CORRESPONDENCE

Letters to the Editor are welcomed and will be published, if found suitable, as space permits. They must be signed, typewritten in double spacing (including references), submitted in duplicate, must not exceed 1½ pages in length and will be subject to editing and possible abridgment. To be considered for publication, letters referring to a recent Journal article should be received within six weeks of the article's publication date.

THERAPY OF ADVANCED OVARIAN CARCINOMA

To the Editor: Several groups of investigators have presented evidence that multiple-agent chemotherapy is superior to single-alkylating-agent treatment of patients with epithelial ovarian cancer. However, statistically significant improved response rates in prospective randomized studies have been difficult to demonstrate. A recent report in the Journal by Young et al.1 purports to provide statistically significant data favoring multiple-agent chemotherapy in this disease.

Most of the statistically significant results (i.e., P<0.05) obtained by the authors are critically dependent on the use of the so-called “one-tailed” (one-sided) test. This method is valid only if before the data were examined, one could be certain that the new treatment would be at least as good as the old treatment.2 Even if such certainty were justified, which it certainly was not, it has been suggested that the use of the one-sided test is unusual for comparison of a new treatment with an old treatment, for one should still retain the contingency that the results with the new treatment may be worse.3

In a similar study4 we reported response-rate differences between melphalan (L-PAM) and AICFUCY (actinomycin-D, 5-fluorouracil and cyclophosphamide) that favored the latter with a P value = 0.07 (two-sided test). Use of the one-sided test would have yielded a p = 0.035.

Also, as pointed out by the authors, the group treated with melphalan had a much higher percentage of patients with lower histologic grade. Patients with tumors of lower histologic grade tend to survive longer, but probably are less responsive to chemotherapy.4 To show an improved median duration of survival in the group treated with hexamethylmelamine, cyclophosphamide, methotrexate and 5-fluorouracil (Hexa-CAF), the authors “adjusted for grade imbalance” by analyzing the high-grade and low-grade tumors separately. No such adjustment for grade imbalance was made in the tumor-response analyses.

The results would have been more revealing and informative with a “two-sided” comparison of response to the treatments according to grade.

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To the Editor: Young and his co-workers are to be complimented on their well designed and well executed study in the December 7, 1978, issue of the Journal. This work sounds a hopeful note for patients with advanced epithelial carcinoma.

It should be noted that the claimed superiority of the combination chemotherapy over melphalan therapy is based on two observations. First of all, the overall response rate (i.e., complete plus partial) is higher in combination-treated patients, resulting in a longer median survival. However, the difference in complete response rates (33 per cent vs. 16 per cent) statistically was not significantly better, and as the authors point out, “the induction of a complete remission...has the most important effect on survival” (that is, only patients who achieve a complete remission have the potential for being cured of their disease). Thus, this study of Young et al. does not yet promise a higher cure rate for patients with ovarian cancer treated with the combination than that obtainable with melphalan. Data presented by these authors at the 14th meeting of the American Society of Clinical Oncology in April, 1978, showed that the actuarial survival curve for the 41 patients on combination chemotherapy was not significantly better than that for the 39 treated with melphalan (i.e., approximately 30 vs. 20 per cent at four years). It would have been pertinent to have included these data in their article in the Journal, particularly since the toxicity of the combination is so much greater than that of melphalan.

Secondly, the survival of patients with well-differentiated tumors was better for patients treated with the combination than for those treated with melphalan. This observation is based on an actuarial survival curve of seven patients only in the former group. Moreover, from the text it is apparent that only four of the seven patients could have achieved complete remission (since nine of 13 complete remissions with combination chemotherapy were in patients with Grade 3 or 4 tumors). The comparison, in my opinion, would have been more appropriate if it had been made between disease-free survival rates rather than survival because the difference was only seen in the slower growing, well differentiated tumors. Unfortunately, the majority of patients with an advanced stage of disease will have poorly differentiated tumors.

One further comment should be made. It would have been useful for comparison with other populations with Stage III and IV carcinoma of the ovary to have known how many of the patients in this series were made eligible for the study as a result of the restaging procedures carried out after the initial operation.

These criticisms notwithstanding, the manner of execution of the study and presentation of the data by these authors are to be lauded, for they provide much valuable information for those involved in the study of this disease.

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To the Editor: Young and his colleagues report improved results with combination chemotherapy as compared to melphalan in the treatment of advanced ovarian carcinoma.

For the past 10 years we have been in a study to test the induction capabilities and the toxicity of the combination regimen. The schedule and doses were similar to those developed by Young et al. A crucial divergence from the trial of the National Cancer Institute is that we also admitted patients to our trial who had previously had extensive radiotherapy or chemotherapy with chlorambucil. In 14 previously untreated patients who received the combination regimen the response rate did not differ greatly from that of Young and his associates, but in the previously treated patients the response was poor; only three out of 13 responded, no complete remissions were obtained, and the hematologic toxicity was more prominent. In six of the patients severe leukopenia developed, and only 63 per cent of the calculated dose could be given in the first cycle. Because of this failure of the regimen as a second-line chemotherapy, we no longer use the combination in pretreated patients.

The report by Young and his co-workers gives no information about previously treated patients, and we wonder whether they have any experience with the combination regimen in such patients.

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The above letters were referred to the authors of the article in question, who offer the following reply:

To the Editor: The letter of Barlow and Blumenson comments on the statistical analysis used in the comparison of response rates. The distribution of objective responses for the combination regimen is significantly better than that for melphalan at a two-sided level of P<0.05, if one takes into account that the remission is better than a partial response when the Wilcoxon rank test is used. The comparison of survival between the two groups resulted in a one-sided significance level of P<0.02, or a two-sided level of P<0.04. When a new therapy is compared to a standard agent, a one-sided statistical significance level is the probability that results as extreme as those obtained in favor of the new treatment will be found by chance alone if the therapies are actually equivalent. The point of view that only two-sided significance levels should be presented is based upon a model in which "statistical significance" is a dichotomous verdict rather than a tool for interpreting results.

Barlow and Blumenson refer to an earlier study reporting a borderline difference in overall response rates between the combination used by them and melphalan.\(^1\) However, in that paper the mean and median durations of remission were the same (nine months), and there was no difference in survival between the two regimens. In fact, the authors state, "the full potential of chemotherapy alone was not evaluable in the patients responding to chemotherapy." The survival difference in our study and the evaluation of chemotherapy alone stands in contrast to their observations in the cited study. The survival benefit seen with our combination regimen occurred in spite of the grade imbalance, which would have favored longer survival with melphalan. We did not adjust our response-rate analysis for grade because our data fail to show a difference in response rates according to histologic grade although grade does influence survival. Degree of response is better (two-sided level of P<0.035) for the combination whether or not one adjusts for grade.

We wish to clarify for Dr. Bush that the significance level P<0.02 (<0.04 two-sided) in Figure 1 of our paper corresponds to the survival comparison of all graded combination-treated patients to all graded melphalan-treated patients, not just for Grade 1 to 2 patients. We analyzed for the grade imbalance in this overall comparison, using the nonparametric Mantel-Haenszel test.\(^2\) Ignoring an imbalance of a truly important measured prognostic factor results in an erroneous conclusion. Dr. Bush's request for true disease-free survival rates would be difficult if not impossible to fulfill without repeated laparotomies. Presumably, this limitation explains why Dr. Bush has not reported his data in that manner either.\(^3\) How ever, the complete response rate to the combination regimen for patients with minimal disease was significantly better than to melphalan (two-sided level of P<0.005), suggesting that long-term disease-free survival will be better for the combination-treated group; 14 of 79 patients (18 per cent) were made eligible for the study as a result of staging procedures carried out after the initial operations. Finally, we are pleased to see the confirmation of our results in untreated patients by Drs. Neijt and Pinedo.\(^4\) We have treated 10 previously treated patients with the combination regimen and have seen only two partial responses. Toxicity in this group is high, and we would not, nor did we, recommend the regimen for previously treated patients.

LITHIUM THERAPY OF APLASTIC ANEMIA

To the Editor: Barrett et al. reported the use of lithium carbonate in two patients with aplastic anemia.\(^1\) One patient had a transient response to lithium, and the second had a sustained improvement in the neutrophil count. An additional patient with aplastic anemia, described below, had a striking improvement in all hematologic findings after lithium carbonate therapy.

This 58-year-old woman was first studied in 1975, when cutaneous purpura was noted. The hemoglobin concentration, white-cell count and differential were normal, but the platelet count was 21,000 per cubic millimeter. A bone-marrow aspirate was normal except for the presence of decreased numbers of megakaryocytes, and the patient was treated with fluoxymesterone, 30 mg daily. She did not improve, and 18 months later, anemia was noted along with mild neutropenia. A needle biopsy of the iliac crest revealed hypoplasia affecting all cell lines. Etocholanolone and prednisolone were given for three months, without any response. By October, 1978, she was receiving transfusions of packed red cells at biweekly intervals, and the platelet count was regularly less than 4000 per cubic millimeter. Vincristine and prednisone were given, without improvement. She became overtly psychotic and was hospitalized on November 4, 1978. The hemoglobin on admission was 7.4 g per deciliter, the white-cell count 2100 per cubic millimeter, with 27 per cent neutrophils, and the platelet count 1000 per cubic millimeter. Over the succeeding four weeks, she required 7 units of packed red cells to maintain her hemoglobin concentration. On December 4, 1978, lithium carbonate, 300 mg three times a day, was started for its psychotropic effects, and she continued to be severely pancytopenic until December 19, when the hemoglobin was noted to have stabilized at 10 g per deciliter; the white-cell count was 5400 per cubic millimeter, with 73 per cent neutrophils, and the platelet count 87,000 per cubic millimeter. The lithium level during this period ranged between 0.45 and 1.3 mg per liter. The improvements in the blood counts persisted, and transfusions were no longer required. She was discharged from the hospital on January 3, 1979, when the hemoglobin concentration was 11.6 g per deciliter, the white-cell count 5100 per cubic millimeter, and the platelet count 134,000 per cubic millimeter.

This patient with severe idiopathic aplastic anemia was treated with many modalities of therapy, but remained severely pancytopenic until two weeks after the initiation of lithium carbonate and subsequently sustained a remarkable improvement in her blood counts. There is evidence that lithium carbonate increases colony-stimulating activity,\(^2\) and this may be the mechanism of its activity. In view of the seriousness of aplastic anemia and its very poor prognosis, the response to lithium in this case suggests that a wider trial of this agent in aplastic anemia is warranted.

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THROMBOCYTOPENIC REACTION TO ASPIRIN AND ACETAMINOPHEN

To the Editor: Acetaminophen (marketed under such brand names as Tylenol, Datriil, Tempra and Liquiprin) is widely advertised and used as an over-the-counter analgesic for patients who cannot take aspirin. Although generally substituted for aspirin because of the latter’s tendency to erode gastric mucosa, acetaminophen has also been used when hypersensitivity to aspirin—an unusual phenomenon—occurs. Although cross-sensitivity between the two drugs must be extremely rare, we report here a case in which severe symptomatic thrombocytopenia seems to have been produced in a young man by both drugs.

In 1972, when he was 29 years old, this patient noted hemoptysis and bruising of his arms and legs, with a huge hematoma on his hip, all without noteworthy trauma. He had been taking aspirin, prophyxedrine (Dristan) and an aspirin-antacid mixture (Bufferin) for a cold for about two weeks before the onset of this bruising. He was in the habit of taking perhaps four aspirin tablets weekly for headaches—attributed to the tension of his work—over the previous six years.

His physician admitted him to a hospital, where, except for the bruises, physical examination was within normal limits, with a blood pressure of 120/70 mm Hg. He was found to have 8500 platelets per cubic millimeter on admission, and a reduced number of megakaryocytes in the bone marrow. Aspirin was discontinued, and he was given a platelet transfusion and 40 mg of prednisone a day. One week later his platelet count was 230,000 per cubic millimeter. On discharge, he was told never to take aspirin or antihistamines.

Except for continued headaches and occasional colds his health was excellent up to the present illness. He took, over these years, an average of 1 g of acetaminophen per week. He was seen for a routine checkup on December 5, 1978, when his blood pressure was 118/80 mm Hg and physical examination gave entirely normal results. The hemoglobin was 14 g per deciliter, and the white-cell count 7000, with a normal differential and adequate platelets on smear; the sedimentation rate was 6 mm per hour; urinalysis, SMA-12 and SMA-6 all gave normal results.

On December 24, he noted multiple hematomas and petechiae on his legs. The platelet count was 30,000 on December 27 and, when seen on the next day, he reported that he had only been taking his regular acetaminophen and a multivitamin preparation. Physical examination gave entirely normal results again except for a dozen hematomas, 2 to 6 cm, over his body and numerous petechiae on the lower legs and beneath the blood-pressure cuff. Acetaminophen was discontinued, as was the multivitamin, and he was given 20 mg of prednisone on that day and 30 mg per day for the next 12 days. After reaching a nadir of 6000 per cubic millimeter on December 29, the platelet count rose progressively thereafter, and reached a level of 170,000 per cubic millimeter on January 9.

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STUDIES OF THE FLUORESCENCE OF FIBROBLASTS FROM HUNTINGTON’S DISEASE: EVIDENCE OF A MEMBRANE ABNORMALITY

To the Editor: Tissue cultures of skin fibroblasts from patients with Huntington’s disease were initially reported to show reduced growth, but subsequent reports demonstrated the fibroblasts to grow to a higher confluent density than was observed in normal persons. This difference may be related to a generalized membrane defect in Huntington’s disease including red cells, neurons, glia and fibroblasts. We have employed fluorescent spectroscopy and microscopy to study possible changes in membrane dynamics in culture between living normal fibroblasts and those from patients with Huntington’s disease. We compared three diseased skin-fibroblast cell lines with three control fibroblast lines matched for age (48 for Huntington’s disease and controls), sex and passage number. Cells were grown to confluency in Dulbecco modified Eagles’ medium with 20 per cent fetal-calf serum (Irvine Scientific) on cover slips designed to fit the diagonal of a 10-mm-square cuvette. The cover slips were stained with a 1 × 10⁻³ M solution of the fluorescent membrane probe (l-anilinonaphthalene-8-sulfonate). Fluorescent studies (Table 1) were performed on a Perkin-Elmer MPF-44A spectrofluorometer with a differential corrected spectrum unit (DCSU-2). At the fourth passage the fibroblasts from the patients, as compared to the normal controls, exhibited an increase of 30 times in excitation and emission intensity, a 30-nm blue shift in the emission maximum and a 0.18 polarization unit increase. These findings suggest that the l-anilinonaphthalene-8-sulfonate molecule in patient skin fibroblasts experiences either increased binding sites or increased quantum yield, a deeper insertion into the nonaqueous (hydrocarbon) region of the membrane and a more restricted motion in the membrane. Continued subculture at higher passages (10) showed a change of these findings toward normal. We believe that these fluorescent studies strongly support the concept that a membrane abnormality is present in Huntington’s disease. Exogenous factors may have influenced these abnormalities in vitro. A systematic study of these factors may help explain the membrane changes.

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INTERACTION BETWEEN CLONAZEPAM AND SODIUM VALPROATE

To the Editor: A potential drug interaction not mentioned in the recent Journal review on clonazepam1 is that between clonazepam and sodium valproate. In 1977, Jeavons, Clark and Maheshwari2 reported the development of absence status in five of 11 patients taking both drugs. Although the mechanism of this interaction in patient not defined, this discrepancy may be a result of an effect of sodium valproate on plasma levels of clonazepam. Baruzzi et al3 evaluated serum levels of valproic acid and clonazepam in epileptic patients, many of whom were being treated with more than one anticonvulsant. A poor correlation was made between the dose of clonazepam and plasma levels, in contrast to other reports.4,5 This observation was attributed to the effects of the concurrent medications, but was not associated specifically with sodium valproate. With the increase in use of both clonazepam and sodium valproate, this adverse interaction may be seen in increasing numbers of patients. Because of its potential implications, this interaction should be considered before these two agents are used in combination.

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Table 1. Fluorescence Studies of Fibroblasts from Patients with Huntington’s Disease and Normal Controls Using l-Anilinonaphthalene-8-Sulfonate.*

<table>
<thead>
<tr>
<th>Type</th>
<th>PASSAGE</th>
<th>EXM</th>
<th>REM1</th>
<th>POI ± SD</th>
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<td>380</td>
<td>1</td>
<td>520</td>
</tr>
<tr>
<td>Patients</td>
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<td>490</td>
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<td></td>
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<td>1</td>
<td>490</td>
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</tbody>
</table>

*EXM denotes excitation maximum, REM1 relative excitation intensity, EM emission maximum, REM 1 relative emission intensity, & POL. polarization.
sarriell adenohypophyseal tissue with hormonal activity and ACTH-secreting cells in other portions of the brain have been reported.1,5 Carbohydration data cannot pinpoint the intracranial ACTH-secreting site, and such venous sampling does not necessarily mean the pituitary is the origin of an ACTH gradient. Without tomographic demonstration of sellar abnormality in mild to moderate Cushing’s disease, we would express some caution in recommending that all such patients have trans-sphenoidal exploration.

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INSULIN AND ATHEROSCLEROSIS

To the Editor: Dr. Stout,5 in response to an article by Dr. Merimee in the Journal, it suggests that a relative insulinopenia may account for the absence of vascular disease in diabetic dwarfs deficient in growth hormone. To my knowledge no specific mechanism is known that would explain the common association of accelerated atherosclerosis and hyperinsulinemia. I should like to propose the following hypothesis: insulin stimulates intracellular synthesis of excess fatty acid, which inhibits hydrolysis of cholesterol ester. Since cholesterol leaves the cell only as unesterified cholesterol its egress from the cell is prevented, resulting in an intracellular accumulation of cholesterol ester.

The major lipid in early atheromas is cholesterol ester. This substance may accumulate either by an increased uptake from circulating cholesterol or an inhibition of cholesterol egress from the cell, or both. Circulating ester (predominantly cholesterol linoleate) undergoes a number of steps in passage into and out of cells that may be summarized as follows: incorporation into cells; hydrolysis in lysosomes by an acid cholesterol esterase; re-esterification in the Golgi apparatus with (presumably) locally synthesized, predominantly oleic acid; rehydrolysis in the cytosol by a neutral cholesterol esterase; and removal from the cell in the form of unesterified cholesterol by high-density lipoprotein.2

Cholesterol egress may be impaired for a variety of reasons.2 A deficiency in acid cholesterol esterase has been suggested as the cause of cholesterol ester storage disease and as a factor in atherosclerosis. However, since cholesterol oleate predominates in early atheroma, it seems more likely that a deficiency or inhibition of pH7 cholesterol esterase would account for the accumulation of cholesterol ester seen in the early atheromatous lesion.

Enzymes that hydrolyze triglyceride and cholesterol ester share many of the same characteristics,2 and an excess of fatty acid has been shown to inhibit both acid cholesterol esterase and a crude preparation of neutral cholesterol esterase as well as triglyceride hydrolysis.3 Insulin stimulates fatty acid synthesis, with oleic acid as the predominant product,4 and fatty acid synthesis is known to take place in both mitochondria and cytosol of aortic cells.2 An influence by insulin on fatty acid synthesis in vascular tissue is suggested in studies showing a decrease in fatty acid production in aortic tissue in experimental diabetes.13 Thus, hyperinsulinemia, by producing an increase in cytoplasmic oleic acid, may inhibit neutral cholesterol esterase, thereby preventing the formation of free cholesterol and its subsequent egress from the cell. It should be noted that aortic cholesterol acid hydrolyse is decreased in experimental diabetes,13 but this observation does not negate the concept of its inhibition by excessive amounts of local fatty acid.

In support of this concept, insulin has been shown to retard the regression of cholesterol deposits after atherogenic diet reversal in experimental atherosclerosis.13

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SOCRERE OF ACTH IN CUSHING’S DISEASE

To the Editor: The report of successful trans-sphenoidal microsurgery for Cushing’s disease by Tyrrell et al. in the April 6, 1978, issue of the Journal encourages this approach as a treatment of choice for this problem. Uncomplicated trans-sphenoidal resection of pituitary microadenomas for the treatment of Cushing’s disease is appealing as a cure, and a conservative approach is probably warranted unless a radiographic abnormality of the sella is apparent. This reservation is illustrated by the following case:

A 39-year-old woman with classically confirmed Cushing’s disease had elevated serum ACTH levels that selective venous catheterization showed to be of intracranial origin. Tomograms of the sella turcica were normal. An apparent pituitary microadenoma was surgically removed by the trans-sphenoidal approach, but the operation was again performed, with complete hypophysectomy. The Cushing’s disease persisted, however, and repeat selective venous sampling still revealed an intracranial source of the elevated ACTH, although she was otherwise functionally hypopituitary by hormonal assessment.

She then underwent bilateral adrenalectomy, with clinical and laboratory improvement except for continued elevation of peripheral ACTH levels.

This patient’s continued ACTH production could be from adenohypophyseal tissue remaining unrecognized in the sella, in a retropharyngeal site, or possibly coming from the hypothalamus. Extra-
ALCOHOL AND HYPERTENSION

To the Editor: Effects of alcohol drinking on blood pressure have been extensively discussed.1-7 Although the mechanisms that have been suggested as contributing to hypertension in alcoholic patients appear worthy of consideration, our recent studies suggest additional explanations. In clinically controlled experiments my colleagues and I have found that plasma renin activity, as well as aldosterone5 and arginine vasopressin release, is stimulated during ethanol intoxication and hangover. Thus, renal tubular mechanisms may cause accumulation of sodium and water and increase blood pressure. Elevated concentration of blood angiotensin II due to stimulated plasma renin activity may also contribute to increased blood pressure associated with ethanol drinking.

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CREASED GLOMERULAR FILTRATION IN BURNED PATIENTS

To the Editor: Loirat and his associates reported1 that glomerular filtration increased in burned patients whom they had studied, and they suggested some possible explanations for their observation. At least one alternative explanation was omitted from their discussion, and I wish to point it out here because it may be readily investigated clinically. Perhaps the most potent known modulators of glomerular filtration are the prostaglandins.2 Prostaglandins are produced in skin after a burn injury.3 Although circulating prostaglandins are usually inactivated rapidly and efficiently, burning apparently stimulates their production sufficiently to mediate the delayed phase of tissue response to burning. Concentrations of circulating prostaglandins or their metabolites might be expected to increase in burned patients at about the time Loirat et al observed increased glomerular filtration. If increased glomerular filtration is a consequence of burn-induced increases in circulating prostaglandin, nonsteroidal anti-inflammatory drugs that inhibit prostaglandin biosynthesis1 should stabilize the glomerular filtration rate and facilitate maintenance in burned patients of plasma concentrations of tobramycin and other clinically important antibiotics.

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FREEDOM OF INFORMATION AND PSRO'S

To the Editor: As a public-interest group seeking access on behalf of consumers to objective PSRO data about hospitals and physicians, we strongly object to the manner in which this issue is discussed by Professor Curran in the Law-Medicine note in the December 14, 1978, issue of the Journal. The title of the note, "Confidentiality of Records in PSRO'S," as well as several textual references, implies that one of the major issues raised by our suit is whether sensitive medical information identifiable to individual patients should be publicly disclosed. Such phrases as "confidentiality of...personal data on patients and providers" and "an action...to open up [PSRO records]" to public examination fail to make the essential distinction between patient records and objective PSRO information about providers that does not identify patients.

Contrary to the impression left by the article, there has never been any dispute about the need to maintain strict confidentiality of patient-identifiable data. Indeed, Public Citizen Health Research Group specifically excluded all patient-identifiable data from its Freedom of Information Act request. Moreover, it is undisputed that the Freedom of Information Act would never require public disclosure of medical information on identified patients, even if requested.

Provider-identifiable PSRO data gathered at taxpayer expense, on the other hand, must not be allowed to remain hidden behind the specious claim of patient confidentiality. Consumers ought to have access to PSRO data showing how often and to what extent hospitals and physicians are paid with public funds comply with the criteria established by their peers in the PSRO. The marketplace cannot operate properly so long as consumers remain ignorant of differences in appropriateness and quality among the health care providers from whom they are seeking services.

The note also contains a factual error concerning the status of the Freedom of Information Act case. The question of whether any of the data requested fall within the Act's exemptions is still being litigated in the Federal District Court. An appeal has not yet been taken, though it is reasonable to expect an appeal upon completion of the litigation in the District Court.

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To the Editor: The December 14 issue included an article by William Curran regarding the applicability of the federal Freedom of Information Act to Professional Standards Review Organizations, and specifically, Judge Gesell's (United States District Court) ruling in the Freedom of Information Act case brought against the District of Columbia PSRO.

We are counsel to the American Association of Professional Standards Review Organizations in that case. Regrettably, the article stated, "The decision itself is now on appeal." This statement is erroneous. The determination that the PSRO was within the purview of the Act was not a final judgment. The court still must consider whether any of the specific exemptions to the Act are applicable. We are now awaiting argument on that issue. If any exemption applies, the information would not have to be provided.

It is also important to recognize that a single lower-court decision would not be binding on other courts. We continue to believe that Congress never intended PSRO's to be federal agencies. For this reason the American Association of Professional Standards Review Organizations stands ready to file amicus curiae briefs on this point on behalf of any other PSRO that is challenged under the Freedom of Information Act.

Finally, the Association is attempting to have Congress enact a clarifying amendment that would reaffirm the original intent in a way that would demonstrate beyond question that PSRO's are not federal agencies and, as a result, not subject to the Act. We hope that such an amendment will be enacted.

We do not wish to minimize the adverse effect of Judge Gesell's ruling on PSRO's. It has made it more difficult for them to operate effectively. Regrettably, Professor Curran's article may compound the problem by making the situation appear worse than it is. We would appreciate your setting the record straight.

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The above letters were referred to Professor Curran, who offers the following reply:

To the Editor: I am pleas ed to have the corrections from the litigant's lawyers in this case. We can always expect these lawyers to know more about the case than any commentator. In my article I referred to "on appeal" as a shorthand to cover the "further litigation" and to indicate to lay readers that the issues were not final.

My comment was not inaccurate about the status of the Freedom of Information Act on the case. I said, "It remains for a further determination to be made as to whether the exemptions in the Freedom of Information Act apply to prevent disclosure of some or all of the data sought by the plaintiffs." This is the point made by Wolfe and his colleagues. I went on at some length in the column to examine the various exemptions under the Act. I am surprised that they did not take note of this discussion, which could not have taken place without realization of these issues.

I am glad to learn that the Health Research Group was not seeking identified-patient information. This point was not clear from Judge Gesell's opinion, since he did not reach it. His opinion did not contain reference to the specifics of the requested information. I did not say that the litigant plaintiffs were seeking information about particular patients or particular physicians. In fact, my discussion was related to what PSRO's and physicians consider the "most sensitive data," the physician profiles that might be used in malpractice cases and other litigation. The Health Research Group was trying "to open up the records of" the PSRO. There is no doubt of that. The extent of availability, as I said in the column, is as yet unestablished.

I agree with Mr. Kopit in his concerns that Congress may never have intended PSRO's to be, or treated as, "federal agencies" under the Freedom of Information Act. However, the lower court did decide just that. A decision of this type in the District of Columbia is of great importance to the rest of the federal court system. The further action by Judge Gesell (no) would affect the scope of exemptions, but not his basic finding of federal agency, unless this issue is appealed and reversed in this particular case. It is important for physicians and PSRO groups to understand that under this type of ruling, a group like PSRO's can be found to be enough like a federal agency to be subject to the same demands for disclosure of information as other, more clearly governmental bodies. Understandably, this threshold decision may well be appealed even after Judge Gesell makes a further decision on the scope of applicability of this plaintiff's request. A later litigant may be seeking other, more sensitive, more personally identifiable data, as in a malpractice case. This was the point of my wider discussion of the issues.

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Boston, MA 02115
BRITISH JOURNAL OF SURGERY ALSO SHOWS CONFIDENCE

To the Editor: Dr. Kenneth J. Rothman, in the December 14, 1978, issue of the Journal, gives a crystal-clear account of the virtue of confidence intervals in assessing the results of clinical trials and suggests that journals should encourage routine use of such intervals in the papers they accept. May I call his and the Journal’s attention to the fact that the British Journal of Surgery has included this point in its instructions to authors over the past two years, with gratifying if modest results in achieving Dr. Rothman’s aims.

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SAVE THE SMALLPOX*

A pox on fiends who scheme to see
The last variola virus wracked!
But wait, such slaughter cannot be:
Bless the Endangered Species Act!

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Note: See p 670 for further comfort. — Ed.

BOOK REVIEWS


The pioneering work of Sir William Harvey, *Exercitatio anatomica de motu cordis et sanguinis in animalibus*, published in 1628, has been admired by scientists around the world. Until the appearance of that scholarly treatise, the nature of the systemic and pulmonary circulations had centered around Galenic concepts and the gradual drift of blood from the right to left heart through invisible pores in the interventricular septum. Harvey’s recognition of the competence and importance of the valves of the heart and venous system, coupled with the pumping capability of the heart, led to his conclusion that “the movement of blood is constantly in a circle and is brought about by the beat of the heart.” In London and New York, Harveyian Societies have been founded in his honor. Harvey was born on April 1, 1578, and died at the age of 79, on June 3, 1657. The present compendium of essays on the circulation has been generated by the Harveyian Society of London to commemorate the quatercentenary of Harvey’s birth. There is little doubt that this book represents an “affectionate festschrift” to Harvey’s memory by a distinguished collection of British physicians and scientists. In June, 1957, the tercentenary of Harvey’s death was commemorated by an international congress in London, and a similar publication, edited by Dr. John McMichael, was created. The present volume seeks to review the state of the art of the circulation by presenting the many recent advances that have taken place since this earlier publication.


If one regards radiology as a form of art, this book has something to recommend it. It is a beautiful book, superbly printed and bound and with many clear illustrations. It is not a useful practical book, however, or a comprehensive reference work. It is primarily a description of the author’s experience applying a variety of technics to lung specimens. The first half of the volume describes the anatomy of the lung and mediastinum. There is an extensive review of the variations of bronchial, arterial and venous anatomy in the lung based on analyses that involve 110 to 180 specimens. Another useful section describes differences in the size of lobes and variations in fissures but lacks documentation of the precise source of the data. Bronchial cartilage, the lobule, the acinus and hilar lymph nodes are other topics discussed. Almost half the section on anatomy is devoted to a chapter, entitled “Stereobronchography and Stereoroangiography of Cadavers,” in which the author correlates the appearance of bronchograms and angiograms with post-mortem preparations using conventional roentgenograms and tomograms, relating them to whole and sliced lungs.

The second half of the book — a detailed description of anatomical radiologic correlations — consists of approximately 150 figures and covers plain roentgenograms in various positions, bronchography, angiography and tomography.

This book will be useful to any person interested in the minutiae of variations of pulmonary anatomy and in the precise identification of anatomic structures in the lung during life. The text is generally comprehensible, but at times it is hard to follow because of the style of writing. Important radiologic topics are not discussed inadequately dealt with or sometimes dealt with erroneously. For example, the descriptions of the lobule and of the acinus do not include the important work by Lynne Reid about lung-lobule anatomy, and the acinus is not precisely or accurately defined. The concept of “conventional” and “accessory” pulmonary arteries and veins is not introduced.

In summary, this book will be of some value to a small number of people, but most radiologists who hope to find a useful guide to anatomicradiologic correlates will be disappointed.

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