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IVF Results: Optimize Not Maximize

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The desire to improve in vitro fertilization (IVF) results has led clinicians to replace more than one embryo in the uterus. As a result, multiple births have increased over the last two decades to epidemic proportions, exposing the field of assisted conception to justified criticism. This review aims to ensure that physicians involved in the field of fertility treatment are aware of the risks and complications related to multiple pregnancies, and to explore possible strategies such as blastocyst culture, preimplantation genetic screening, and embryo cryopreservation, which can help to control and reverse the tide of multiple pregnancies without reducing the good success rate that modern IVF treatment enjoys. A brief overview of the respective U.K. legislative system is also presented.

Critical Care Medicine

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The Intensivist in a Spiritual Care Training Program Adapted for Clinicians

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and Mary Martha Thiel*

Background: Critical illness is a crisis for the total person, not just for the physical body. Patients and their loved ones often reflect on spiritual, religious, and existential questions when seriously ill. Surveys have demonstrated that most patients wish physicians would concern themselves with their patients' spiritual and religious needs, thus indicating that this part of their care has been neglected or avoided. With the well-documented desire of patients to have their caregivers include the patient's spiritual values in their health care, and the well-documented reality that caregivers are often hesitant to do so because of lack of training and comfort in this realm, clinical pastoral education for health-care providers fills a significant gap in continuing education for caregivers. *Objectives:* To report on the first six years of a unique training program in clinical pastoral education adapted for clinicians and its effect on the experience of the health-care worker in the intensive care unit. The authors describe the didactic and reflective process whereby skills of relating to the ultimate concerns of patients and families are acquired and refined. *Design and Setting:* Clinical pastoral education designed for clergy was adapted for the health-care worker committed to developing skills in the diagnosis and management of spiritual distress. Clinician participants (approximately ten to twelve) meet weekly for five months (four hundred hours of supervised clinical pastoral care training). The program is designed to incorporate essential elements of pastoral care training, namely experience, reflection, insight, action, and integration. *Results:* This accredited program has been in

continuous operation training clinicians for the past six years. Fifty-three clinicians have since graduated from the program. Graduates have incorporated clinical pastoral education training into clinical medical practice, research, and/or further training in clinical pastoral education. Outcomes reported by graduates include the following: Clinical practice became infused with new awareness, sensitivity, and language; graduates learned to relate more meaningfully to patients/families of patients and discover a richer relationship with them; spiritual distress was (newly) recognizable in patients, caregivers, and self. *Conclusions:* This unique clinical pastoral education program provides the clinician with knowledge, language, and understanding to explore and support spiritual and religious issues confronting critically ill patients and their families. The authors propose that incorporating spiritual care of the patient and family into clinical practice is an important step in addressing the goal of caring for the whole person.

JAMA: The Journal of the American Medical Association

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Use of Gastric Acid-Suppressive Agents and the Risk of Community- Acquired *Clostridium difficile*- Associated Disease

Sandra Dial et al.

Context: Recent reports suggest an increasing occurrence and severity of *Clostridium difficile*-associated disease. The authors assessed whether the use of gastric acid-suppressive agents is associated with an increased risk in the community. *Objective:* To determine whether the use of gastric acid-suppressive agents increases the risk of *C. difficile*-associated disease in a community population. *Design, Setting, and Patients:*

The authors conducted two population-based case-control studies using the U.K. General Practice Research Database. In the first study, they identified all 1,672 cases of *C. difficile* recorded between 1994 and 2004 among all patients registered for at least two years in each practice. Each case was matched to ten controls on calendar time and the general practice. In the second study, a subset of these cases defined as community-acquired, that is, not hospitalized in the prior year, were matched on practice and age with controls also not hospitalized in the prior year. *Main Outcome Measures:* The incidence of *C. difficile* and risk associated with gastric acid-suppressive agent use. *Results:* The incidence of *C. difficile* in patients diagnosed by their general practitioners in the General Practice Research Database increased from less than one case per one-hundred thousand in 1994 to twenty-two per one-hundred thousand in 2004. The adjusted rate ratio of *C. difficile*-associated disease with current use of proton pump inhibitors was 2.9 (95 percent confidence interval [95% CI], 2.4–3.4) and with H₂-receptor antagonists the rate ratio was 2.0 (95% CI, 1.6–2.7). An elevated rate was also found with the use of nonsteroidal anti-inflammatory drugs (rate ratio, 1.3; 95% CI, 1.2–1.5). *Conclusions:* The use of acid-suppressive therapy, particularly proton pump inhibitors, is associated with an increased risk of community-acquired *C. difficile*. The unexpected increase in risk with nonsteroidal anti-inflammatory drug use should be investigated further.

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Health Industry Practices that Create Conflicts of Interest: A Policy Proposal for Academic Medical Centers

Troyen A. Brennan et al.

Conflicts of interest between physicians' commitment to patient care and the desire of pharmaceutical companies and their representatives to sell their products pose challenges to the principles of medical professionalism. These conflicts occur when physicians have

motives or are in situations for which reasonable observers could conclude that the moral requirements of the physician's roles are or will be compromised. Although physician groups, the manufacturers, and the federal government have instituted self-regulation of marketing, research in the psychology and social science of gift receipt and giving indicates that current controls will not satisfactorily protect the interests of patients. More stringent regulation is necessary, including the elimination or modification of common practices related to small gifts, pharmaceutical samples, continuing medical education, funds for physician travel, speakers bureaus, ghost-writing, and consulting and research contracts. The authors propose a policy under which academic medical centers would take the lead in eliminating the conflicts of interest that still characterize the relationship between physicians and the health-care industry.

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**Association of Socioeconomic Status
with Functional Capacity, Heart Rate
Recovery, and All-Cause Mortality**

Mehdi H. Shishehbor et al.

Context: Lower socioeconomic status (SES) confers heightened cardiovascular risk and mortality, although the mediating pathways are unclear. *Objective:* To evaluate the extent to which exercise physiologic characteristics account for the association between lower SES and mortality. *Design, Setting, and Participants:* Prospective cohort study of 30,043 consecutive patients living in seven counties in northeast Ohio referred between 1990 and 2002 for symptom-limited stress testing for evaluation of known or suspected coronary artery disease. Follow-up for mortality continued through February 2004. *Main Outcome Measures:* Estimated functional capacity in metabolic equivalents and heart rate recovery, physiologic characteristics that are determined directly from exercise; testing and all-cause mortality during a median follow-up of 6.5 years. *Results:* Multivariable models adjusting for demographics, insurance status, smoking status, and clinical con-

founders demonstrated a strong association between a composite SES score based on census block data and functional capacity (adjusted odds ratio comparing twenty-fifth with seventy-fifth percentile values, 1.72; 95 percent confidence interval [95% CI], 1.56–1.89; $P<.001$) as well as heart rate recovery (adjusted odds ratio comparing twenty-fifth with seventy-fifth percentile values, 1.18; 95% CI, 1.07–1.30; $P<.001$). There were 2,174 deaths, with mortality risk increasing from 5 to 10 percent as SES decreased by quartile ($P<.001$). Cox proportional hazards models that included all confounding variables except exercise physiologic characteristics demonstrated increased mortality as SES decreased (adjusted hazard ratio comparing twenty-fifth with seventy-fifth percentile values, 1.32; 95% CI, 1.22–1.42; $P<.001$). After further adding functional capacity and heart rate recovery, the magnitude of this relationship was reduced (comparing twenty-fifth with seventy-fifth percentile values; adjusted hazard ratio, 1.17; 95% CI, 1.08–1.26; $P<.001$), with these variables explaining 47 percent of the association. *Conclusions:* Impaired functional capacity and abnormal heart rate recovery were strongly associated with lower SES and accounted for a major proportion of the correlation between SES and mortality. Efforts to modify these clinical features among patients with low SES may narrow disparities in mortality.

**Journal of Child Psychology
and Psychiatry**

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**Abortion in Young Women and
Subsequent Mental Health**

*David M. Fergusson, L. John Horwood,
and Elizabeth M. Ridder*

Background: The extent to which abortion has harmful consequences for mental health remains controversial. The authors aimed to examine the linkages between having an abor-

tion and mental health outcomes over the interval from age fifteen to twenty-five years. *Methods:* Data were gathered as part of the Christchurch Health and Development Study, a twenty-five-year longitudinal study of a birth cohort of New Zealand children. Information was obtained on (a) the history of pregnancy and abortion for female participants over the interval from age fifteen to twenty-five years; (b) measures of DSM-IV mental disorders and suicidal behaviour over the intervals from age fifteen to eighteen years, eighteen to twenty-one years, and twenty-one to twenty-five years; and (c) childhood, family, and related confounding factors. *Results:* Forty-one percent of women had become pregnant on at least one occasion prior to age twenty-five years, and 14.6 percent had had an abortion. Those who had an abortion had elevated rates of subsequent mental health problems, including depression, anxiety, suicidal behaviors, and substance use disorders. This association persisted after adjustment for confounding factors. *Conclusions:* The findings suggest that abortion in young women may be associated with increased risks of mental health problems.

The Lancet

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Banking on Human Embryonic Stem Cells: Estimating the Number of Donor Cell Lines Needed for HLA Matching

Craig J. Taylor et al.

Background: Human embryonic stem (hES) cells are a promising source for transplantation to replace diseased or damaged tissue, but their differentiated progeny express human leukocyte antigens (HLAs) that will probably cause graft rejection. The creation of a bank of HLA-typed hES cells, from which a best match could be selected, would help reduce the likelihood of graft rejection. The authors investigated how many hES cell

lines would be needed to make matching possible in most cases. *Methods:* The number of hES cell lines needed to achieve varying degrees of HLA match was estimated by use of, as a surrogate for hES-cell donor embryos, blood group and HLA types on a series of ten thousand consecutive U.K. cadaveric organ donors. The degree of blood group compatibility and HLA matching for a recipient population consisting of 6,577 patients registered on the U.K. kidney transplant waiting list was determined, assuming all donor hES cell lines could provide a transplant for an unlimited number of recipients. *Findings:* A bank of 150 consecutive donors provided a full match at HLA-A, HLA-B, and HLA-DR for a minority of recipients (less than 20 percent); a beneficial match (defined as one HLA-A or one HLA-B mismatch only) or better for 37.9 percent (range, 27.9–47.5); and an HLA-DR match or better for 84.9 percent (77.5–90.0). Extending the number of donors beyond 150 conferred only a very gradual incremental benefit with respect to HLA matching. A panel of only ten donors homozygous for common HLA types selected from ten thousand donors provided a complete HLA-A, HLA-B and HLA-DR match for 37.7 percent of recipients, and a beneficial match for 67.4 percent. *Interpretation:* Approximately 150 consecutive blood-group-compatible donors, 100 consecutive blood group O donors, or 10 highly selected homozygous donors could provide the maximum practical benefit for HLA matching. The findings from these simulations have practical, political, and ethical implications for the establishment of hES-cell banks.

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Fruit and Vegetable Consumption and Stroke: Meta-Analysis of Cohort Studies

Feng J He, Caryl A. Nowson, and
Graham A. MacGregor

Background: Increased consumption of fruit and vegetables has been shown to be associated with a reduced risk of stroke in most

epidemiological studies, although the extent of the association is uncertain. The authors quantitatively assessed the relation between fruit and vegetable intake and incidence of stroke in a meta-analysis of cohort studies. *Methods:* The authors searched MEDLINE, EMBASE, the Cochrane Library, and bibliographies of retrieved articles. Studies were included if they reported relative risks and corresponding 95 percent confidence intervals (95% CIs) of stroke with respect to frequency of fruit and vegetable intake. *Findings:* Eight studies, consisting of nine independent cohorts, met the inclusion criteria. These groups included 257,551 individuals (4,917 stroke events) with an average follow-up of thirteen years. Compared with individuals who had less than three servings of fruit and vegetables per day, the pooled relative risk of stroke was 0.89 (95% CI, 0.83–0.97) for those with three to five servings per day, and 0.74 (95% CI, 0.69–0.79) for those with more than five servings per day. Subgroup analyses showed that fruit and vegetables had a significant protective effect on both ischemic and hemorrhagic stroke. *Interpretation:* Increased fruit and vegetable intake in the range commonly consumed is associated with a reduced risk of stroke. Our results provide strong support for the recommendations to consume more than five servings of fruit and vegetables per day, which is likely to cause a major reduction in strokes.

New England Journal of Medicine

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Fatal Toxic Shock Syndrome Associated with *Clostridium sordellii* after Medical Abortion

Marc Fischer et al.

Endometritis and toxic shock syndrome associated with *Clostridium sordellii* have previously been reported after childbirth and, in one case, after medical abortion. The authors

describe four deaths due to endometritis and toxic shock syndrome associated with *C. sordellii* that occurred within one week after medically induced abortions. Clinical findings included tachycardia, hypotension, edema, hemoconcentration, profound leukocytosis, and absence of fever. These cases indicate the need for physician awareness of this syndrome and for further study of its association with medical abortion.

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Disciplinary Action by Medical Boards and Prior Behavior in Medical School

Maxine A. Papadakis et al.

Background: Evidence supporting professionalism as a critical measure of competence in medical education is limited. In this case-control study, the authors investigated the association of disciplinary action against practicing physicians with prior unprofessional behavior in medical school. They also examined the specific types of behavior that are most predictive of disciplinary action against practicing physicians with unprofessional behavior in medical school. *Methods:* The study included 235 graduates of three medical schools who were disciplined by one of forty state medical boards between 1990 and 2003 (case physicians). The 469 control physicians were matched with the case physicians according to medical school and graduation year. Predictor variables from medical school included the presence or absence of narratives describing unprofessional behavior, grades, standardized-test scores, and demographic characteristics. Narratives were assigned an overall rating for unprofessional behavior. Those that met the threshold for unprofessional behavior were further classified among eight types of behavior and assigned a severity rating (moderate to severe). *Results:* Disciplinary action by a medical board was strongly associated with prior unprofessional behavior in medical school (odds ratio, 3.0; 95 percent confidence interval [95% CI], 1.9–4.8), for a population attributable risk of disciplinary

action of 26 percent. The types of unprofessional behavior most strongly linked with disciplinary action were severe irresponsibility (odds ratio, 8.5; 95% CI, 1.8–40.1) and severely diminished capacity for self-improvement (odds ratio, 3.1; 95% CI, 1.2–8.2). Disciplinary action by a medical board was also associated with low scores on the Medical College Admission Test and poor grades in the first two years of medical school (1 percent and 7 percent population attributable risk, respectively), but the association with these variables was less strong than that with unprofessional behavior. **Conclusions:** In this case-control study, disciplinary action among practicing physicians by medical boards was strongly associated with unprofessional behavior in medical school. Students with the strongest association were those who were described as irresponsible or as having diminished ability to improve their behavior. Professionalism should have a central role in medical academics and throughout one's medical career.

Volume 354, Number 1
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Is Our Behavior Written in Our Genes?

Dennis Drayna

Scientists recently reached an important milestone in the understanding of genetic contributions to behavior. A new study demonstrated the role of a single gene in specifying sexual behavior in the fruit fly *Drosophila melanogaster*. The findings prompt provocative thinking about the contribution of genetic factors to sexual orientation in humans, as well as about genes that might underlie a broader spectrum of human behaviors.

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Mortality after the Hospitalization of a Spouse

*Nicholas A. Christakis and
Paul D. Allison*

Background: The illness of a spouse can affect the health of a caregiving partner. The

authors examined the association between the hospitalization of a spouse and a partner's risk of death among elderly people. **Methods:** The authors studied 518,240 couples who were enrolled in Medicare in 1993. They used Cox regression analysis and fixed-effects (case–time–control) methods to assess hospitalizations and deaths during nine years of follow-up. **Results:** Overall, 383,480 husbands (74 percent) and 347,269 wives (67 percent) were hospitalized at least once, and 252,557 husbands (49 percent) and 156,004 wives (30 percent) died. Mortality after the hospitalization of a spouse varied according to the spouse's diagnosis. Among men, 6.4 percent died within a year after a spouse's hospitalization for colon cancer, 6.9 percent after a spouse's hospitalization for stroke, 7.5 percent after a spouse's hospitalization for psychiatric disease, and 8.6 percent after a spouse's hospitalization for dementia. Among women, 3.0 percent died within a year after a spouse's hospitalization for colon cancer, 3.7 percent after a spouse's hospitalization for stroke, 5.7 percent after a spouse's hospitalization for psychiatric disease, and 5.0 percent after a spouse's hospitalization for dementia. After adjustment for measured covariates, the risk of death for men was not significantly higher after a spouse's hospitalization for colon cancer (hazard ratio, 1.02; 95 percent confidence interval [95% CI], 0.95–1.09) but was higher after hospitalization for stroke (hazard ratio, 1.06; 95% CI, 1.03–1.09), congestive heart failure (hazard ratio, 1.12; 95% CI, 1.07–1.16), hip fracture (hazard ratio, 1.15; 95% CI, 1.11–1.18), psychiatric disease (hazard ratio, 1.19; 95% CI, 1.12–1.26), or dementia (hazard ratio, 1.22; 95% CI, 1.12–1.32). For women, the various risks of death after a spouse's hospitalization were similar. Overall, for men, the risk of death associated with a spouse's hospitalization was 22 percent of that associated with a spouse's death (95% CI, 17–27 percent); for women, the risk was 16 percent of that associated with death (95% CI, 8–24 percent). **Conclusions:** Among elderly people, hospitalization of a spouse is associated with an in-

creased risk of death, and the effect of the illness of a spouse varies among diagnoses. Such interpersonal health effects have clinical and policy implications for the care of patients and their families.

Sleep

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Relative Treatment Rates for Sleep Disorders and Sleep Disturbances following Abortion and Childbirth: A Prospective Record-Based Study

*David C. Reardon and
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Sleep disorders are linked with mood disorders and other psychiatric illnesses. Many women attribute sleep difficulties to abortion, but this self-diagnosis has not been tested using record-based evidence. Examination of records for 56,824 women with no known history of sleep disorders or sleep disturbances revealed that women were more likely to be treated for sleep disorders or disturbances following an induced abortion compared to a birth. The difference was most pronounced in the first 180 days after pregnancy resolution and was not significant after the third year.

Theoretical Medicine and Bioethics

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Some Things Ought Never Be Done: Moral Absolutes In Clinical Ethics

Edmund D. Pellegrino

Moral absolutes have little or no moral standing in our morally diverse modern society. Moral relativism is far more palatable to most ethicists and to the public at large. Yet, when pressed, every moral relativist will finally admit that there are some things which ought never be done. It is the rarest of moral relativists that will take rape, murder, theft, child sacrifice as morally neutral choices. In general ethics, the list of those things that must never be done will vary from person to person. In clinical ethics, however, the nature of the physician–patient relationship is such that certain moral absolutes are essential to the attainment of the good of the patient – the end of the relationship itself. These are all derivatives of the first moral absolute of all morality: Do good and avoid evil. In the clinical encounter, this absolute entails several subsidiary absolutes – act for the good of the patient, do not kill, keep promises, protect the dignity of the patient, do not lie, avoid complicity with evil. Each absolute is intrinsic to the healing and helping ends of the clinical encounter.