Introduction: The Challenge of Incidental Findings
Susan M. Wolf

Managing Incidental Findings in Human Subjects Research: Analysis and Recommendations
Susan M. Wolf et al.
No consensus yet exists on how to handle incidental findings (IFs) in human subjects research. Yet empirical studies document IFs in a wide range of research studies, where IFs are findings beyond the aims of the study that are of potential health or reproductive importance to the individual research participant. This paper reports recommendations of a two-year project group funded by NIH to study how to manage IFs in genetic and genomic research, as well as imaging research. We conclude that researchers have an obligation to address the possibility of discovering IFs in their protocol and communications with the IRB, and in their consent forms and communications with research participants. Researchers should establish a pathway for handling IFs and communicate that to the IRB and research participants. We recommend a pathway and categorize IFs into those that must be disclosed to research participants, those that may be disclosed, and those that should not be disclosed.

Empirical Analysis of Current Approaches to Incidental Findings
Frances Lawrenz and Suzanne Sobotka
This paper presents results found through searching publicly available U.S. data sources for information about how to handle incidental findings (IF) in human subjects research, especially in genetics and genomics research, neuroimaging research, and CT colonography research. We searched the Web sites of 14 federal agencies, 22 professional societies, and 100 universities, as well as used the search engine Google for actual consent forms that had been posted on the Internet. Our analysis of these documents showed that there is very little public guidance available for researchers as to how to deal with incidental findings. Moreover, the guidance available is not consistent.

Incidental Findings and Ancillary-Care Obligations
Henry S. Richardson
Recent work on incidental findings, concentrating on the difficult problems posed by the ambiguous results often generated by high-tech medicine, has proceeded largely independently from recent work on medical researchers’ ancillary-care obligations, the obligations that researchers have to deal with diseases or conditions besides the one(s) under study. This paper contends that the two topics are morally linked, and specifically that a sound understanding of ancillary-care obligations will center them on incidental findings. The paper sets out and defends an understanding of ancillary-care obligations, which is based on the idea that when participants signed up for a study they may — independently of their beliefs and expectations and of those of the researchers — be taken to have partially entrusted certain aspects of their health into the researchers’ hands. This partial-entrustment model of ancillary-care obligations, in turn, has substantive implications for how to deal ethically with incidental findings; for instance, it suggests that researchers have no moral obligation to hunt for incidental findings.

Incidental Findings in Human Subjects Research: What Do Investigators Owe Research Participants?
Franklin G. Miller, Michelle M. Mello, and Steven Joffe
The use of brain imaging technology as a common tool of research has spawned concern and debate over how investigators should respond to incidental findings discovered in the course of research. In this article, we argue that investigators have an obligation to respond to incidental findings in view of their entering into a professional relationship with research participants in which they are granted privileged access to private information with potential relevance to participants’ health. We discuss the scope and limits of this professional obligation to respond to incidental findings, bearing in mind that the relationship between investigators and research participants differs fundamentally from the doctor-patient relationship.
Understanding Incidental Findings in the Context of Genetics and Genomics
Mildred K. Cho

Human genetic and genomic research can yield information that may be of clinical relevance to the individuals who participate as subjects of the research. It has been common practice among researchers to notify participants during the informed consent process that no individual results will be disclosed, “incidental” or otherwise. However, as genetic information obtained in research becomes orders of magnitude more voluminous, increasingly accessible online, and more informative, this precedent may no longer be appropriate. There is not yet consensus on the responsibilities of researchers to disclose individual research results to research participants. Empirical research suggests that participants want to know individual research results. On the other hand, the increased resolution and power afforded by new genomic analyses may lead to findings of statistical, but not necessarily clinical, significance. This paper addresses the issues to be considered in deciding whether and how to disclose “incidental” findings or other findings of clinical significance that arise in the course of human genomic and genetic research. What research results should be offered, and what should not be offered? For which research should individual results be offered to research participants, when should they be offered, how, and to whom?

Genomic Research and Incidental Findings
Brian Van Ness

The Human Genome Project showed that there is significant genetic variation within the population. Current research is accumulating large databases that may reveal genetic variations associated with disease or health risks, even if not intended as part of the study design. These incidental findings create legal, ethical, and financial challenges for researchers. Current federal and international guidelines are not adequate. Plans for dealing with incidental findings need to be established in the study design and reviewed and approved by the Institutional Review Board.

Bridging Philosophical and Practical Implications of Incidental Findings in Brain Research
Judy Illes and Vivian Nora Chin

Empirical studies and ethical-legal analyses have demonstrated that incidental findings in the brain, most commonly vascular in origin, must be addressed in the current era of brain research. The challenges, however, are substantial. The discovery and management of incidental findings vary, at minimum, by institutional setting, professional background of investigators, and the inherent differences between research and clinical protocols. In the context of human subjects protections, the challenges of disclosure of unexpected and potentially meaningful clinical information concern privacy and confidentiality, communication, and responsibility for follow-up. Risks, including a blurring of boundaries between research and clinical practice, must be weighed against the possible benefit to subjects and a moral duty to inform. Identification and examination of these challenges have been met by scientific interest and a robust, interdisciplinary response resulting in the pragmatic recommendations discussed here.

The Risks and Benefits of Searching for Incidental Findings in MRI Research Scans
Jason M. Royal and Bradley S. Peterson

We weigh the presumed benefits of routinely searching all research scans for incidental findings (IFs) against its substantial risks, including false-positive and false-negative findings, and the possibility of triggering unnecessary, costly evaluations and perhaps harmful treatments. We argue that routinely searching for IFs may not maximize benefits and minimize risks to participants.
Incidental Findings in Magnetic Resonance Imaging (MRI) Brain Research
Charles A. Nelson
The use of magnetic resonance imaging (MRI) to investigate brain structure (“structural MRI”) and function (so-called “functional MRI”) has become increasingly common among neuroscientists, psychologists, and even economists in recent years. Yet, despite this increase in use, relatively little attention has been paid to the issue of incidental findings. The current paper discusses these issues, and anticipates the future of incidental findings in the context of other neuroimaging tools currently being used to investigate the living brain.

Incidental Findings in CT Colonography: Literature Review and Survey of Current Research Practice
Hassan Siddiki, J. G. Fletcher, Beth McFarland, Nora Dajani, Nicholas Orme, Barbara Koenig, Marguerite Strobel, and Susan M. Wolf
Incidental findings (IFs) of potential medical significance are seen in approximately 5–8 percent of asymptomatic subjects and 16 percent of symptomatic subjects participating in large computed tomography (CT) colonography (CTC) studies, with the incidence varying further by CT acquisition technique. While most CTC research programs have a well-defined plan to detect and disclose IFs, such plans are largely communicated only verbally. Written consent documents should also inform subjects of how IFs of potential medical significance will be detected and reported in CTC research studies.

Incidental Findings in Pediatric Research
Benjamin S. Wilfond and Katherine J. Carpenter
The approach to incidental research findings in children emerges by considering the child-parent relationship and balancing divergent interests and preferences. Incidental findings with clear and proximate clinical importance should be disclosed to both. We recommend that particularly sensitive or private information (e.g., pregnancy or drug use) should be disclosed to the adolescent first, while particularly serious information (e.g., cancer) should first be disclosed to the parent. These approaches allow the researcher to form an alliance with one party prior to engaging the other. However, unlike clinical settings, where there may be presumptive expectations of confidentiality about sharing information within the family, in most research settings it is reasonable to plan to disclose such information to both parties. It is important to communicate this plan during the informed consent process separately to adolescents to avoid enrolling adolescents when sensitive incidental findings such as pregnancy and drug use may be detected. The approach to incidental findings without clear and proximate benefit is challenging. Researchers should plan more limited disclosure of such incidental findings for pediatric participants than for adult participants.

The Future of Incidental Findings: Should They be Viewed as Benefits?
Lisa S. Parker
This paper argues against considering incidental findings (IFs) as potential benefits of research when assessing the social value of proposed research, determining the appropriateness of a study’s risk/benefit ratio, and identifying and disclosing the risks and benefits of participation during informed consent. The possibility of generating IFs should be disclosed during informed consent as neither a risk nor benefit, but as a possible outcome collateral to participation. Whether specific IFs will be disclosed when identified is a separate question whose answer is material to determining whether IFs constitute a risk or a potential indirect benefit of participation. Finally, three types of IF should be distinguished and treated differently during informed consent: those that will be routinely generated (e.g., results of testing to determine study eligibility), those that can reasonably be characterized in terms of their nature and frequency of generation (e.g., misattributed parentage), and those of unpredictable nature and frequency that can be characterized only in general terms. Research protocols should provide a rationale for sharing or not sharing IFs of these three types with participants. Regulatory review of such plans should not, however, be confused with regarding IFs as potential benefits when assessing the study’s risk/benefit ratio or merit.

Institutional Review Board Approaches to the Incidental Findings Problem
Moira A. Keane
Institutional Review Boards (IRBs) are confronted with new challenges in the face of expanding technologies while fulfilling their existing regulatory mandate to ensure that plans are in place to protect subjects and to inform them of risks and benefits of research participation. Existing regulations and guidance do not address the issue of incidental findings (IFs), thus leaving awareness of the issue and the application of ethical principles to IRB judgment alone. In order to assure that researchers are aware of the potential for IFs, IRBs must identify which studies are likely to identify IFs and establish what plans should be put into place prior to study initiation to assure the subjects are appropriately informed of the likelihood of IFs, how IFs will be communicated to subjects, and whether the burden of follow-up falls on the researchers or is the subject’s responsibility.
Independent Articles

356
Research Malpractice and the Issue of Incidental Findings
Alan C. Milstein
Human subject research involving brain imaging is likely to reveal significant incidental findings of abnormal brain morphology. Because of this fact and because of the fiduciary relationship between researcher and subject, board-certified or board-eligible radiologists should review the scans to look for any abnormality, the scans should be conducted in accordance with standard medical practice for reviewing the clinical status of the whole brain, and the informed consent process should disclose the possibility that incidental findings may be revealed and what consequences will follow. In the event such findings are revealed, qualified physicians should explain to the subject the significance of the findings and the alternatives available.

361
The Law of Incidental Findings in Human Subjects Research: Establishing Researchers’ Duties
Susan M. Wolf, Jordan Paradise, and Charlisse Caga-anan
Research technologies can now produce so much information that there is significant potential for incidental findings (IFs). These are findings generated in research that are beyond the aims of the study. Current law and federal regulations offer no direct guidance on how to deal with IFs in research, nor is there adequate professional or institutional guidance. We advocate a defined set of researcher duties based on law and ethics and recommend a pathway to be followed in handling IFs in research. This article traces the underlying ethical and legal theories supporting researcher duties to manage IFs, including duties to develop a plan for management in the research protocol, to discuss the possibility of and management plan for IFs in the informed consent process, and to address, evaluate, and ultimately offer to disclose IFs of potential clinical or reproductive significance to research participants when they arise.

384
Assessing Mandatory HPV Vaccination: Who Should Call the Shots?
Gail Javitt, Deena Berkowitz, and Lawrence O. Gostin
In 2007, many legislatures considered, and two enacted, bills mandating HPV vaccination for young girls as a condition of school attendance. Such mandates raise significant legal, ethical, and social concerns. This paper argues that mandating HPV vaccination for minor females is premature since long-term safety and effectiveness of the vaccine has not been established, HPV does not pose imminent and significant risk of harm to others, a sex specific mandate raises constitutional concerns, and a mandate will burden financially existing government health programs and private physicians. Absent careful consideration and public conversation, HPV mandates may undermine coverage rates for other vaccines.

396
Reactions of Potential Jurors to a Hypothetical Malpractice Suit Alleging Failure to Perform a Prostate-Specific Antigen Test
Michael J. Barry, Pamela H. Wescott, Ellen J. Reifler, Yuchaio Chang, and Benjamin W. Moulton
We conducted focus groups with 47 potential jurors who were presented with different scenarios in a hypothetical malpractice case involving failure to order a PSA test. Better documentation that a patient made an informed decision to decline a PSA test appeared to provide more medical-legal protection for physicians, especially with the use of a decision aid.

403
Premption of Local Smoke-Free Air Ordinances: The Implications of Judicial Opinions for Meeting National Health Objectives
Jean C. O’Connor, Allison MacNeil, Jamie F. Chriqui, Michael Tynan, Hannalori Bates, and Shelby K. S. Eidson
Elimination of state laws that preempt local antismoking ordinances is a national health objective. However, the tobacco industry and its supporters have continued to pursue state-level preemption of local tobacco control ordinances as part of an apparent strategy to avoid the diffusion of grassroots antismoking initiatives. And, an increasing number of challenges to local ordinances by the tobacco industry and persons supported by the tobacco industry are being decided in state supreme courts and courts of appeals. The outcomes of seemingly similar cases about the validity of local smoke-free air ordinances vary significantly by state. This paper examines the common and unique aspects of the decisions and the potential implications of court rulings on preemption for future state tobacco control efforts and achievement of national health objectives around the elimination of preemption. Using a search strategy developed for the Centers for Disease Control and Prevention’s State Tobacco Activities Tracking and Evaluation (STATE) System, cases where a state or federal appellate level court made a finding on the validity of a local smoke-free air ordinance or regulation were identified in 19 states. In contrast to previous studies, we found that cases in approximately half of states were decided for local governments. We also found that across the states, courts were considering similar factors in their decisions including the extent to which: (1) the local government possessed the authority to pass the ordinance, (2) the ordinance conflicted with the state constitution, and (3) state statutes preempt the ordinance.
Symposium articles are solicited by the guest editor for the purposes of creating a comprehensive and definitive collection of articles on a topic relevant to the study of law, medicine and ethics. Each article is peer reviewed.

Independent articles are essays unrelated to the symposium topic, and can cover a wide variety of subjects within the larger medical and legal ethics fields. These articles are peer reviewed.

Columns are written or edited by leaders in their fields and appear in each issue of JLME.

Columns

413
Currents in Contemporary Ethics
Ana S. Iltis, Hisako Matsuo, and Shannon R. DeVader

419
Reviews in Medical Ethics
Ana S. Iltis

425
Recent Developments in Health Law
Harvard Law and Health Care Society

435
Calendar of Events

Next Issue:
Race, Pharmaceuticals, and Medical Technology
A Symposium Guest Edited by David Jones, Gregory M. Dorr, and Anne Pollock