada bayi yang tidak mendapatkan ASI, tetap diberikan susu formula seperti biasanya dan tidak diencerkan atau dikurangi porsinya.


Pada diare yang disertai darah (disentri), diare berkepanjangan dan disertai gejala sistemik atau demam berkepanjangan, dapat dipertimbangkan pemberian antibiotik. Pada anak dengan imunokompromis, juga dapat diberikan antibiotik.

Selanjutnya dr. Hegar memaparkan disentri atau diare cair yang disertai darah (nyata terlihat) sebagian besar disebabkan oleh shigella (50-60%), dengan gejala nyeri perut, demam, letargi dan prolaps rektum. Hampsia kasus disentri memerlukan antibiotik dan rawat inap dilakukan bila dialami oleh anak dengan gizi buruk, usia < 2 bulan, berisiko sepsis (toksik, letargi, kembung, nyeri tekan pada abdomen dan kejang).

**Peran zink pada diare**

Zink pada kesehatan saluran cerna berperan dalam menjaga integritas sawar epitel, perbaikan jaringan dan fungsi imun. Zink saat ini direkomendasikan dalam tatalaksana diare. Penelitian membuktikan, zink memberikan manfaat dalam mencegah kejadian diare berulang selama 2-3 bulan mendatang (60%). WHO/UNICEF merekomendasikan suplementasi zink selama 10-14 hari dengan dosis 20 mg/hari untuk anak berusia > 6 bulan atau 10 mg/hari pada bayi < 6 bulan.

Efikasi zink telah beberapa penelitian di negara-negara berkembang yang menunjukkan, zink dapat mencegah infeksi usus, menurunkan kejadian-durasi-rekurensi diare dan menurunkan penggunaan antibiotik.

Kunci utama pencegahan diare pada anak adalah ASI, disinfeksi arena bermain dan mainan, mencuci tangan, melakukan praktik menjaga kebersihan di bangsal rumah sakit dan imunisasi.

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**Pentingnya nutrisi lengkap pada ibu hamil**

Hardini Arivianti

Agar kebutuhan gizi anak untuk tumbuh sehat dan berkembang secara optimal terpenuhi, perlu perencanaan dengan baik karena semua harus diawali sejak 270 hari kehidupan janin dalam kandungan.

Asupan gizi yang tepat dan lengkap pada ibu hamil menjadi hal yang sangat esensial dalam masa kehamilan karena ibu merupakan satu-satunya sumber nutrisi bagi janin. Hal ini diungkapkan oleh dr. Samuel Oetoro, MS, SpGK pada acara peluncuran susu ibu hamil Frisian Flag Mama.

Ibu hamil dengan status gizi kurang akan mempengaruhi berat bayi saat lahir dan dapat
berakibat timbulnya penyakit kronik-degeneratif saat dewasa nanti. Sebelum hamil, tubuh ibu juga harus dipersiapkan supaya sistem reproduksi-nya siap untuk melahirkan bayi sehat.

Persiapan dengan nutrisi

“Peran nutrisi dalam mencegah kematian ibu sangat banyak misalnya dapat mencegah perdarahan, pre-eklamsi dan infeksi,” tukas Dr. dr. Noroyono Wibowo, SpOG (K) dalam acara yang sama. Contohnya dari sebuah data WHO, setiap 100.000 ada 400 orang yang mengalami ketidakmampuan melakukan apa pun akibat defisiensi zat besi. Ibu dengan defisiensi zat besi di awal kehamilan ternyata memiliki cenderungan mengalami post partum depression dan melakukan bunuh diri. Dampak pada bayi, defisiensi zat besi menambahkan penurunan IQ hingga 20%. Zat besi ini berperan memperkokoh bumbung saraf.

Selain itu, defisiensi vitamin A juga mengganggu berbagai fungsi karena vitamin ini berperan sebagai regulator berbagai proses dalam tubuh, sebagai regulator pembentukan sel darah merah, pembentukan/pematangan jantung janin, dll.


Pada masa pra kehamilan pre-valensi talasemia 5-8% (Jakarta) dan 13-20% (NTB). Ini sebabnya perlu skrining awal. “Diharapkan ada semacam lompatan strategi agar general check up tidak hanya dilakukan oleh orang tua, namun juga pada anak dan dimulai beberapa saat setelah lahir dan dilakukan secara rutin tahunan,” harap dr. Noroyono.

Selanjutnya, dr. Noroyono menjelaskan, dari penelitian di RSCM bila ibu memiliki kadar vitamin B6 > 250 mg/ml dan kadar albumin > 4 gr/dL maka 100% ibu tidak akan mual dan muntah. Itu sebabnya pengukuran juga perlu dilakukan agar persiapan hadapi kehamilan jadi lebih baik.

Untuk itu kehamilan perlu dipersiapkan dengan status nutrisi yang adekuat, higiene, vaksinasi dan finansial. “Kita harus kemapian, hamil itu bukan sekadar hamil, namun harus diingat kehamilan juga merupakan persiapan generasi di masa yang akan datang.”
Memahami gangguan bipolar

Hardini Arivianti

Gangguan bipolar merupakan gangguan yang kronik dan siklik sehingga pengobatan diperlukan di fase akut, pemeliharaan, maupun jangka panjang. Tujuan terapi adalah untuk mengatasi gejala-gejala perilaku yang mengganggu, mengurangi frekuensi siklus, dan mencegah relaps.


“Penegakan diagnosis GB seringkali mengalami keterlambatan. Menurut penelitian kami di dalam mengevaluasi status rekam medik di RSCM, pasien mengalami keterlambatan diagnosa hampir 9 tahun atau lebih dan hal ini sesuai dengan penelitian di luar negeri yang mengalami keterlambatan hampir 10 tahun,” tukas Kepala Departemen Psikiatri RSCM ini. Komorbiditas tersering adalah gangguan cemas yang seringkali terjadi akibat penyelahagunaan benzodiazepin. Yang perlu dihindari adalah keterlambatan diagnosis. Penegakan diagnosis GB memiliki beberapa tantangan tersendiri bagi psikiater. Tantangan tersebut berupa usia awitan dan tampilan gejala ber variasi; seringkali ditemukan saat fase depresi dan salah diagnosis sebagai depresi unipolar; onset depresi atau dis timia saat prepubertas memiliki risiko 20-40% menjadi GB; simtom tumpang tindih dengan gangguan psikiatrik lainnya; sering terjadi missdiagnosis; dan banyak komorbiditas dengan berbagai gangguan psikiatri dan gangguan medis lainnya.

Untuk memprediksi kondisi ini yang bersifat rekuren dan long life, dr. Agung menjelaskan, dapat menggunakan rumus ‘tiga’ yaitu bila seseorang memiliki tiga atau lebih dari kategori yang terdiri dari episode depresi mayor, kegagalan perkawinan, kegagalan merespon terhadap antidepressan, memiliki profesi yang berbeda, memiliki saudara kandung (generasi pertama) menderita gangguan mood, terindikasi penyalahgunaan zat, berprilaku impulsif, berpacaran secara simultan, pekerjaan simultan, terdiagnosis gangguan kepribadian, histrionik, psikotik atau ambang, dan menyukai warna merah atau menyolok.

Angka bunuh diri pada GB ini berkisar 0,4% per tahun pada yang terdiagnosis GB. Bunuh diri ini biasanya sering terjadi saat awal sakit dan berhubungan dengan episode depresi berat dan disforik agitatif khususnya setelah episode depresi berulang.

Selanjutnya, Prof. dr. Tuti Wahmurti A S, SpKJ sebagai Perwakilan Majelis Kehormatan Profesi PDSKJI menjelaskan, penyebab...
GB bersifat multifaktor meliputi genetik, biologi otak, peristiwa kehidupan dan perubahan sistem hormonal yang memengaruhi zat kimia alami otak. Gen berfungsi sebagai regulator yang akan mengatur keseimbangan terjaga dengan baik. “Pada orang-orang tertentu dengan gen yang lemah terhadap GB, keseimbangan dopaminergik, serotonergik dan noradrenergik tidak bisa dijaga sehingga timbul kekacauan dan timbul gejala GB.”

Atasi GB

Pengobatan secara langsung terkait dengan fase episodenya dan bertujuan utnuk mengobati kekacauan mood, juga mencegah kekambuhan yang berulang. Untuk itu, pemberian mood stabilizer dan antipsikotik atipik cukup efektif.

Strateginya disesuaikan dengan kondisi pasien. Ada fase terapi akut, berkelanjutan dan pemeliharaan. Terapi akut bertujuan untuk mengendalikan gejala hingga mencapai perbaikan dan biasanya diberikan mood stabilizer dan psikoedukasi. Terapi berkelanjutan merupakan jembatan atau fase terapi akut dan pemeliharaan. Fase terapi berkelanjutan memerlukan 2-6 bulan tergantung sifat individu. Fase terapi pemeliharaan ditujukan untuk memelihara kestabilan mood, mencegah kekambuhan dan memberikan kemudahan agar pasien dapat berfungsi sepenuhnya.


Divalproex sodium diindikasikan sebagai terapi pada masa akut atau episode campuran yang dikaitkan dengan GB, dengan atau tanpa gambaran psikotik. Menurut buku Panduan Tatalaksana Gangguan Bipolar (POKJA SPM dan Seksi Bipolar PDSKJI 2010), obat tersebut efektif untuk mania akut, campuran akut, depresi mayor akut, terapi rumatan GB, mania sekunder, GB yang tidak respon dengan litium, siklus cepat, GB pada anak dan remaja, dan GB pada lanjut usia.
Telehealth helps reduce mortality, emergency admissions

Alexandra Kirsten

The use of telehealth programs is associated with lower mortality and emergency hospital admission rates in patients with chronic diseases, the findings of a recent UK study suggest.

The study, one of the largest of its kind ever conducted, involved the recruitment at three sites in England between May 2008 and November 2009 of more than 3,000 patients with various chronic diseases including diabetes, chronic obstructive pulmonary disease (COPD) and heart failure. Patients were randomized to either home-based telehealth interventions or standard non-telehealth management approaches (control group). [BMJ 2012;344:e3874]

“Telehealth involves the remote exchange of data between a patient and healthcare professionals.”

“Telehealth involves the remote exchange of data between a patient and healthcare professionals as part of the patient’s diagnosis and healthcare management,” the authors explained. Communication technologies differ and may contain videoconferencing, the internet, store-and-forward imaging, streaming media, and terrestrial and wireless communications.

The study included a broad class of technologies and the choices of communication varied among the three trial sites. Nevertheless, all patients used the same monitoring devices such as a pulse oximeter for COPD, a glucometer for diabetes, and weighing scales for heart failure. Patient characteristics were similar at baseline.

The participants were asked to take clinical readings at the same time each day for up to 5 days per week. In addition, practitioners sent symptom questions and educational messages either via the telehealth base unit or via a set top box connected to a television.

Compared with controls, the intervention group had a significantly lower rate of emergency admissions within the 12 months of follow-up (42.9% vs. 48.2%, P=0.017). Mortality rate was also lower in the telehealth group than in the control group (4.6% vs. 8.3%, P<0.001).

“The reduced mortality observed in the intervention group will be an important motivator to invest in these interventions and similar technologies,” the authors said.

The underlying reasons or mechanisms for these benefits of telehealth remain unclear. Telehealth could help patients manage their conditions better and therefore reduce the incidence of acute exacerbations that need emergency admissions. Additionally these new technologies may change people’s perception of when they need to seek additional support, as well as professionals’ decisions about whether to refer or admit patients.

“Further analyses will provide insights into the mechanisms by which telehealth can lead to reductions in admission rates,” the authors concluded. “There is great potential but also still much to be done.”
A high intake of caffeine may protect against basal cell carcinoma (BCC), the most common form of skin cancer, data from two large cohorts have shown.

People who had more caffeine in their diet had a lower risk of BCC compared with those who had less ($P<0.001$). High consumption of caffeinated coffee was also inversely associated with BCC. The association applies to other sources of caffeine such as tea, cola and chocolate. [Cancer Res 2012;72;3282-3289]

“Our results add basal cell carcinoma to a list of conditions for which risk is decreased with increasing coffee consumption,” said study author Associate Professor Jiali Han, from Harvard Medical School and Harvard School of Public Health in Boston, Massachusetts, US. “This included conditions such as type 2 diabetes and Parkinson’s disease.”

Han and colleagues analyzed the relationship between skin cancer and caffeine intake in 112,987 adult women and men participating in the Nurses’ Health Study and the Health Professionals Follow-up Study, two long-running studies investigating factors that affect health.

Of the total study population, 22,786 developed BCC within >20 years of follow-up. Women who consumed >3 cups of caffeinated coffee per day had a 21 percent reduction in BCC risk (RR 0.79; 95% CI 0.74-0.85, $P<0.0001$) compared with those who consumed <1 cup a month. For men, the corresponding risk reduction was still significant, albeit less marked (RR 0.90; 95% CI 0.80-1.01; $P=0.003$).

Consumption of decaffeinated coffee, on the other hand, was not associated with a decrease in BCC risk. “The results suggest that it is the caffeine in coffee that is responsible for the anti-cancer effect,” said Han.

The findings support studies in mice which demonstrated that caffeine may block the formation of skin tumors. However, Han said he would not recommend increasing a person’s coffee intake based on these data alone. “We need more studies in different populations and additional mechanistic studies before we can say this definitively.”

Contrary to the findings for BCC, caffeine intake was not inversely associated with two other forms of skin cancer – squamous cell carcinoma and melanoma. There were 1,953 cases of squamous cell carcinoma and 741 cases of melanoma in the study, and Han said these numbers may be insufficient to establish an association with coffee consumption.
Shanghai set for regional respiratory forum

Elvira Manzano

The 8th International Symposium on Respiratory Diseases (ISRD) and American Thoracic Society (ATS) in China Forum to be held in Shanghai from 9-11 this November is expected to attract delegates and leaders in pulmonary and respiratory medicine from all over the world.

The 4-day conference at the Shanghai International Convention Center will consist of plenary and state-of-the-art lectures, oral presentations and satellite symposia, including a session on translational respiratory medicine. Some of the main highlights in the scientific program include latest trends in the diagnosis and management of COPD and lung cancer, as well as updates on sleep medicine and mechanical ventilation.

Conference president Professor Chunxue Bai, chairman of the Shanghai Respiratory Research Institute (SRRI), which is hosting the event, and chairman of the Respiratory Department of Zhongshan Hospital and Fudan University, Shanghai, China, said 2012 marks a significant milestone for the ISRD, with its inaugural joint scientific sessions with the ATS.

“[The] ATS in China Forum reinforces our ‘east meets west’ approach where renowned speakers from the US, Europe, Asia Pacific and China will share their insights, knowledge and experiences in respiratory research and clinical practice for better disease management outcome.”

Bai expects around 1,500 delegates, 80 percent of which are from China, to attend the conference. He said the event will provide a forum for clinical and scientific researchers with complementary experience and expertise to debate and foster collaboration towards prevention and management of respiratory diseases and its complications.

“It is our hope that, with the support and contribution from delegates, speakers and industrial companies, ISRD will grow to become an international academic brand attracting more respirologists as well as clinical and translational researches,” Bai said.
Beijing ready for regional cardiology congress

The 23rd Great Wall International Congress of Cardiology (GW-ICC) Asia Pacific Heart Congress (APHC) 2012 in Beijing, China from 11-14 October will showcase the latest research and clinical advances in cardiology in the Asia Pacific.

This year’s congress will be held in over 30 venues, with around 13,000 delegates anticipated to participate in 400 academic exchanges, thematic sessions, training presentations and exhibitions.

Congress president Professor Dayi Hu, chief of the Cardiology Division, Peking University’s People’s Hospital, Beijing, China, said participants can also look forward to keynote lectures, post-graduate courses, workshops and 17 joint symposia with leading international societies including the American College of Cardiology (ACC), European Society of Cardiology (ESC) and World Heart Federation.

Discussions will focus on opportunities and challenges in cardiovascular care in the US and China, advances in the management of heart failure and acute coronary syndromes, cardiac and stroke rehabilitation care, updates in cardiovascular imaging, cardiac catheterization and revascularization, new approaches to AF ablation and latest recommendations in pharmacotherapy, among other topics. Both English and Chinese sessions will be provided.

“We hope this congress will be an exciting and productive gathering of cardiologists from all over the world and provide [them] an opportunity to share knowledge, experience and views on current cardiology topics,” said Hu.

Over the years, the GW-ICC APHC has brought together leading cardiologists and researchers to discuss developments in cardiovascular research and practice. The congress has been attracting participation from a number of international academic organizations annually.

This year’s theme is “Emphasis on Rehabilitation and Secondary Prevention, from hospital back to home.”

The GW-ICC and APHC is organized by the GWICC congress committee together with 23 leading international academic societies.
Patients with a fever lasting more than 2 weeks where there is no sign of localized infection should be treated with the common antimicrobial agent doxycycline, according to an expert.

“Empirical treatment with doxycycline is the most cost-effective strategy for the management of patients with acute undifferentiated fever in Asia,” said Professor Yupin Suputtamongkol, from the Faculty of Medicine, Siriraj Hospital, Mahidol University in Bangkok, Thailand. “This sub-group of patients has a very good prognosis and clinical response is dramatic with appropriate antimicrobial therapy.”

For severe cases, a combination treatment with either ceftriaxone or penicillin G is recommended, she added.

The diagnosis of acute undifferentiated febrile illness has been a challenge for physicians in Southeast Asia. “Acute undifferentiated fever is very common in this region but its specific etiology is often unknown, making accurate diagnosis and effective treatment difficult,” Suputtamongkol said.

The majority of patients present with non-specific symptoms such as fever, headache, chills, nausea, muscle ache and vomiting that mimic clinical manifestations of secondary sepsis caused by different circulating pathogens. “Physicians should be aware that malaria, dengue infection, ricketsial infections, and leptospirosis are major causes of acute undifferentiated fever in Asia. Travelers to endemic areas are also at risk.”

Currently, there is no single rapid test that would differentiate one disease from the other. Even when dengue fever and leptospirosis are suspected, available rapid serologic tests cannot reliably detect IgM antibodies until at least the sixth day of clinical illness. Rapid serologic testing was able to identify only half of the cases of leptospirosis in Thailand during an outbreak between 1999 and 2003.

“It’s not practical to request for a serial diagnostic test for dengue, leptospirosis or scrub typhus because most of the time it’s only about 50 percent accurate. We need a test that can detect these three infectious diseases in one go,” Suputtamongkol said.

“We came up with clinical practice guidelines in the management of acute febrile illness after conducting a series of clinical trials on patients in various hospitals in Thailand during an outbreak of leptospirosis in 1999. The guideline has four components - investigations, severity assessment, empirical therapy and follow-up,” she said.

“This is diagnosis by exclusion. Exclude malaria and dengue first. Then consider rickettsial infection or leptospirosis. If scrub typhus is the cause of fever, the patient will improve in 48 hours following doxycycline therapy. If there’s no clinical response and the patient remains febrile, then the cycle of strategy has to be repeated.”

Patients with severe leptospirosis could die of lung hemorrhage. As for scrub typhus, the important cause of death is acute respiratory disease syndrome so respiratory support is also very important, Suputtamongkol added.

“Early diagnosis of the cause of acute fever is important to guide appropriate antimicrobial therapy. Empirical treatment is necessary because rapid, sensitive and affordable diagnostic tests for scrub typhus, leptospirosis and murine typhus are not available,” she concluded.
Sustained suppression of Hep B virus a critical measure of treatment response

Hepatitis B e antigen (HBeAg) seroconversion is an inadequate end-point in hepatitis B management because it does not indicate or guarantee long-term remission and virus inactivity, according to a leading hepatologist.

“While hepatitis B surface antigen (HBsAg) seroconversion comes as a near ‘cure’ for chronic hepatitis B (CHB), it is only achievable in 10 percent of patients with all current therapies,” said Dr. Ching-Lung Lai, chair professor of hepatology and medicine, and chief of the Gastroenterology and Hepatology Division, Department of Medicine, University of Hong Kong. “It is also genotype-dependent, and rarely achieved in patients with genotypes B and C, which are the common genotypes in Asia.”

In a study in Hong Kong, 60 percent of 85 HBeAg-positive patients had HBeAg seroconversion following pegylated interferon therapy at year 5, however only 11 percent had undetectable HBV DNA (≤400 copies/mL). About 2.4 percent of patients achieved HBsAg seroclearance at 2.6 and 84 months post-treatment. [Hepatology 2010; 51:1945-1953]

“HBeAg seroconversion to anti-HBe is thus only a half-way process in the natural history of CHB in patients who acquire the disease during early childhood,” said Lai.

In another study, more than 60 percent of patients had no significant decline in HBsAg levels following 2 years of treatment with entecavir, a mononucleos(t)ide analogue agent. Early decline in HBsAg levels at weeks 12 and 24 was not associated with HBV DNA suppression or HBeAg seroconversion. [Am J Gastroenterol 2011;106:1766-1773]

“HBeAg seroconversion in patients with chronic hepatitis B is only meaningful when accompanied with permanently low and undetectable HBV DNA,” said Lai. “This is very important if we are to reduce the risk of the disease developing into cirrhosis and hepatocarcinoma.”

Sustained virologic suppression is critical to CHB therapy. “Five-year treatment with tenofovir and entecavir has resulted in a continuing HBV DNA suppression of up to <3-400 copies/mL in more than 90 percent of patients. This is associated with histologic improvement, including reversal of severe fibrosis.”

Entecavir and tenofovir are potent, safe and associated with little or no resistance, Lai added.
Personal Perspectives

“...The talk on HIV today, which tackled new areas we need to look into in terms of development and cure for HIV, was so revealing. Another interesting lecture was on global biosurveillance. But coming from Nigeria, we have so many limitations. They are going too high when we haven’t even reached where they are now. We are lagging behind [and] we need their support. Africa is famous for malaria, TB and intestinal helminths. If they could help research in our country, then that would be great.”

– Dr. Chinenyee Afonne, field epidemiologist, Department of Epidemiology and Medical Statistics, College of Medicine, University of Ibadan, Ibadan, Nigeria

“All the lectures I’ve been to have been great. It’s good to have an Asian perspective. There’s a lot of data on emerging infections and a lot of epidemiology that we don’t necessarily get to hear about unless we come to conferences like this.”

– Dr. Sanchia Warren, Royal Hobart Hospital, Hobart, Tasmania, Australia

“One of the ICID highlights to me was looking at all the new diagnostic tools that are available for infectious diseases. It’s very interesting to think about diagnostic testing in the clinic and being able to give patients the results immediately. That is one of the major strides that we are making. By using point-of-care diagnostics, we could treat millions of people who mostly live in low-resource settings.”

– Dr. Ruanne Barnabas, post-doctoral research fellow, Fred Hutchinson Cancer Research Center, Seattle, Washington, US.
Studies demolish theories of glargine-cancer link

Rajesh Kumar

Three major observational studies examining the use of long-acting insulin have found no increased risk of a wide range of cancers in patients using glargine, contradicting previous suggestions of a glargine-cancer link.

Researchers in the US and Europe independently compared the use of insulin glargine for diabetes patients with other long-acting insulins and found no basis for the previous suggestion made by a series of studies published in 2009.

One study group from Kaiser Permanente examined data for 115,000 patients with diabetes who were taking either insulin glargine or neutral protamine Hagedorn (NPH) insulin. They compared cancer risk in new insulin users as well as patients who had switched from NPH to glargine. There was a median duration of 1.2 years for glargine use and 1.4 years for NPH. This study found a “suggestion” of an association between insulin glargine use and a modest increase in breast cancer risk, but only among new insulin users (HR 1.6, 95% CI 1.0 to 2.8). However, in patients who had been on insulin for a longer period of time and had switched from NPH to glargine, there was no increased risk.

“We think this may be a chance finding,” said principal investigator Dr. Laurel Habel, research scientist at the Kaiser Permanente Northern California division of research in Oakland, California, US, adding there was no biological reason why the cancer risk would be seen only in new users.

The group found no association with prostate, colorectal cancer or all cancers combined in new users or in prior users.

“The preponderance of the evidence suggests that there is no increased risk of cancer associated with relatively short-term use of insulin,” said Dr. John Buse, director of the diabetes center at the University of North Carolina School of Medicine in Chapel Hill, North Carolina, US.

The second group of researchers at the University of North Carolina used a large automated healthcare database to identify 43,306 patients initiating glargine and 9,147 initiating NPH, all of whom were free of cancer when they initiated insulin use. The mean duration of treatment was 1.2 years for the glargine group and 1.1 years for those taking NPH. Follow-up was discontinued when a patient experienced a change in their insulin treatment.

“We found no evidence of an increased risk for cancer and we specifically found no increased risk for breast cancer in the small group that stayed on these drugs for more than 24 months,” said principal investigator Dr. Til Stürmer, professor of epidemiology and director of the center of excellence in pharmacoepidemiology and public health at the University of North Carolina Gillings school of global public health.

“Our study adds to the important evidence about long-term outcomes of these antidiabetic treatments,” said Stürmer.

The Northern European Study of Insulin...
and Cancer, is the largest of the three studies comprising 447,821 diabetic patients using insulin, over 1.5 million person-years of observation and 17,500 new cases of cancer in the cohorts. The average follow-up time is longer at 3.1 years for those on glargine and 3.5 years for other insulins.

This study looked at the risk for all cancers, as well as individually for breast, lung, pancreas, colorectal and prostate cancers.

“There was no difference in risk between glargine and other insulins found in any of the pre-defined primary and secondary hypotheses of this study,” said principal investigator Dr. Peter Boyle, President of the International Prevention Research Institute in Lyon, France.

Linagliptin effective in combination with insulin, metformin

Rajesh Kumar

The DPP-4 inhibitor linagliptin (Trajenta®, Boehringer Ingelheim) has been shown to be effective when combined with other antidiabetic therapies in achieving clinically meaningful blood glucose control in adults with type 2 diabetes.

In a randomized phase III clinical trial involving 1,261 adult patients with type 2 diabetes, linagliptin 5mg once daily was significantly more effective at lowering blood glucose levels compared with placebo when used as an add-on therapy to basal insulin alone or in combination with metformin and/or pioglitazone.

It demonstrated a placebo-adjusted reduction in HbA1c of 0.65 percent (P≤0.0001) from a baseline HbA1c of 8.3 percent at 24 weeks, without weight gain or additional risk of hypoglycaemia.

“Once patients are on insulin, there is not much you can do to make their diabetes control better, [therefore a] 0.65 percent reduction in HbA1c is a very good reduction in insulin treated patients,” said Dr. Mark Cooper, director of the Danielle Alberti Memorial Centre for Diabetes Complications and head of the diabetes division at the Baker IDI Heart and Diabetes Institute in Melbourne, Australia.

“Linagliptin, which we have always considered better to use in earlier stage of diabetes, can actually be used in any stage – early, middle or late,” said Cooper.

 Patients were eligible for the study if they had inadequate glycemic control with a stable dose of basal insulin (ie, insulin glargine, insulin detemir or NPH insulin) with or without metformin and/or pioglitazone.

There was a similar overall frequency of adverse events (linagliptin 71.8 percent, placebo 72.5 percent) and hypoglycemia (linagliptin 25.7 percent, placebo 27.3 percent) in each group. In addition, body weight did not significantly change from the baseline in the linagliptin and placebo groups (-0.17 kg and +0.13 kg, respectively; P=0.07).

A post-hoc analysis from a second phase III trial found that on a background of metformin randomized to add linagliptin or glimepiride, a greater proportion of patients taking linagliptin achieved the target of HbA1c <7 percent without weight gain and/or hypoglycemia than those taking glimepiride after 104 weeks (54 percent vs.
23 percent). The overall reduction in HbA1c was similar in both groups.

In patients who were at high risk of declining renal function, yet another post-hoc analysis showed that linagliptin achieved significant reduction in urinary albumin-to-creatinine ratio (UACR) of 33 percent from baseline ($P \leq 0.05$), in addition to a 0.71 reduction in HbA1c.

The analysis included pooled data from four 24-week trials involving a total of 227 patients at high risk of declining renal function who were on stable treatment with angiotensin-converting enzyme inhibitors (ACEs) or angiotensin receptor blockers (ARBs).

“This analysis is important because approximately 65 percent of patients living with type 2 diabetes are at risk of declining renal function, which can limit treatment options,” said Professor Per Henrik Groop of the division of nephrology at Helsinki University Central Hospital in Helsinki, Finland.

“Patients treated with linagliptin showed improvements in blood glucose levels and reduction of albumin in the urine, a sign for renal dysfunction. We will continue to further investigate this area as we recognize the importance of considering declining renal function when treating type 2 diabetes patients.”
The investigational antidiabetic drug empagliflozin, a sodium glucose co-transporter-2 (SGLT-2) inhibitor, has demonstrated promising results in a phase II trial.

SGLT-2 inhibitors, which lower high blood glucose independently of insulin by blocking glucose re-uptake in the kidneys and thereby excreting excess glucose via the urine, lower HbA1c and weight, irrespective of beta cell function or insulin resistance.

In the trial, 659 adults with type 2 diabetes who had participated in earlier 12-week phase II-b trials of the drug, were then randomized to receive open-label treatment with either 10 mg or 25 mg of empagliflozin (as monotherapy or add-on to metformin), metformin alone, or sitagliptin plus metformin for an additional 78 weeks.

At week 90, patients assigned to empagliflozin 10 mg alone achieved a 0.34 percent reduction in Hb1Ac from baseline and a weight loss of 2.24 kg. Monotherapy with the 25mg dose led to a HbA1c reduction of -0.47 percent, along with weight loss of 2.61 kg, versus metformin alone (-0.56 percent and 1.28 kg, respectively).

When used as an add-on to metformin, significant decreases from baseline in mean HbA1c levels and weight loss were observed with empagliflozin 10 mg (-0.34 percent; -3.14 kg) and 25 mg (-0.63 percent; 4.03 kg), versus sitagliptin (-0.40 percent, 0.41 kg).

The Boehringer Ingelheim/Eli Lilly-sponsored study showed the drug in both 10 mg or 25 mg doses was generally well tolerated. More than 90 percent of the adverse events (AEs) reported in the trial were mild or moderate in severity. Between 0.9 percent and 3.6 percent of patients on empagliflozin reported hypoglycemic vents, versus 7.1 percent on metformin monotherapy and 5.4 percent on sitagliptin.

AEs related to urinary tract infections were reported in 3.8 to 12.7 percent of patients on empagliflozin, 3.6 percent of patients on metformin monotherapy, and 12.5 percent of patients on sitagliptin. AEs related to genital infections were reported in 3.0 percent to 5.5 percent of patients on empagliflozin, 1.8 percent of patients on metformin monotherapy, and none of the patients on sitagliptin.

Empagliflozin is now in phase III clinical development, with more than 14,500 patients planned to be enrolled.

“Type 2 diabetes is characterized by three main factors: persistent hyperglycemia, impaired insulin secretion and increased insulin resistance,” said Dr. Hans-Juergen Woerle, vice-president of the medicine therapeutic area (metabolism) at Boehringer Ingelheim, Ingelheim am Rhein, Germany.

“SGLT-2 inhibitors such as empagliflozin represent an innovative, insulin-independent mode of action. To date, clinical data have demonstrated that these drugs have the potential to improve persistent hyperglycemia irrespective of the two other factors.”
Ethical clinical decisions must consider both mother and fetus

Radha Chitale

The rights of both mother and fetus must be considered when managing pregnancy because unilateral clinical decisions breach clinical ethical standards, said Dr. Frank Chervenak, Weill Cornell Medical College, New York, New York, US.

Perinatal ethics span a wide variety of situations, including abortion, stem cell research, mental health and pregnancy, and caesarean delivery.

Clinicians’ professional responsibility to the mother and fetus can seem conflicted, requiring unacceptable compromises.

However, considering the rights of only the mother or the fetus (at all gestational ages) is simplistic and, Chervenak said, will result in conceptual and clinical failure.

Instead of this kind of counterproductive reductionism, the professional responsibility model of obstetric ethics should gird clinical decisions, he added, and be comprised of medical science and compassionate clinical care for both the pregnant and fetal patients. [Am J Obstet Gynecol 2011;205:315.e1-5]

“Incorporating the psychological and social dimensions is required to have a clinically adequate model to guide obstetric care and avoid clinical tunnel vision,” Chervenak said.

The professional responsibility model also hinges on high quality informed consent of the pregnant patient to encourage autonomy.

According to the American College of Obstetricians and Gynecologists, “screening and invasive diagnostic testing for aneuploidy should be available to all women who present for prenatal care before 20 weeks of gestation regardless of maternal age.” [Obstet Gynecol 2007;109:217-227]

In a study to evaluate how pregnant women use risk assessment information for trisomy 21, 30,564 consecutive, singleton pregnancies were assessed based on maternal age, fetal nuchal translucency thickness and maternal proteins during the first trimester. [Am J Obstet Gynecol 2005;193:322-326]

Patients were counselled about estimated risk and informed that invasive testing, which has miscarriage risks of about 1 percent, were necessary to determine whether the fetus had chromosomal abnormalities.

Women were informed of the possibility of a 1 in 300 risk of fetal trisomy 21 but that the choice of whether or not to test was theirs. Median maternal age was 34 years.

The rate of invasive testing increased exponentially with increasing estimated risk ($P<0.0001$). Estimated risk for trisomy 21 was at least 1 in 300 in 8.4 percent of patients, of which 77.6 percent had invasive testing. Among the 91.6 percent of women whose estimated risk for trisomy 21 was less than 1 in 300, 4.6 percent had invasive testing.

“These empiric data compliment the arguments of normative ethics to create evidence-based ethical standards for informed consent regarding invasive testing,” the researchers said.
Chervenak noted that women were able to use sophisticated risk assessment data to make informed, rational decisions about invasive fetal testing. Given that high quality informed consent on behalf of the mother and fetus requires adequate time, he suggested that clinicians who cannot meet this ethical standard should refer patients to centers that can.
Three-dimensional (3-D) sonographic imaging technology could be helpful for more than examining babies in utero.

As “one of the most important advances in modern sonography,” according to Dr. Beryl Benacerraf, of Harvard Medical School and president of Diagnostic Ultrasound Associates in Boston, Massachusetts, US, 3-D volume acquisition of 2-D ultrasound has a variety of applications including identifying intrauterine devices (IUDs) that are embedded within the uterus, a potentially dangerous condition.

Volume displays make use of tomographic ultrasound imaging in which a number of image “slices” are taken about 1-4 mm apart, which can capture all the relevant anatomy over about 30 minutes.

Volume imaging allows doctors to see anatomic sections from any angle, not just the one at which the image was taken.

“This has the potential of making the acquisition plane irrelevant in the future,” Benacerraf said.

The benefit of 3-D sonography is a more accurate picture of what is inside the uterus.

This application is particularly useful for IUD insertion and monitoring in women, whose cervixes can vary significantly in size and shape, which can affect the IUD.

In one study, 167 consecutive women with a uterine IUD were evaluated with 3-D sonography for the width of the endometrial cavity at the base of the uterus to evaluate variations in size between women who had an embedded IUD and those who did not. [J Ultrasound Med 2010;29:1453-1456]

The data showed that 28 (16.5 percent) women had an IUD embedded in the myometrium or the cervix and that all of the IUDs that appeared to be placed low in a 2-D rendering were in fact embedded after examination of a 3-D rendering.

Women with embedded IUDs also had more bleeding and pain compared to women with normally placed IUDs ($P=0.0001$).

Width measurements of 29 women with embedded IUDs and 132 with non-embedded IUDs showed that the former had smaller fundal uterine cavities ($25 \pm 0.8$ mm) compared with those with nonembedded IUDs ($32 \pm 1.0$ mm, $P=0.0003$).

Benacerraf noted that the average uterine cavity is 29 mm, for nulliparous women it is 27 mm, and for those with at least one pregnancy it is 32 mm.

“[The mean widths suggest] that patients should consider an ultrasound to measure the uterine cavity prior to having an IUD inserted,” she said.
New guidelines to manage osteoporosis in men

Radha Chitale

New guidelines from the US-based Endocrine Society outline a clinical approach for managing osteoporosis, which results in lost bone density, bone weakness and increased risk of fracture, in men. [J Clin Endocrinol Metab 2012;97:1802-1822]

Osteoporosis is most often associated with women but the disorder causes significant morbidity and mortality in men.

“One in five [men] will experience an osteoporosis-related fracture in their lifetime,” said authoring task force chair Dr. Nelson Watts, Mercy Health Osteoporosis and Bone Health Services in Cincinnati, Ohio, US. “Mortality after fracture is [two to three times] higher in men than in women. Of the 10 million Americans with osteoporosis, 2 million are men. Of the 2 million fractures due to osteoporosis that occur each year, 600,000 are in men.”

Testing was recommended in high-risk men when they are age 70 or older or when they are between ages 50-69 and have risk factors for osteoporosis including low body weight or a history of smoking.

A history of adult bone fractures, particularly after age 50, is a strong indicator of osteoporosis risk.

The task force said clinicians should recommend reducing alcohol intake and smoking, increase weight-bearing exercises, and get sufficient calcium and vitamin D in order to promote good bone health.

“In contrast to the large fracture-end point trials of osteoporosis therapies in women, studies in men have generally been small, with change in bone mineral density as the primary end point,” the authors said.

However, trials have shown positive effects of drug therapies on bone mineral density and markers for bone remodelling, so “we conclude that available therapies are likely to be effective in men and that it is appropriate to recommend pharmacological therapy in men with increased fracture risk.”

Men over 50 who have had spine or hip fractures, who have low bone mineral density or any other clinical or lifestyle risk factors are recommended for pharmacological treatment with any approved osteoporosis drugs, including alendronate, risedronate and teripatatide.

Zolendronic acid is recommended for men with recent hip fractures.

Use of a risk assessment tool that calculates the 10-year risk of fracture, like the FRAX questionnaire, to help plan therapy can also be helpful as it may identify more men in need of treatment than bone density tests alone.

“Acknowledging the shortcomings of the available data, we recognize the need to be sufficiently inclusive to identify both an adequate number of the men at risk and to incorporate multivariable risk models,” the researchers said.
Few drinks per day may prevent bone loss among postmenopausal women. New research showed a drop in markers for bone turnover – the process of bone breakdown and reformation – after 2 weeks of abstaining from alcohol followed by a quick rise again to pre-abstinence levels after consumption resumption.

“After less than 24 hours to see such a measurable effect was really unexpected,” said study author Dr. Urszula Iwaniec, associate professor in the College of Public Health and Human Sciences at Oregon State University, Corvallis, Oregon, US.

Although alcohol abuse is associated with reduced bone mineral density, moderate alcohol consumption, about 28 grams per day, has been linked previously to increased bone mineral density, though the effect of confounding variables has not been teased out.

Forty healthy postmenopausal women, mean age 56.3, who consumed between 18-20 grams of alcohol per day were included in the study. [Menopause 2012 Jul 9. Epub ahead of print]

Immunoassays for the bone formation marker serum osteocalcin and the bone resorption marker C-terminal telopeptide (CTx) were done at baseline, after 14 days of abstaining from alcohol, and again 12-14 hours following alcohol resumption.

Serum levels for both markers increased during the abstinent period compared to baseline after assessment at 14 days (osteocalcin 4.1 ± 1.6 percent, \( P=0.01 \); CTx 5.8 ± 2.6 percent, \( P=0.02 \)), indicating increased turnover.

After the women were allowed to drink alcohol normally, serum levels for both osteocalcin and CTx fell immediately, within 12-14 hours, upon testing the next day to levels similar to baseline (osteocalcin 3.4 ± 1.4 percent, \( P=0.01 \) and 3.5 ± 2.1 percent, \( P=0.05 \)).

The study was not ethnically diverse and therefore not generalizable and the type of drink was not controlled for, the researchers noted.

In addition, the process of bone remodeling, whereby reabsorbed bone cavities are filled with new bone, takes about 4 months, and the study results may have underestimated the effects of alcohol due to residual effects of long-term alcohol use.

“Nevertheless, the small but significant increases in osteocalcin and CTx after short-term abstinence provide substantial evidence that moderate alcohol consumption decreases bone turnover,” they said.

Eighty percent of patients with osteoporosis are postmenopausal women and while pharmacological interventions are available, they are costly and have side effects.

“It is therefore important to identify modifiable lifestyle factors that influence the risk of osteoporosis,” said the researchers, but added that abstinence for longer than the 14-day trial would be required to determine the total effects of alcohol on bone turnover.
The global death toll from the 2009 influenza A H1N1 pandemic was 15 times higher than reported, according to estimates from the US Centers for Disease Control and Prevention (CDC).

During the pandemic in 2009, countries worldwide reported to the World Health Organization that 18,500 deaths were attributable to H1N1, as confirmed through laboratory testing results. But this figure was widely acknowledged to be a significant underestimate of the true mortality caused by ‘swine flu’, said Dr. Fatimah Dawood from the CDC influenza division.

“Counting only deaths in people with laboratory-confirmed 2009 H1N1 influenza will miss deaths for at least two reasons,” she pointed out. “First, some people who die from influenza are not tested. Second, some people die from influenza-related complications that may occur many days after the initial infection when the virus is no longer detectable with commonly-used diagnostic tests.”

In a study published recently, Dawood and colleagues derived a different estimate by using H1N1 symptomatic attack rates from 12 countries of different income levels and fatality ratios from five high-income countries. [Lancet Infect Dis 2012 Jun 26. Epub ahead of print]

The attack rates were found to vary widely between countries, ranging from 4 to 33 percent in children and from 0 to 22 percent in adults. Fatality rates were also variable. To adjust for such differences, which could be caused by socioeconomic and healthcare disparities, they applied multiplier factors based on respiratory disease mortality before the pandemic.

With this approach, the investigators pegged the worldwide H1N1 respiratory death toll at 201,200 and cardiovascular deaths at 83,000. Added together, this estimate (284,200) is about 15 times higher than the laboratory-confirmed death counts.

Such results will “help public health officials make decisions about the allocation and delivery of influenza prevention and treatment measures,” Dawood noted.

Indeed, the study findings suggested that a disproportionate number of deaths occurred in Africa and Southeast Asia. Although only 38 percent of the world’s population live in these regions, they accounted for 51 percent of all deaths.

Original reports of laboratory-confirmed deaths had Africa and Southeast Asia contributing to less than 12 percent of all H1N1-associated deaths, according to a commentary by Dr. Cecile Viboud of the National Institutes of Health, Maryland, US, and Professor Lone

The study also reported that 80 percent of deaths occurred in those younger than 65 years of age.

“These findings highlight the importance of influenza prevention tools such as vaccines and the need to ensure that regions of the world that suffer more deaths have access to influenza prevention and treatment tools during future pandemics,” said Dawood.
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Mr GAN Kim Yong
Minister for Health, Republic of Singapore

Opening Keynote by
Dr Blackford MIDDLETON
Corporate Director, Clinical Informatics Research & Development, Partners HealthCare System, Harvard Medical School, Brigham & Women’s Hospital

Closing Keynote by
Dr Charles SAWYER
MD, FACP
Associate Chief Health Information Officer Geisinger Health System
August

60th Annual Scientific Meeting of the Cardiac Society of Australia & New Zealand
16/8/2012 to 19/8/2012
Location: Brisbane, Australia
Info: The Conference Company
Tel: (64) 9-360 1240
Fax: (64) 9-360 1242
Email: csanz@icc.co.nz
Website: www.csanz2012.com/

11th Asian Congress of Urology of The Urological Association of Asia
22/8/2012 to 26/8/2012
Location: Pattaya, Thailand
Info: 11th ACU Local Organiser
Tel: (662) 287 3942 to 3
Fax: (662) 677 5868
Email: secretariat@11thacu2012.org
Website: http://www.11thacu2012.org/

European Society of Cardiology Congress 2012
25/8/2012 to 29/8/2012
Location: Munich, Germany
Info: European Society of Cardiology
Tel: (33) 4 9294 7600
Fax : (33) 4 9294 7601
E-Mail: ascoregistration@jspargo.com
Website: www.escardio.org/congresses/esc-2012

September

European Respiratory Society Annual Congress
1/9/2012 to 5/9/2012
Location: Vienna, Austria
Info: European Respiratory Society
Tel: (41) 21 213 01 01
Fax: (41) 21 213 01 00
E-Mail: ers2012groups@kit-group.org
Website: www.erscongress2012.org/

14th Congress of the International Society for Peritoneal Dialysis
9/9/2012 to 12/9/2012
Location: Kuala Lumpur, Malaysia
Info: International Society for Peritoneal Dialysis
Tel: (603) 2162 0566
Fax: (603) 2161 6560
E-Mail: ispd2012@console.com.my
Website: www.ispd2012.org.my

Hospital Management Asia 2012
13/9/2012 to 14/9/2012
Location: Hanoi, Vietnam
Info: Ms. Sheila Pepito
Tel: (632) 846 8339
Email: shilapepito@exedraevents.com
Website: hospitalmanagementasia.com

London College of Clinical Hypnosis (LCCH-Asia) Certificate in Clinical Hypnosis
22/9/2012 to 23/9/2012
Location: University of Malaya, Kuala Lumpur, Malaysia
Info: LCCH Secretariat
Tel: (60) 3-7960 6439 / 7960 6449
Email: info@hypnosis-malaysia.com
Website: www.hypnosis-malaysia.com

Upcoming

15th Biennial Meeting of the European Society for Immunodeficiencies (ESID 2012)
3/10/2012 to 6/10/2012
Location: Florence, Italy
Info: Secretariat Office of GW-ICC & APHC (Shanghai Office)
Tel: (86) 21-6157 3888 Extn: 3861/62/64/65
Fax: (86) 21-6157 3899
Email: secretariat@heartcongress.org
Website: www.heartcongress.org

23rd Great Wall International Congress of Cardiology (GW-ICC) – Asia Pacific Heart Congress (APHC) 2012
11/10/2012 to 14/10/2012
Location: Beijing, China
Info: Secretariat Office of GW-ICC & APHC (Shanghai Office)
Tel: (86) 21-6157 3888 Extn: 3861/62/64/65
Fax: (86) 21-6157 3899
Email: secretariat@heartcongress.org
Website: www.heartcongress.org

42nd Annual Meeting of the International Continence Society
15/10/2012 to 19/10/2012
Location: Beijing, China
Tel: (41) 22 908 0488
Fax: (41) 22 906 9140
Email: ics@kenes.com
Website: www.kenes.com/ics
8th International Symposium on Respiratory Diseases & ATS in China Forum 2012
9/11/2012 to 11/11/2012
Location: Shanghai, China
Info: UBM Medica Shanghai Ltd.
Tel: (86) 21-6157 3888 Extn: 3861/62/64/65
Fax: (86) 21-6157 3899
Email: secretariat@isrd.org
Website: www.isrd.org

National Diagnostic Imaging Symposium
2/12/2012 to 6/12/2012
Location: Orlando, Florida, US
Info: World Class CME
Tel: (980) 819 5095
Email: office@worldclaswscme.com

Asian Pacific Digestive Week 2012
5/12/2012 to 8/12/2012
Location: Bangkok, Thailand
Tel: (66) 2 748 7881 ext. 111
Fax: (66) 2 748 7880
E-mail: secretariat@apdw2012.org
Website: www.apdw2012.org

World Allergy Organization International Scientific Conference (WISC 2012)
6/12/2012 to 9/12/2012
Location: Hyderabad, India
Info: World Allergy Organization
Tel: (1) 414 276 1791
Fax: (1) 414 276 3349
E-mail: WISC@worldallergy.org
Website: www.worldallergy.org

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The sun glistens on the Amstel River, forming a seemingly endless pathway of diamonds, an illusion interrupted only by small boats. The boats, largely ferrying tourists on the edge of their seats attempting to get the best views of the narrow, gabled houses leaning into one another, weave in and out of the canal network, skillfully avoiding docked houseboats. Occasionally, a ‘party boat’ breaks the monotony with a boisterous crowd on board lost in their heady fog of loud music and alcohol.

Amsterdam, touted as ‘the Venice of the North,’ blends history, art and culture seamlessly with hedonism. From the various tourist attractions, parks and pleins (squares) to the bars, clubs and the red-light district which come alive at sundown, this city has something to offer everyone.

With over 60 museums, 50 theaters and 140 art galleries, Amsterdam is a mecca for culture vultures. The aptly named Museumplein alone boasts three very popular Dutch museum institutions, the Rembrandt-heavy Rijksmuseum (Dutch National Museum), which houses an impressive collection of paintings from the Dutch Golden Age, the Van Gogh museum, and the modern art Stedelijk museum.
The Anne Frank Museum, drawing almost a million visitors annually, is a moving experience. The restored cramped, dark secret annexe where two Jewish families hid from persecution by the Nazis, provides a bleak contrast to the optimistic journal entries of Anne.

Various markets selling a hodgepodge of items guarantee you will score a bargain or two. The Albert Cuyp street market sells everything from fruits to clothes, cosmetics and spices. A personal favorite is the Bloemenmarkt, the floating flower market on the Singel canal. Roses, peonies and tulips in full bloom spill from the stalls onto the pavement in an explosion of colors.

Options are a plenty for getting from one place to another in Amsterdam. Arm yourself with a map and you will find that most places are within walking distance through the charming, distinctly European cobbled streets. The city is also serviced by frequent trams, convenient after a long day of sightseeing.

A more favorable option is hiring a bicycle. The number of bicycles in Amsterdam is said to outnumber the population, and this is very apparent with the multi-story bicycle parking lot in the heart of the city, visible as soon as you step out of Amsterdam Central Station.

Stepping out of the flurry of activity in the capital, a visit to the Netherlands is not complete without visiting the Dutch countryside. The immediate scenery change sees breathtaking views of vast farmland dotted by lazily grazing cows. Head to the picturesque village of Zaanse Schans and gape in awe at the six remaining windmills that line the River Zaan. A cheese-making factory close by lets you sample Dutch cheese and take home an assortment of cheeses, chocolates and Delftware (blue pottery).

A ferry ride away, the postcard-worthy fishing villages of Volendam and Marken make for perfect spots to bask in the sun by the waterfront and devour fresh seafood or indulge in an assortment of desserts sold by the harbor front.

The sights and sounds are sure to reel you in and leave you feeling like you’ve left a piece of your heart in the Netherlands.
“As far as I can see, it could be anything!”

“So, your wife had a doctor’s appointment and you couldn’t find a babysitter?”

“Lucy, I think we should get a divorce!”

“Darn it Dr. Flask, you shouldn’t have touched that thing!”

“The patient in the next bed is highly contagious. Please Harry, don’t go near him!”

“Should I take this medicine orally or in written form?”

“Don’t worry, it takes time to get used to progressive lenses!”