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1 April 2003 138 7 525-612

ARTICLES

Changing Use of Antibiotics in Community-Based Outpatient Practice, 1991–1999 525

M.A. Steinman, R. Gonzales, J.A. Linder, and C.S. Landefeld
Antibiotic use in ambulatory patients is decreasing in the United States. However, physicians increasingly prescribe expensive, broad-spectrum agents, even when there is little clinical rationale for their use.

Variation within Genes Encoding Interleukin-1 and the Interleukin-1 Receptor Antagonist Influence the Severity of Meningococcal Disease 534

R.C. Read, C. Cannings, S.C. Naylor, J.M. Timms, R. Maheswaran, R. Borrow, E.B. Kaczmarski, and G.W. Duff
Genotype at the interleukin-1 gene locus influences the likelihood of surviving meningococcal infection but does not affect susceptibility to the infection. Increasing age and infection with serogroup C also influence the likelihood of death.

Cardiovascular Outcomes in the Irbesartan Diabetic Nephropathy Trial of Patients with Type 2 Diabetes and Overt Nephropathy 542

T. Berl, L.G. Hunsicker, J.B. Lewis, M.A. Pfeffer, J.G. Porush, J.-L. Rouleau, P.L. Drury, E. Esmatjes, D. Hricik, C.R. Parikh, I. Raz, P. Vanhille, T.B. Wiegmann, B.M. Wolfe, F. Locatelli, S.Z. Goldhaber, and E.J. Lewis, for the Collaborative Study Group
Treatment with irbesartan, amlodipine, or placebo led to the same composite cardiovascular event rate (cardiovascular death, myocardial infarction, congestive heart failure, strokes, and coronary revascularization) in patients with type 2 diabetes and overt nephropathy who also received conventional antihypertensive therapy.

REVIEWS

Gene Vaccines 550

I.K. Srivastava and M.A. Liu
This article describes the immunologic rationale, design, and evaluation of gene vaccines for various clinical applications.

The Hereditary Nonpolyposis Colorectal Cancer Syndrome: Genetics and Clinical Implications 560

D.C. Chung and A.K. Rustgi
This review highlights the key features of normal DNA replication and the genetic and biochemical mechanisms that ensure the fidelity of this process. It then shows how mutations in the genes involved in DNA mismatch repair

lead to hereditary nonpolyposis colorectal cancer and describes how knowledge of the genetic origins of this disease inform the management of patients who are at increased risk for it.

PERSPECTIVES

“Genetic Exceptionalism” in Medicine: Clarifying the Differences between Genetic and Nongenetic Tests 571

M.J. Green and J.R. Botkin
This paper examines the arguments for “genetic exceptionalism” (the idea that genetic tests are unique and therefore justify special consideration for informed consent and privacy) and concludes that the same principles that informs the use of nongenetic tests also apply to genetic tests.

Genomics and Medicine: Distraction, Incremental Progress, or the Dawn of a New Age? 576

R.S. Cooper and B.M. Psaty
The authors suggest how to use currently accepted principles to assess the potential contribution of genomics to medicine and public health. They also speculate about the broader context that makes the rhetoric of the genomics revolution so compelling yet so likely to lead to misinterpretation of its potential impact.

HISTORY OF MEDICINE

Reprint: Molecular Structure of Nucleic Acids 581

J.D. Watson and F.H.C. Crick
We have reprinted Watson and Crick’s original paper from the 25 April 1953 issue of *Nature* (with permission of the publisher). It repays careful reading for its scientific content; the spare, precise prose; and the careful references to unpublished experimental results, which we now know gave the authors ample cause for confidence in their proposed structure for DNA.

Celebrating Complementarity 583

M.B. Hoagland
From the mid-1940s to the late 1950s, biological science focused on 1) the nature of the gene and genetic information and 2) the mechanism of protein synthesis. The former was the realm of molecular biologists; the latter attracted the classical biochemists. Although a wide scientific cultural gap separated these two approaches, they were complementary to one another and were destined to merge, unexpectedly and dramatically, 3 years after Watson and Crick published their celebrated paper.

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CLINICAL GUIDELINES

The Evidence Base for Tight Blood Pressure Control in the Management of Type 2 Diabetes Mellitus 587

V. Snow, K.B. Weiss, and C. Mottur-Pilson, for the Clinical Efficacy Assessment Subcommittee of the American College of Physicians

This article describes the American College of Physicians' guidelines for managing hypertension in patients with type 2 diabetes mellitus. It answers the following questions: 1) What are the benefits of tight blood pressure control in type 2 diabetes? 2) What are appropriate target levels of systolic blood pressure and diastolic blood pressure for patients with type 2 diabetes? and 3) Are certain antihypertensive agents more effective in patients with diabetes?

Treatment of Hypertension in Type 2 Diabetes Mellitus: Blood Pressure Goals, Choice of Agents, and Setting Priorities in Diabetes Care 593

S. Vijan and R.A. Hayward

The authors use the accumulated results of research on the effects of blood pressure on the complications of type 2 diabetes to recommend optimal blood pressure goals and preferred antihypertensive drugs. This paper provides the rationale for the American College of Physicians' clinical guidelines and provides an evidence base to guide clinicians in setting hypertension treatment goals and priorities in patients with type 2 diabetes.

EDITORIALS

From the Double Helix to Genomic Medicine 603

W.N. Kelley

What we take for granted in the clinical literature today was just recently considered basic science. As we begin to reap the benefits of the scientific progress achieved over the past 50 years, we must, as a nation, continue to support our basic science and clinical research enterprise and the training

of physician-scientists, who are most critical to conducting the necessary translational research. Failing this, we will not fully realize the ultimate promise inherent in Watson and Crick's discovery.

Antimicrobial Prescribing in the United States: Good News, Bad News 605

R.E. Besser

In this issue, Steinman and colleagues look at the changing patterns of antimicrobial selection during the 1990s. While overall prescribing declined during the 1990s, use of targeted therapy shifted to use of broader-spectrum agents. Does it matter that broader-spectrum agents are being overused? What is the cost?

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