Correspondence

Building-Related Illnesses

To the Editor: As occupational and environmental physicians, we disagree with Menzies and Bourbeau's assessment of building-related illnesses with respect to fungal and bacterial contamination (Nov. 20 issue).[1] In a growing number of investigations we are encountering problems in office workers associated with moisture- and water-related microbial contamination resulting in fungal growth and marked bioaerosol exposure. Building materials made of cellulose are particularly susceptible to fungal growth. The clinically important information with respect to exposure is not necessarily the absolute quantity of colony-forming units, but the fact that fungal species are atypical and that the concentrations are higher than in the outside air, used as a normal reference. In well-documented clinical case evaluations and epidemiologic studies, we and other authors have found clear evidence of an association of mucous membrane irritation, allergy, asthma, and inflammatory effects with allergenic or toxigenic fungal bioaerosol exposures.[2-6]

Medical treatment of fungal building-related illnesses is primarily aimed at symptoms, and the intervention needs to focus on exposure cessation, moisture control, and antifungal measures. The public and occupational health message is to control flooding, water leaks, and other moisture problems in buildings as soon as possible in order to prevent unnecessary building-related illnesses. Improved industrial-hygiene sampling and characterization of bioaerosol exposure will provide better data so that the examining physician can improve the assessment of clinical outcomes and establish a correct diagnosis of building-related illnesses.

ECKARDT JOHANNING, M.D.
Mount Sinai Medical Center
New York, NY 10029-6574

PIERRE L. AUGER, M.D.
Direction de Santé Publique de la Région de Québec
Beauport, QC G1E 7G9, Canada

KARI REIJULA, M.D., PH.D.
Finnish Institute of Occupational Health
FIN 00370 Helsinki, Finland

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To the Editor: In their review of building-related illnesses, Menzies and Bourbeau comprehensively cover physiologic and environmental theories of causation while minimizing the possibility of psychosocial factors. The authors simply state, "The association of symptoms with psychosocial factors does not mean that 'the problem is all in the workers' heads.'" Apparently, concern about stigma continues to make psychosocial causes undesirable candidates in the differential diagnosis.

Few would debate the evidence of discrete causes of specific building-related illnesses. However, nonspecific building-related illnesses remain a conundrum, and some evi-

dence suggests that nonphysiologic factors deserve more serious consideration. Menzies and Bourbeau cite seven studies, involving 21,762 patients, that found an association between psychosocial factors and nonspecific building-related illness, and none that showed the absence of an association (their Table 2). In a landmark study, changes in ventilation failed to ameliorate the symptoms of the sick building syndrome.[1] Three recent reviews suggest an important contributory role of psychosocial factors in some patients.[2-4] Moreover, physical symptoms are exceptionally prevalent in both clinical and community populations and often remain unattributable to a discrete disease.[5] Psychosocial factors should not be narrowly defined as simply depression, anxiety, or other psychiatric disorders. Worries about the meaning of symptoms and increased attention to normal bodily sensations may contribute to the reporting of symptoms in the absence of a specific disease.

This is not to say that nonspecific building-related symptoms are not real or are "all in the head." However, the exhaustive search for occult environmental causes (and the ensuing disruption of the workplace) should not preclude due consideration of nonphysiologic causes. Psychosocial factors merit a fairer hearing.

KURT KROENKE, M.D.
Regenstrief Institute for Health Care
Indianapolis, IN 46202-2859

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The authors reply:

To the Editor: Dr. Kroenke's comments are valid. Psychosocial factors, such as job-related stress[1] or job-related strain,[2] have been associated with a greater prevalence of symptoms in cross-sectional studies of nonspecific building-related illnesses. An index of psychosocial dissatisfaction has been associated with the initial prevalence of symptoms, as well as with the incidence of new symptoms during follow-up.[3] We agree that such psychosocial factors should not be narrowly defined and that they merit serious consideration. Whether job-related stress or strain, which results from high psychosocial demands and low latitude in decisions, causes symptoms or mediates a change in the susceptibility to symptoms requires further investigation.

Johanning and colleagues appear to disagree not with our assessment of the potential importance of microbial contaminants but rather with our assessment of the strength of the current evidence. One of the studies they cite[4] is an uncontrolled case series of chronic fatigue syndrome in which persons reported the relief of symptoms after they had moved out of the contaminated environment or the contaminant had been removed. Another study that Johanning and colleagues cite[5] compared workers in a work area known to be problematic with a nonexposed reference group. The workers in the problematic area reported significantly more symptoms, but objective measures, such as antibody response, did not differ between the two groups. Given the potential for selection and reporting bias in these studies, we would be much more cautious than Johanning and colleagues in interpreting the results as strong epidemiologic evidence. The review the authors cite[6] similarly concluded that the evidence of an association of symptoms with indicators of fungal exposure was strong but that the evidence of an association of symptoms or objective health measures with measured microbial levels was much less consistent.

In our review, we outlined the considerable indirect evidence suggesting that microbial contamination may play a part in the pathogenesis of nonspecific building-related illnesses, and we recommended avoiding or eliminating potential sources of microbial proliferation. Our recommendations are more cautious than those of Johanning and colleagues but are better supported by the current epidemiologic evidence. Given the indirect evidence, as well as the considerable body of experience, it is likely that fungi and other microbes are important. Their role must be more precisely defined to allow more rapid diagnosis and effective intervention, in order to improve the health and well-being of workers in modern nonindustrial environments.

DICK MENZIES, M.D.
JEAN BOURBEAU, M.D.
McGill University
Montreal, QC H3A 1A3, Canada

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Effect of Inhaled Formoterol and Budesonide on Exacerbations of Asthma

To the Editor: Pauwels et al. (Nov. 13 issue)[1] found that in patients with persistent symptoms of asthma despite treatment with inhaled glucocorticoids, the addition of formoterol to budesonide therapy or the use of a higher dose of budesonide may be beneficial. Three features of the study design may have helped increase the size of the effect seen and reduce its generalizability to clinical practice. First, the high rate of exacerbations of asthma in the group given low-dose budesonide is not surprising. In this group, the mean dose of inhaled corticosteroids was similar to that in the other groups (range, 818 to 856 μg daily) before the study. Second, most exacerbations of asthma

were defined in terms of clinical measures. Only 27 percent of severe exacerbations were associated with a fall in the peak expiratory flow rate of more than 30 percent on two successive days. Few clinicians would initiate prednisone therapy for patients who had a peak expiratory flow rate in the range of 70 to 100 percent of the predicted value. The current consensus regarding treatment, although not proved,[2] would be to double the dose of inhaled corticosteroids and try to prevent a more severe exacerbation requiring prednisone. The study design most likely did not allow changes in the maintenance dose of inhaled corticosteroids, and this again would amplify the differences between the groups. Third, the importance of the high-dose induction phase is unclear, and again this would not usually be used in clinical practice.

J. MARK FITZGERALD, M.D.
Vancouver Hospital and Health Sciences Center
Vancouver, BC V5Z 3J5, Canada

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To the Editor: Airway hyperresponsiveness, which is one of the hallmarks of asthma, has been shown to be increased after long-term or regular use of β_2-agonists. This is one of the major reasons for the controversy associated with the regular use of β_2-agonists in the management of asthma. Pauwels et al. mentioned this in their introduction but did not address this issue in their study. The only outcomes monitored were changes in lung functions, extent of symptoms, and the need for rescue medications. Drazen et al.[1] have shown that although regular use of β_2-agonists was not associated with worsening of symptoms, worsening of lung function, or an increased need for rescue medication, it increased bronchial hyperresponsiveness significantly during the treatment period, and this increase was associated with a greater variability in peak flow and an increased requirement for rescue medication when the medications were withdrawn. Pauwels et al. did not include a withdrawal period in their study. How might the patients who were regularly receiving formoterol have fared once this medication was stopped after one year?

SUNDEEP SALVI, M.D.
University of Southampton
Highfield, Southampton SO17 1BJ, United Kingdom

1. Drazen JM, Israel E, Boushey HA, et al. Comparison of regularly scheduled with as-needed use of albuterol in mild asthma. N Engl J Med 1996;335:841-7.

The authors reply:

To the Editor: There are several reasons why we did not measure bronchial responsiveness. Although bronchial hyperresponsiveness is an important characteristic of asthma, it is only an intermediate outcome. Bronchial responsiveness to a direct agonist such as histamine is poorly related to clinical outcomes.[1] There is still debate as to whether bronchial responsiveness to a direct or an indirect agonist is a better correlate of disease activity.[2] Furthermore, most studies have shown a decrease but not a loss of protective activity for bronchoconstrictor agonists during prolonged treatment with long-acting β_2-agonists. We therefore decided that it was more important to look at clinically important outcome measures such as severe and mild exacerbations, symptoms, and use of rescue medication.

FitzGerald suggests that the severe exacerbations, defined in terms of clinical variables, did not justify treatment with oral glucocorticoids. We have compared symptom scores, changes in peak expiratory flow, and use of rescue medication in the days preceding the course of oral glucocorticoids in the patients with severe exacerbations that were identified on the basis of clinical judgment and on the basis of peak-expiratory-flow criteria and found that the changes were similar in both groups. No patients with a peak expiratory flow that was 70 to 100 percent of the predicted value were defined as having a severe exacerbation of asthma, as suggested by FitzGerald. In fact, we added the peak-expiratory-flow criteria to protect patients who were unaware that they had had a significant decrease in their lung function from having a life-threatening exacerbation. Our study therefore confirms that clinical judgment is in most instances an adequate means to identify severe exacerbations of asthma.

We cannot make a definitive statement about the influence of the high-dose induction phase on the long-term effects of the various treatments, since no control group was included. The principal reason for the high-dose induction phase was to exclude patients whose asthma could not be controlled with a very high dose of inhaled budesonide and who were therefore at greater risk when randomly assigned to the low dose. The use of this phase may have contributed to the long-term effect. A study with a similar design showed that the effects of a high-dose induction phase on measures of airway inflammation were maintained for one year of therapy with lower doses of inhaled glucocorticoids.[3] The high-dose induction phase has been recommended in guidelines on the treatment of asthma.[4]

ROMAIN A. PAUWELS, M.D.
University Hospital
B9000 Ghent, Belgium

ANNE E. TATTERSFIELD, M.D.
City Hospital
Nottingham NG5 1PB, United Kingdom

CLAES-GÖRAN LÖFDAHL, M.D.
University Hospital
S-221 85 Lund, Sweden

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The Interleukin-4 Receptor Variant Q576R in Hyper-IgE Syndrome

To the Editor: The hyper-IgE recurrent-infection syndrome (Online Mendelian Inheritance in Man no. 243700), also called Job's syndrome, is a rare immunodeficiency disorder that is characterized by recurrent staphylococcal skin abscesses, pneumonia, and elevated serum IgE concentrations (>2000 IU per milliliter).[1,2] The known involvement of the interleukin-4 pathway in atopy and IgE isotype switching[3] led Hershey et al. (Dec. 11 issue)[4] to search for mutations in the α subunit of the interleukin-4 receptor. All three of their patients with the hyper-IgE syndrome were heterozygous for an interleukin-4 receptor variant allele (Q576R). The Q576R mutation was also found in 10 percent of the interleukin-4 receptor alleles in normal subjects, but it was significantly more common among patients with severe atopic disease.

We investigated the frequency of Q576R in 25 control subjects and 20 unrelated patients with the hyper-IgE syndrome who were followed in collaboration with Drs. John Gallin and Harry Malech at the National Institutes of Health Clinical Center. Q576R was detected in DNA samples by single-strand conformation polymorphism analysis (Fig. 1) and confirmed by sequence analysis (data not shown). Only 4 of 20 patients with the hyper-IgE syndrome had the Q576R mutation (allelic frequency, 10 percent), which was not significantly different from the frequency of 12 percent in the control subjects (6 of 25). In the case of nine of the patients, family members were also studied. In five families Q576R was not detected, and in three families an unaffected parent was heterozygous for the mutation but did not transmit this variant allele to the affected child. In one family (Fig. 1), the healthy, nonatopic mother (Subject I-1) was homozygous for Q576R and her three children were heterozygous for the mutation, but only one child (Subject 20) had the hyper-IgE syndrome.

All the patients in our cohort had elevated serum IgE concentrations (Fig. 1). If Q576R predisposes persons to atopy, as suggested by Hershey et al., one might expect patients with the hyper-IgE syndrome and the Q576R mutation to have higher IgE concentrations. However, it is clear from Figure 1 that this was not the case.

It is possible that other mutations in the interleukin-4 receptor gene or mutations in a nearby gene could be

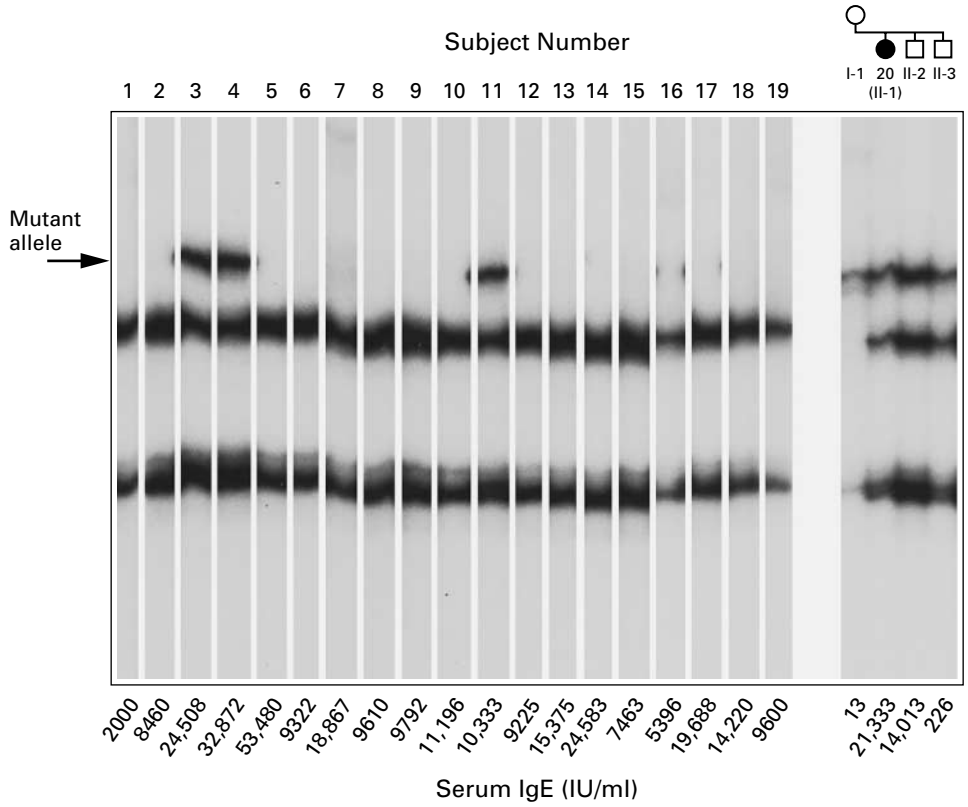

Figure 1. Single-Strand Conformation Polymorphism Analysis of the Interleukin-4 Receptor Gene in 20 Unrelated Patients with the Hyper-IgE Syndrome and Three Relatives of Subject 20.

The Q576R variant was detected as a band migrating above the two bands produced by the wild-type allele.[3] Subject I-1, who was homozygous for Q576R, has only the variant band. The highest measured serum IgE values are indicated below each lane. Circles denote female family members, squares male family members, and the solid symbol a family member with the hyper-IgE syndrome.

causally associated with the hyper-IgE syndrome. To evaluate whether the syndrome is genetically linked to the interleukin-4 receptor gene on chromosome 16, seven families with autosomal dominant hyper-IgE syndrome were genotyped with polymorphic markers surrounding the interleukin-4 receptor locus. After conducting multiple analyses using programs from the Fastlink package,[5] we concluded that the interleukin-4 receptor gene is not linked to the hyper-IgE syndrome. For example, four-point Linkmap analysis with the ordered markers D16S769, D16S753, and ATA55A11 (the outer two are known to flank the interleukin-4 receptor gene) gave a maximal lod score of less than −2.5 for the location of the hyper-IgE syndrome between the first two markers, and of less than −5.0 for its location between the second two markers.

Our data agree with those of Hershey et al. in suggesting that the Q576R variant occurs in about 10 percent of interleukin-4 receptor gene alleles in healthy persons. However, our analysis of a large cohort of patients with the hyper-IgE syndrome not only showed no increase in the frequency of Q576R as compared with that in normal subjects, but also ruled out the possibility of genetic linkage between the syndrome and the interleukin-4 receptor locus.

BODO GRIMBACHER, M.D.
National Human Genome Research Institute

STEVEN M. HOLLAND, M.D.
National Institute for Allergy and Infectious Diseases

JENNIFER M. PUCK, M.D.
National Human Genome Research Institute
Bethesda, MD 20892

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The authors reply:

To the Editor: Grimbacher and colleagues analyzed the frequency of the interleukin-4 receptor R576 allele in 20 patients with the hyper-IgE syndrome and found no increase in the frequency of this allele in patients relative to that in healthy control subjects. Our identification of nonatopic subjects who are heterozygous and even homozygous for the R576 allele effectively ruled it out as a cause of hyper-IgE syndrome, although its presence in all three patients with the syndrome whom we examined suggested a contribution of this allele to the pathogenesis of the syndrome. The data of Grimbacher et al. suggest otherwise, and it remains to be determined whether the presence of the R576 allele in all three of our patients was a chance occurrence or reflective of differences in the patients' characteristics (e.g., our patients had sporadic cases of disease rather than familial forms).

The failure of Grimbacher et al. to find a correlation between IgE levels in their patients and the presence of the R576 allele is not surprising. IgE levels are extremely elevated in this syndrome, presumably because of a distinct primary genetic defect, which may obscure a contribution by atopy-susceptibility alleles. The association of IL-4R alleles with atopy has been established by another recent study.[1] The contribution of these alleles to atopic diseases remains the subject of ongoing studies.

GURJIT K. KHURANA HERSHEY, M.D.
Children's Hospital Medical Center
Cincinnati, OH 45229

TALAL A. CHATILA, M.D.
Washington University School of Medicine
St. Louis, MO 63110

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Improvement in CD4+ Cell Counts despite Persistently Detectable HIV Load

To the Editor: A major goal of antiretroviral therapy for human immunodeficiency virus (HIV) infection should be to keep the viral load undetectable or at least suppressed as fully as possible.[1,2] For patients with detectable viral loads, changes in medication have been advocated on the basis of studies demonstrating that viral load is a surrogate marker for the clinical progression of HIV infection. However, patients who have persistently elevated viral loads despite treatment with highly active antiretroviral agents (generally a protease inhibitor and two reverse-transcriptase inhibitors) have few therapeutic options. There are a limited number of drugs available, and medication cross-resistance, antagonism, and side effects are matters of concern.[3]

I describe two patients with AIDS treated with salvage regimens of antiretroviral therapy who had dramatic increases in CD4+ T-cell counts and improvement in clinical status despite the presence of persistently elevated HIV viral loads. Patient 1 was a 35-year-old woman who presented in 1992 with eosinophilic folliculitis and a CD4+ T-cell count of 40 per microliter. Patient 2 was a 38-year-old man who presented in 1993 with cryptococcal meningitis and a CD4+ T-cell count of 30 per microliter. The course of both patients was complicated by *Pneumocystis carinii* pneumonia, recurrent herpes, and severely depressed CD4+ T-cell counts despite treatment with zidovudine, didanosine, stavudine, and lamivudine, alone or in combination. Both patients began a regimen of zidovudine, lamivudine, and indinavir but had elevated viral loads and persistently low CD4+ T-cell counts (Fig. 1). Patient 1 was switched to a regimen of nelfinavir, didanosine, lamivudine, and stavudine in October 1996. Patient 2 was switched to a regimen of ritonavir, saquinavir, didanosine, and stavudine in March 1997. Compliance with medication, as indicated by pharmacy records and patient reporting, was excellent. At the most recent assessment, CD4+

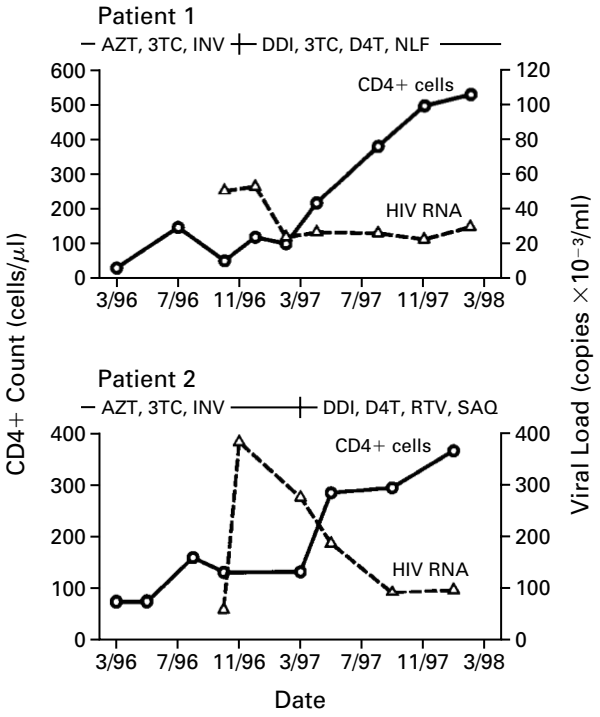

Figure 1. Changes in Peripheral-Blood CD4+ T-Cell Counts and HIV Viral Load in Patients 1 and 2.

CD4+ cells were enumerated by flow cytometry, and the viral load was quantified by a branched-chain DNA assay. The medications that the patients received are indicated. AZT denotes zidovudine, 3TC lamivudine, INV indinavir, DDI didanosine, D4T stavudine, NLF nelfinavir, RTV ritonavir, and SAQ saquinavir.

T-cell counts in Patients 1 and 2 had risen to 528 and 375 cells per microliter, respectively, despite only modest falls in the viral load of less than 1 log to 46,110 and 92,850 copies per milliliter, respectively. Neither patient has had further opportunistic infections, and both have returned to work or school.

It remains to be seen how long the patients' responses will be maintained. Moreover, the extent to which the elevations in CD4+ T-cell counts reflect other variables pertaining to immunologic reconstitution is unknown.[4] Although controlled trials are needed to determine the optimal salvage regimens in patients with elevated viral loads despite treatment with highly active antiretroviral agents, dramatic increases in the CD4+ T-cell count may occur despite the presence of relatively large viral loads. It may be premature for one to change antiretroviral therapy solely on the finding of a detectable viral load, especially in patients for whom therapeutic options are limited.

STUART M. LEVITZ, M.D.
Boston Medical Center
Boston, MA 02118

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Performance of Two Rapid Tests for *Plasmodium falciparum* Malaria in Patients with Rheumatoid Factors

To the Editor: Light-microscopical examination of blood smears is the cornerstone of the diagnosis of malaria. Recently, two rapid immunodiagnostic tests, the ParaSight F test (Becton Dickinson, Cockeysville, Md.)[1] and the ICT Malaria Pf test (ICT Diagnostics, Balgowlah, Australia),[2] were developed for the diagnosis of *Plasmodium falciparum* infection. Both are immunochromatographic tests based on the detection of circulating *P. falciparum* histidine-rich protein-2 antigen in whole blood.[3] Recently, Laferl [not Laferi, as published] et al., in a letter to the editor,[4] and Bartoloni et al.[5] reported false positive results of ParaSight F tests in 67 percent and 68 percent of patients with rheumatoid factors, respectively. Since the production of rheumatoid factors occurs commonly in patients with a variety of infectious and noninfectious diseases, as well as in 5 percent of the healthy people, caution was urged in the use of the ParaSight F test.

With the aim of determining whether the ICT Malaria Pf test presents the same limitation as the ParaSight F test, we performed both tests on whole-blood samples obtained from 23 patients with rheumatoid factors and thick blood films that were negative for malaria. The ParaSight F test was positive in 19 patients (83 percent), whereas the ICT Malaria Pf test had no false positive results. The different performance of the two rapid tests, both based on the capture of histidine-rich protein-2 antigen, is probably due to the fact that the antibody used in the ICT Malaria Pf test is different from that used in the ParaSight F test.

ALESSANDRO BARTOLONI, M.D.
Università di Firenze
50121 Florence, Italy

GUIDO SABATINELLI, M.D.
Istituto Superiore di Sanità
00161 Rome, Italy

MAURIZIO BENUCCI, M.D.
Azienda Sanitaria Firenze
50122 Florence, Italy

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Privacy and Medical-Records Research

To the Editor: In his Sounding Board article (Nov. 13 issue),[1] Melton ignores the very reasons he lists for why many people support legislation that requires specific consent on the part of patients for access to medical records by medical researchers. Even more disturbing is his incorrect assertion that there is an absence of documented abuses related to approved research projects. Abuses of genetic testing have been amply documented.[2]

Researchers, members of institutional review boards (IRBs), and health advocacy groups have acknowledged the fact that we can no longer guarantee privacy and confidentiality in an age of electronic medical records.[3] The logistic hurdles associated with medical- and research-record gatekeeping make errors inevitable. Because of this reality, it is more important than ever to ensure the use of informed-consent procedures that convey this potential loss of privacy as one of the risks of research. And because the misuse of genetic information could be especially damaging, we need public policies that specifically address genetics research.

Although there are greater costs associated with recontacting individual subjects and gaining renewed consent for any additional research uses of tissue samples or medical records, this is a price we must be willing to pay. Much valuable research will still be able to go forward, and society will not be harmed in any meaningful fashion.

As we move to create better public policies in this area, we must retain our tradition of protecting human subjects and their right to consent or to refuse to consent before any use is made of their medical information for research. As a staff lawyer with the Office for Protection from Research Risks recently stated: "If there's any possible way that you can go back to one identifiable human being, then you have to provide the twin protection of Institutional Review Board review *and* informed consent. . . . It may be difficult in the context of tissue banking, but at the moment, that is the standard."[4]

As long as we have no national health plan with guaranteed access to health and medical care, and thus the release of research-related information can result in the loss of access to services, the need to guarantee confidentiality will remain essential.

JUDY NORSIGIAN
SALLY WHELAN
Boston Women's Health Book Collective
Somerville, MA 02144

PAUL BILLINGS, M.D., PH.D.
Council for Responsible Genetics
Cambridge, MA 02140

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To the Editor: In the belief that society can only benefit from epidemiologic studies, Melton proposes that IRBs make all decisions concerning the release of medical records to researchers. He assumes these boards will do little or nothing to impede the kinds of studies that have become possible, or soon will, as a result of the computerization of medical records and the creation of a national system of electronically linked records.

Others are less sanguine than he. The Privacy Commissioner of Canada has written in his recent annual report: "Easy as it is to rationalize data gathering as beneficial for the individual and society, the information might not be used for benevolent purposes. The collection of medical data can slide imperceptibly from health care to medical supervision to lifestyle surveillance and, ultimately, to a more generalized form of surveillance by the state."[1] By Melton's own account, Mayo's patients are concerned about such dangers and about the migration of their records without their knowledge.

As Edgar and Rothman have noted, the current IRB system is not well designed to protect patients' rights and patients' interests.[2] In a recent report to the Department of Health and Human Services, Lowrance questions whether IRBs are "able and willing" to "become more deeply engaged with the privacy and confidentiality aspects of subject protection than they have been."[3] In recent years, a number of commentators have argued that the IRB system needs restructuring, a view with which I concur.[2,4]

Some of the issues raised by Melton, including those pertaining to making medical records anonymous, are discussed more fully in a group of papers from a 1997 symposium on medical-record confidentiality and data collection.[5] Much more reflection and debate are needed if we are to design satisfactory policies with respect to the handling of personal medical information.

BEVERLY WOODWARD, PH.D.
Brandeis University
Waltham, MA 02254

1. Phillips B. Privacy Commissioner of Canada, 1996–97 annual report. Ottawa: Privacy Commissioner of Canada, 1997. (Or see http://infoweb.magi.com/uprivcan/annrep/english/table.html).
2. Edgar H, Rothman DJ. The institutional review board and beyond: future challenges to the ethics of human experimentation. Milbank Q 1995; 73:489-506.
3. Lowrance WW. Privacy and health research: a report to the U.S. Secretary of Health and Human Services. Washington, D.C.: Department of Health and Human Services, May 1997.
4. Katz J. Do we need another advisory commission on human experimentation? Hastings Cent Rep 1995;25(1):29-31.
5. Symposium: medical confidentiality & research. J Law Med Ethics 1997;25(2&3):85-138.

To the Editor: Melton states that the Rochester Epidemiology Project, begun 30 years ago, was possible because state law allowed researchers access to medical records. Not so. Melton's quotation of the law supporting his assertion actually comes from a 1992 statute.[1] Thirty years ago, Minnesota statutes were silent on the confidentiality of patients' records, but in 1976, a new state law granted that patients of health care facilities "shall be assured confidential treatment of their personal and medical records, and may approve or refuse their release to any individual outside the facility."[2] Melton's article fails to clarify under

what statutory authority this sharing of identified patient records in the Rochester Project occurred.

Melton also neglects to mention that because of lobbying by the Mayo Clinic in 1996 and 1997, the new consent requirement pertains only to records generated on or after January 1, 1997, and only to releases to external researchers.[3]

In addition, Mayo supported the full release of medical records to external researchers without consent after "reasonable efforts" had been made to obtain consent. The final language of the 1997 law authorizes the release of records without the patient's consent if the patient has not responded within 60 days after the second request for authorization is mailed.[4] Therefore, because of Mayo's lobbying efforts, many medical records in Minnesota can be used by researchers without the patients' consent.

It is not comforting to patients that a physician would advocate either "constructed consent" (majority-conferred obligation) or decisions by IRBs as methods to bypass the patients' concern about privacy.

TWILA BRASE, R.N., P.H.N.
Citizens for Choice in Health Care
St. Paul, MN 55104

1. 1992 Minnesota Statutes, Chapter 144.335, p. 1159. St. Paul: State of Minnesota, 1992.
2. 1976 Minnesota Statutes, Chapter 144.651, No. 15, p. 2158. St. Paul: State of Minnesota, 1976.
3. 1997 Minnesota Statutes, Chapter 144.335. St. Paul: State of Minnesota, 1997.
4. 1997 Laws of Minnesota, Chapter 144.335, p. 3199. St. Paul: State of Minnesota, 1997.

To the Editor: Melton describes an environment at the Mayo Clinic in which there has been a long tradition of researchers' using patients' records in an open manner. But until recently, there existed natural limits that protected patients' privacy; technology now erodes these limits at an alarming rate. For example, the physical labor previously involved in manually reviewing records provided an economic boundary that restricted the dissemination of person-specific data. Researchers were once physically limited to the records facility itself to gather needed information, but in a globally networked society it is possible for a researcher located anywhere in the world to gain immediate electronic access to patients' files. Today's technology does pose unparalleled threats to patients' privacy, but today's technology also offers solutions.

Many details about our lives are documented on computers, and when this information is linked together, the resulting profiles can identify individual persons as accurately as fingerprints, even when the information contains no explicit identifiers such as name and address.[1,2] The increase in the availability of detailed data, as well as inexpensive technology to process it, is having a dramatic impact on research. Having more clinical information available will probably lead to more epidemiologic studies, especially since it can help ensure the validity and generalizability of specific studies. Most likely this will result in a dramatic increase in the number of records released.

A Harris–Equifax poll[3] implies that the public would be willing to share information for research, provided researchers and others could not identify any person included in the released data. Melton seems intent on complete access to identifiable information. But he could have conducted his hip-fracture study without identifiable data. All he needed was age, sex, diagnosis (i.e., hip fracture), and date of diagnosis for each stratum. Generalization, suppression, and anonymous linking are among the various computational techniques currently available.[1,4] These techniques are intended to release the minimal data needed in the most general format possible, ensuring confidentiality, on the one hand, and usefulness, on the other. In cases in which identifying information is required, these techniques reduce unnecessary risk.

Fear and concern about privacy in the computer age are justified, but the options are not limited to past practices; a new spectrum of solutions is emerging. If researchers want patients to release sensitive data, they should be willing to use technology that ensures patients' privacy within the released data.

LATANYA SWEENEY, S.M.
Massachusetts Institute of Technology
Cambridge, MA 02139

1. Sweeney L. Weaving technology and policy together to maintain confidentiality. J Law Med Ethics 1997;25(2&3):98-110.
2. A guide to state-level ambulatory care data collection activities. Falls Church, Va.: National Association of Health Data Organizations, 1996.
3. Louis Harris and Associates. The Equifax-Harris consumer privacy survey. Atlanta: Equifax, 1994.
4. Sweeney L. Datafly: a system for providing anonymity in medical data. In: Lin T, Qian S, eds. Database security XI: status and prospects. New York: IFIP/IEEE/Chapman & Hall, 1998:356-81.

Dr. Melton replies:

To the Editor: Norsigian and colleagues distort my attempt to report on testimony to the National Committee on Vital and Health Statistics indicating that there were no documented abuses specifically related to approved research projects involving medical-records review,[1] the topic of my article. There is legitimate widespread concern about possible abuses of genetic information by insurers and employers, as emphasized by our focus group, whose members also worried about encroaching governmental surveillance and recognized greater risks associated with electronic data. However, informed consent does not solve any of these problems, and my recommendation was that regulations be focused more directly on the potential abuses of medical data.

As Brase points out, there were no restrictions on the release of medical data 30 years ago, although data for the Rochester Epidemiology Project were obtained under custodial agreements with the other providers. When restrictions were imposed, Minnesota legislators provided the exception for epidemiologic studies that I described. The new Minnesota law governing the external release of medical data took effect on January 1, 1997. "External" release was subsequently clarified to be consistent with Minnesota law relating to private data generally. At the Mayo Clinic, however, research access to medical records is denied even within the institution when patients have refused the research authorization.

Investigators in epidemiologic studies would have no interest in patients' identities were it not for the need to link events with their outcomes and to distinguish unique pa-

tients cared for by multiple providers. It is obvious that even a patient with a discrete event like hip fracture might be seen at an emergency room, a hospital, an extended care facility, and an outpatient clinic, all of which might report data on the same patient independently. Sweeney's comments in this regard indicate little experience in the conduct of such studies, where these problems have been amply documented.

Ultimately, it seems futile to debate these issues philosophically. In my opinion, the issue is not whether privacy is intruded upon or whether research is hampered but, instead, whether patients are being helped or harmed. It is naive to believe that no unintended adverse consequences will attend more restricted access to medical records for research, and it is irresponsible to ignore them as Norsigian and her colleagues do. Although the issues are complicated, there needs to be a balancing of the concern for privacy with patients' need for accurate data on outcomes and with society's need for information about the causes of disease and the effectiveness of medical care.

L. Joseph Melton III, M.D.
Mayo Clinic and Foundation
Rochester, MN 55905

1. Health privacy and confidentiality recommendations. Washington, D.C.: National Committee on Vital and Health Statistics, June 25, 1997.

Organophosphorus Poisoning in the Kashmir Valley, 1994 to 1997

To the Editor: An estimated 1 million serious accidental poisonings and 2 million suicide attempts involving organophosphorus compounds occur each year worldwide.[1] India ranks second in Asia in annual pesticide consumption.[2]

We prospectively studied 164 patients (age range, 14 to 58 years) from different districts of the Kashmir valley, who were seen in the casualty department of SMHS Hospital, Srinagar, India, with a history of exposure to organophosphorus compounds between April 1994 and July 1997 (Table 1). Most of the patients (74.4 percent) had consumed these agents to attempt suicide. Phosphamidon was the agent most frequently ingested. Two thirds of the patients lived in districts with large areas of apple orchards. About 90 percent had consumed 5 to 50 ml of various agents; the rest had taken more. About 80 percent were seen within two to four hours. Thirty-eight patients (23.2 percent) initially denied consumption of these agents, though they had clinical features of poisoning. The precipitation factors in the suicide attempts were strained social relations (in 30.3 percent, mainly caused by the death of a close relative in the current political unrest), failure in examinations (20.5 percent), unemployment (18.0 percent), failure in love affairs (14.0 percent), and others (17.1 percent). Nine patients died, and 155 recovered.

Table 1. Characteristics of 164 Patients with Organophosphorus Poisoning.

Characteristic	No. of Patients (%)
Sex	
Male	50 (30.5)
Female	114 (69.5)
Age — (yr)	
14 to <25	55 (33.5)
25 to <50	86 (52.4)
≥50	23 (14.0)
Mode of poisoning	
Suicide attempt	122 (74.4)
Accident	42 (25.6)
Agent	
Phosphamidon	91 (55.5)
Malathion	20 (12.2)
Dichlorvos	14 (8.5)
Tic-20	17 (10.4)
Unknown	22 (13.4)
Means of exposure	
Ingestion	140 (85.4)
Inhalation	7 (4.3)
Topical application	17 (10.4)
Outcome	
Recovery	155 (94.5)
Death	9 (5.5)

Organophosphorus compounds are commonly used as insecticides, pesticides, and fungicides in Kashmir. Since 1990, political unrest has caused great suffering and mental trauma among the residents of Kashmir. The high incidence of organophosphorus poisoning with suicidal intent is but one of many manifestations of the tragic consequences of this unrest.

G.M. Malik, M.D.
M. Mubarik, M.D.
G.J. Romshoo, M.D.
Government Medical College
Srinagar, 190010, Kashmir, India

1. Jayaratnam J. Acute pesticide poisoning: a major global health problem. World Healthstate Q 1990;43:139-44.
2. O'Malley M. Clinical evaluation of pesticide exposure and poisonings. Lancet 1997;349:1161-6.