LETTERS AND CORRECTIONS

"The power and the beauty of science do not rest upon infallibility, which it has not, but on corrigibility, without which it is nothing."—Howard E. Gruber*

Letters submitted for publication must be typed double-spaced. Text length must not exceed 500 words, and no more than five references may be used. Complete references must be furnished, as specified in "Information for Authors" (page I-6). Specific permission to publish should be appended as a postscript. Publication depends on availability of space: We give preference to comment on recent content and new information. Letters for this section should be concise—the Editor reserves the right to shorten them and make changes that accord with our style.

Hodgkin's Disease and the ABVD Regimen

TO THE EDITOR: Santoro and colleagues (1) have reported a 59% complete response rate using the ABVD regimen (doxorubicin, bleomycin, vinblastine, and decarbazine) in patients with Hodgkin's disease resistant to MOPP chemotherapy (mechlorethamine, vincristine, procarbazine, and prednisone). For uncertain reasons other investigators (2-4) using approximately the same regimen and dose schedule have not achieved a similarly favorable rate of complete remission. One possible reason for this difference is that Santoro and associates state that 11 of their 54 evaluable patients had irradiation as "consolidation therapy" after receiving ABVD treatment. Either some of these 11 patients did not achieve a complete response with ABVD regimen alone or for unknown reasons the complete response was not expected to be durable without additional treatment. I believe that either way the treatment results in these irradiated patients cannot be ascribed solely to the ABVD chemotherapy. Perhaps the investigators could provide additional information about these 11 patients and recalculate their treatment results to reflect the effect of ABVD chemotherapy alone.

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In reply: The high complete response rate found in our series is probably due to two factors: Only 27 of 54 patients had extranodal involvement of Hodgkin's disease before starting ABVD chemotherapy, and ABVD was the first treatment in all our patients once they were considered to be resistant to MOPP chemotherapy. Because a number of clinical factors (such as extranodal involvement, systemic symptoms) were found in our series to lower considerably the likelihood of attaining complete remission with salvage ABVD treatment, it is not surprising that other investigators have obtained inferior results if their series mainly consisted of patients with unfavorable pretreatment characteristics. Probably for the same biological reasons (1, 2), if other forms of treatment are applied before starting ABVD therapy in MOPP-resistant patients, the possibility that the fraction of permanent multidrug-resistant cells will increase becomes very high.

We confirm that the reported 59% complete response rate is to be ascribed solely to ABVD chemotherapy. In other words, radiation therapy was attempted as consolidation treatment in 11 patients once clinical and pathologic complete remission was unequivocally documented after drug treatment alone. This is probably the reason why, as described in our original report, the remission duration was not affected by consolidation therapy with irradiation.

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The Thyroid Nodule

TO THE EDITOR: We suggest an alternative to the methods discussed by Van Herle and associates (1) for evaluating the thyroid nodule. After being screened with radionuclide scans, 34 patients with discrete cold nodules had fine needle aspiration of these nodules and a simultaneous ultrasound examination. Appropriate sweeps with the transducer of our static B-mode ultrasound equipment during the aspiration have enabled us to both identify cystic areas and improve biopsy accuracy by confirming the needle's position while in the nodule. Even in patients with solid nodules, we have found subtle differences in tissue density and have improved localization of these lesions in all but one patient.

We have been impressed by the depth of many nodules that felt superficial and suspect that this technique has significantly decreased sampling error and the number of inadequate specimens. It has also allowed for the systematic guided aspiration of mixed cystic-solid nodules so that fluid can be more easily removed, often with resultant shrinkage of the neck mass. Although this technique is more expensive per diagnosis than the other methods outlined by Van Herle and discussants, we suspect that fewer false negatives and inadequate specimens may make the average cost per correct diagnosis competitive. The possibility of fewer missed malignan-

*GRUBER HE. The origin of the origin of species. Review of *Darwin and the Mysterious Mr. X: New Light on the Evolutionists.* By EISELEY L. *The New York Times Book Review.* 1979 July 22:16.

cies might also ease the minds of both patients and physicians. To determine the advantage of this technique follow-up of those patients with negative biopsies is currently in progress.

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REFERENCE

1. VAN HERLE AJ, RICH P, LJUNG BME, ASHCRAFT MW, SOLOMON DH, KELLER EB. The thyroid nodule. *Ann Intern Med.* 1982;**96**: 221-32.

TO THE EDITOR: The recent UCLA conference (1) was an extremely useful analysis of the thyroid nodule as a diagnostic and therapeutic problem. I enter one plea, however. Although the analysis was lucid in terms of medical decision making in the technical sense, there was not even passing mention of the patient's preference for a thyroid scan or echothyrography as opposed to a needle aspiration. Although the needle aspiration entails very little risk and is an extremely useful study, patients whom I have seen undergoing this procedure in which the neck is approached by a needle show fear and trembling that we, as objective physicians, may well be able to placate but cannot ignore. It is a very short step from the elegant cost analysis to a utility analysis of the diagnostic sequence for each patient. I hope that, in future analyses of this kind, at least a passing mention will be made of the likely perceptions of a patient who is undergoing a procedure having any degree of invasiveness.

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Small-Cell Lung Cancer and Limbic Encephalitis

TO THE EDITOR: Remote effects of cancer on the nervous system have been well described clinically but the pathophysiologic basis of such events is poorly understood (1-3). Similarly, little information is available on the response of these paraneoplastic syndromes to specific antitumor therapy. We describe a patient with limbic encephalitis secondary to small-cell carcinoma of the lung whose neurologic manifestations reversed dramatically after treatment.

A 45-year-old woman with no history of neurologic dysfunction had the sudden onset of temporal lobe seizures characterized by uncontrolled grimacing, vocalization, disorientation, and bilateral hyperextension of her arms and legs. An electroencephalogram (EEG) showed a seizure focus in the left temporal region. A lumbar puncture and computed tomographic (CT) scan of the brain were normal. Anticonvulsant therapy was only partially successful in controlling the seizures and the patient persisted in having episodes of confusion and severe retrograde amnesia. Subsequent evaluation including three repeat CT scans and four lumbar punctures was completely normal, including negative cytologic examinations of cerebrospinal fluid. Four months after she had had her first seizure a chest roentgenogram showed a right hilar mass. After bronchoscopy, biopsy, and staging, the patient was found to have small-cell carcinoma limited to the right lung. Combination chemotherapy was started and resulted in significant tumor regression. Chest and prophylactic cranial radiotherapy (2100 rad) was administered 4 months later. In the several months after institution of chemotherapy, the patient's neurologic status changed markedly with the cessation of seizure activity and dramatic improvement in memory. A repeat EEG was minimally abnormal without a seizure focus being shown.

Fourteen months after the institution of therapy, the patient was found to have recurrent disease in the lung. Neurologic examination was normal at that time. She died 2 years after first developing symptoms without having recurrence of seizure activity or difficulty with memory. A request for an autopsy was refused.

Although we cannot be absolutely certain this patient did not have direct central nervous system involvement with tumor at the time of presentation, all attempts to implicate the tumor were unsuccessful. Also, even with therapy the prognosis of patients with brain involvement with small-cell carcinoma is extremely poor, and this patient's clinical course is inconsistent with that diagnosis (4).

The development of neurologic symptoms consistent with a paraneoplastic process should lead to a prompt search for cancer. Should the patient have small-cell carcinoma, a common cause of such syndromes (2, 3), antitumor therapy can result in amelioration of symptoms as well as prolongation of survival (5).

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Edema in the Ectopic ACTH Syndrome

TO THE EDITOR: Peripheral edema may be a prominent feature of the ectopic adrenocorticotropic hormone (ACTH) syndrome, and has been attributed to mineralocorticoid excess (1, 2). However, in other cases of mineralocorticoid excess, such as primary aldosteronism, escape from the salt-retaining effects of mineralocorticoids prevents the formation of edema. Escape from these effects has also been shown after constant daily exogenous ACTH infusion (3). The mechanism of the failure of sodium escape in the ectopic ACTH syndrome is uncertain. Conceivably, some factors associated with underlying malignancy, such as protein-calorie malnutrition or profound potassium depletion, could favor salt retention and prevent escape.

Because there is edema formation in ectopic ACTH syndrome, urinary salt excretion must be relatively low, at least lower than dietary intake. Nevertheless it is usually assumed that, analogous to other states of primary mineralocorticoid excess, urine chloride (and sodium) levels are relatively high and thus of diagnostic value in this syndrome (4). The following case report shows that such an assumption may be misleading.

A 75-year-old man with a history of lung carcinoma and liver metastases had progressive and marked peripheral edema and hypokalemic metabolic alkalosis. Medications included methyldopa and hydrochlorothiazide. Serum sodium was 144 meq/L; potassium, 2.4 meq/L; chloride, 90 meq/L; and total CO_2, 40 meq/L. Blood urea nitrogen was 46 mg/dL; creatinine, 2.6 mg/dL; glucose, 525 mg/dL; and albumin, 3.6 g/dL. Arterial pH was 7.52; Po_2, 49 mm Hg; and Pco_2, 46 mm Hg. The urine electrolytes were sodium, 4 meq/L; chloride, 2 meq/L; and potassium, 37 meq/L. Subsequent studies showed no evidence of congestive heart failure, cor pulmonale, nephrotic syndrome, venous obstruction, or

obstructive uropathy. Volume contraction due to diuretic use was initially suspected; the administration of normal saline with a weight gain of 4 kg produced a marked increase in peripheral edema but multiple measurements of urine sodium and chloride remained below 10 meq/L. Plasma cortisol after high dose dexamethasone was 91.2 μg/dL. Plasma ACTH was 222 pg/mL (normal, up to 80). Spironolactone and aminoglutethimide were administered but the patient died before an adequate therapeutic response could be obtained.

The markedly reduced urine sodium and chloride levels in this patient caused some diagnostic confusion. An initial diagnosis of diuretic-induced metabolic alkalosis was postulated but was not supported when a trial of saline expansion markedly worsened edema without any effect on metabolic alkalosis or urine electrolytes. Thus the metabolic alkalosis of the ectopic ACTH syndrome may be associated with markedly reduced urinary chloride and sodium concentrations, particularly when edema formation is a prominent finding. In other cases of ectopic ACTH syndrome, where edema was minimal or absent, we have observed relatively high urine chloride (greater than 20 meq/L).

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Cortisol, Valproic Acid, and ACTH Suppression

TO THE EDITOR: We read with interest the article by Koletsky and associates (1) on the cortisol suppression test in patients with elevated adrenocorticotropic hormone (ACTH) levels. In a previous study (2), we showed that cortisol failed to normalize ACTH values in patients with Nelson's syndrome, but was effective in lowering ACTH values after bilateral adrenalectomy for Cushing's disease. The ACTH values were not suppressed in our patients with Nelson's tumor, even when serum cortisol concentrations were greater than 300 μg/dL, a level much higher than that used by Koletsky and colleagues.

Failure of cortisol to suppress ACTH secretion from certain pituitary adenomas may be due to a difference in the genesis of some of these tumors with resultant differences in responsiveness to the feedback effects of cortisol and the influence of agents that affect brain neurotransmitters. The study by Lamberts and associates (3) that showed the existence of two types of ACTH-producing tumors supports this concept. The commoner tumor that appears in the anterior part of the anterior pituitary tends to be more responsive to the negative feedback effects of glucocorticoids. The other type of tumor that generally lies in the area of the pituitary, which corresponds to the pars intermedia in the rat, is less responsive to glucocorticoid suppression. Although cortisol suppression tests may prove helpful in differentiating patients with Nelson's syndrome from adrenalectomized patients with Cushing's disease, we found the response of such patients to be more definitive when valproic acid was administered (2). This gamma-aminobutyric acid transaminase inhibitor lowered ACTH levels in Nelson's syndrome, but produced no effect in adrenalectomized patients with Cushing's disease.

Our findings with respect to this action of valproic acid are confirmed by the studies of Jones and colleagues (4) who used valproic acid to treat patients with Nelson's syndrome, and by the more recent studies of Allolio and coworkers (5). Finally, the different response to cortisol and valproic acid tends to support the concept of two types of ACTH-producing tumors as proposed by Lamberts and associates (3).

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Hypercapnia in Hyperalimentation

TO THE EDITOR: We write to clarify a potential misunderstanding that could result from the provocative short paper by Covelli and associates (1) on hypercapnia in hyperalimentation.

The authors intimate that the increase in CO_2 production ($\dot{V}CO_2$) and consequent increase in arterial PCO_2 were due to an increase in carbohydrate calories supplied by total parenteral nutrition. This suggestion may lead the reader to assume that the finding is an unusual and unexpected consequence and would not be expected with a simple increases in caloric intake (oral, enteral, or parenteral). As more medical centers become capable of measuring $\dot{V}O_2$, it will become common knowledge that the $\dot{V}CO_2$ increase as a consequence of increased caloric intake by any route and with all caloric substrates. The implication of total parenteral nutrition, and especially carbohydrates supplied with total parenteral nutrition, is fallacious. Of course, total parenteral nutrition should not be used in patients who can receive nutrition by other routes. However, if a patient needs total parenteral nutrition, it should be initiated without hesitation. The increase in $\dot{V}CO_2$ should be anticipated and measures taken to compensate for this increase. Also, the patient's $\dot{V}O_2$ should be measured and calories supplied to meet, but not exceed, the patient's measured energy needs. This will limit the increase in $\dot{V}CO_2$ while supplying the patient with needed nutrients. To withhold nutrition or reduce the nutrients below requirements to avoid an increase in $\dot{V}CO_2$ is analogous to withholding blood from a bleeding patient to stop the bleeding.

One final observation is that the uninitiated reader could conclude (although Covelli and associates did not suggest this idea) that lipid calories should be substituted for carbohydrate calories to avoid hypercapnia. It should be emphasized that the maximum decrease in $\dot{V}CO_2$ realized by this maneuver is only 17%, which is not likely to be clinically significant. Also, there is the potential risk of increasing the $\dot{V}O_2$; this risk is due to the lower caloric yield per litre of O_2 consumed with fat as the caloric substrate. Theoretically, there is also the risk of exacerbating the hypoxemia

that will be present in these critically ill patients because of the increase in right to left shunt shown in the experimental model reported by Rosegger and colleagues (2). The conclusions to be drawn from the report by Covelli and associates are the following: Caloric requirements should be determined by direct measurement of $\dot{V}O_2$ and $\dot{V}CO_2$ in critically ill patients, especially those with mechanical ventilation (3); patients should be fed quantities to meet, not exceed, measured caloric requirements; and excess feeding can result in signficant complications including hypercapnia as seen in the three patients reported.

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Cimetidine and Allergy Skin Testing

TO THE EDITOR: Although the primary action of cimetidine is gastric acid suppression, other effects have been noted related to its H_2 antihistamine effect (1). H_2 sites are present in the skin (2), and cimetidine can cause a mild reduction of histamine-induced wheals and flares (3). The studies cited were done with oral cimetidine, but evidence from two patients we have seen suggests that this medication may be a more potent skin suppressor when given intravenously.

We were asked to see two patients with a possible penicillin allergy who were in an intensive care unit. Both patients were critically ill and were receiving intravenous cimetidine to suppress gastric acid production and prevent gastric ulceration. In this setting, histamine (1.0 mg/mL) was applied intradermally in addition to the penicillin antigens. Results of all skin tests, including the histamine, were negative. One patient's condition allowed discontinuation of cimetidine with retesting 24 hours later. This patient then was positive to histamine as well as to benzylpenicilloyl-polylysine and was successfully desensitized. The other patient's condition did not allow delay, and he was started on penicillin on a rapid desensitizing schedule, without incident.

This information indicates that intravenous cimetidine may be a more potent suppressor of wheal and flare reactions than the oral preparation. When evaluating patients who are receiving this drug, usually in an intensive care unit, care must be taken in interpreting the results of immediate-type skin tests. Also, histamine should be used routinely in this situation to evaluate the dermal reactivity in these patients.

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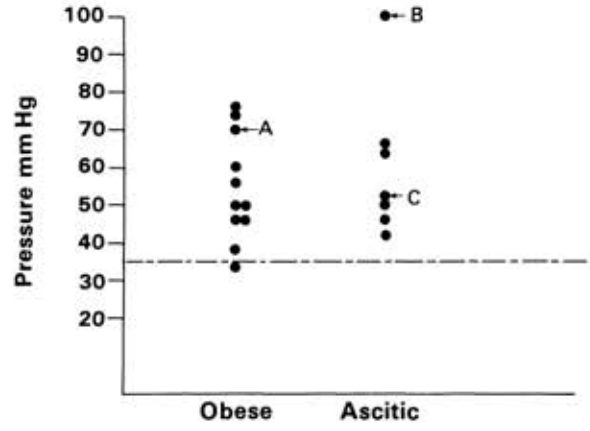

Figure 1. Groin pressures in obese and ascitic patients while sitting with legs dangling: index case (*A*), cases of meralgia paresthetica found during study (*B, C*). Dashed line is highest pressure recorded in normal-weight patients.

Meralgia Paresthetica and Large Abdomens

TO THE EDITOR: We read with great interest the letter by Radvan and Vidikan (1) on meralgia paresthetica in patients with liver disease, in which they suggested that entrapment of the lateral cutaneous nerve of the thigh results from mechanical factors such as stretching of the abdominal wall caused by ascites or massive hepatomegaly.

The recent observation of an obese patient whose symptoms of meralgia paresthetica were triggered when sitting but relieved when lying down led us to consider an additional pathogenetic mechanism: external compression of the nerve by the weight of a big abdomen. We studied groin pressures in 10 patients with normal weight, 11 obese patients, and seven ascitic patients. A folded sphygmomanometer cuff—in the manner used by rheumatologists to assess grip strength (2)—was placed over the inguinal ligament between the abdominal flap and thigh. Patients were then asked to assume their usual sitting position and pressures were recorded. After the pressure recordings were done, careful histories were taken for symptoms of meralgia paresthetica.

The mean weights of the patients with normal weight, obese patients, and ascitic patients were 61 kg (range, 50 to 76 kg), 107 kg (68 to 172 kg), and 92 kg (52 to 149 kg), respectively, with corresponding mean abdominal girths of 81 cm (range, 66 to 96 cm), 121 cm (102 to 153 cm), and 118 cm (84 to 144 cm). Pressures are shown in Figure 1. Whereas the highest pressure in patients with normal weight was 35 mm Hg, pressures above 50 mm Hg were observed in five of the 11 obese patients, and five of the seven patients with ascites. Interestingly, two of the five ascitic patients with pressures above 50 mm Hg were found to have previously undiagnosed meralgia paresthetica.

Our data suggest that the weight of the protuberant abdomen may be a contributory factor leading to meralgia paresthetica in obese and ascitic patients. Experimental data indicate that tissue pressures greater than 50 mm Hg result in nerve ischemia (3). Whereas interstitial fluid pressure represents approximately 70% of externally applied pressures, it may approach 100% when excess tissue fluid is present (4)—as in patients with cirrhosis of the liver and ascites.

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TO THE EDITOR: In their recent letter (1), Radvan and Vidikan describe 15 patients with meralgia paresthetica and alcoholic liver disease, including 13 with severe ascites. Although they state "meralgia paresthetica has not been described previously in patients with liver disease or ascites," such a case was reported as early as 1938 by Ecker and Woltman (2). Additional cases of meralgia paresthetica with ascites were reported in 1972 by Kitchen and Simpson (3).

Mechanical factors have long been recognized as having an important causal role. Stookey (4) stated that the sharp angulation of the lateral femoral cutaneous nerve as it leaves the pelvis subjects it to constant low grade trauma. Undoubtedly the patients described by Radvan and Vidikan had important mechanical factors because all but one patient had abdominal distension. Radvan and Vidikan have misinterpreted the scholarly work by Wartenberg (5) on the subject. He did not ". . . deny the importance of the mechanical factor . . . [but] intended to deprive the mechanical factor of its unique validity." He emphasized the role of generalized toxic or infectious processes that predispose the lateral femoral cutaneous nerve to disease. The alcoholic patients described with severe liver disease certainly have potential toxic causal factors. Conclusions about the relative role of local mechanical and systemic factors cannot be made on the basis of a review of the patients described.

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Reversible Hepatic Veno-Occlusive Disease and 6-Thioguanine

TO THE EDITOR: We read with interest the article by Gill and associates (1). We report another case of reversible veno-occlusive disease of the liver caused by 6-thioguanine in a patient with acute leukemia in remission who was concomitantly treated with methotrexate.

A 46-year-old man was hospitalized in April 1976 for evaluation of acute diffuse abdominal pain, fever, and sudden ascites that began 1 week before admission. In January 1976 he had been started on 6-thioguanine, 120 mg/d, and methotrexate, 30 mg/week. One week before hospitalization a bone marrow aspiration was done that did not show leukemic activity. At the time of hospitalization he was still taking 6-thioguanine and methotrexate.

On admission, he had fever, ascites, tender hepatomegaly, and painless splenomegaly. His hemoglobin level and leukocyte differential count were normal. His platelet count was 94 × 10^9/L; alkaline phosphatase, 997 IU/L; bilirubin, 24 μmol/L; and his aspartate transaminase level was 5 times the normal value. Celiac angiography and cavography were normal. A ^{99m}Tc sulfur colloid liver and spleen scintiscan showed an enlarged liver and spleen with nonhomogenous distribution of the colloid in the liver, and a region of increased activity in the caudate lobe.

Chemotherapy was discontinued on admission. On the fourth hospital day a needle biopsy of the liver was done, which showed severe centrolubular congestion with slight degeneration of hepatocytes in the same area but no leukemic infiltration. The histologic and scintiscan findings confirmed the diagnosis of hepatic veno-occlusive disease (2, 3).

He was treated with diuretics and improved gradually. A second needle biopsy of the liver was done on the 23rd hospital day, which showed slight congestion in the centrolobular area; liver and spleen scintigraphy was normal. In July 1978 he died during a relapse of his disease and a postmortem histologic examination of the liver showed a normal liver parenchyma.

This patient had been treated with 6-thioguanine daily and methotrexate weekly; after 3 months on therapy he developed a transient hepatic veno-occlusive disease. The diagnosis was made from findings of a needle biopsy and scintiscans of the liver. The rapid improvement on stopping 6-thioguanine and methotrexate therapy strongly indicates that the use of 6-thioguanine was the cause of this disease, as in the case previously described (1). It is noteworthy that when the patient died 2 years later the histologic findings in the liver were normal.

Methotrexate has been implicated as the cause of various forms of liver damage, such as hepatocellular necrosis, cholestasis, cirrhosis, and steatosis. Those injuries, however, were not transient. Hepatic veno-occlusive disease has been not described (5). Because of the potential reversibility of this lesion, it is important to be aware of this complication so that an early diagnosis can be made.

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Hepatic Dysfunction and Ketoconazole Therapy

TO THE EDITOR: A previous communication from our institution described a case of biopsy-proven toxic hepatitis in a patient treated with ketoconazole (1). We recently saw a second patient. Ketoconazole has been widely used (with an estimated 300 000 prescriptions) since it became licensed in the United States in 1981 for treatment of deep mycoses and candidiasis (2). The need for informing physicians of this drug's rare but potentially serious danger is even more acute since the recent advisory from the manufacturer (Janssen Pharmaceutica, Inc., Berse, Belgium) reporting the death of a patient who developed hepatitis during ketoconazole therapy (2).

A 48-year-old physician was included in an open, multicenter study of ketoconazole for treatment of fingernail onychomycosis. The infection had been unresponsive to treatment with griseofulvin over a 4-month period

Table 1. Laboratory Tests

	Normal Values	Hospital Day					
		0	84	86	98	113	141
Total bilirubin, *μmol/L*	2-17	...	...	107	111	51	14
Alkaline phosphatase, *U/L*	50-275	...	...	450	480	240	158
Aspartate transaminase, *U/L*	10-40	13	1030	1900	1450	480	31
Lactic dehydrogenase, *U/L*	150-450	...	...	800	600	350	248

and that drug had to be discontinued because of diarrhea. The patient had no history of liver disease nor of excessive ethanol intake and took no other medications. Ketoconazole was administered in a single oral daily dose of 200 mg. Hematologic values and serum alanine transaminase (ALT) were normal at the start of therapy. Improvement of the nail infection was obvious after 8 weeks of therapy and a slight increase, although still within normal limits, in serum ALT was found. One month later, fatigue and nausea suddenly occurred, leading to cessation of therapy after 81 days. Laboratory studies showed markedly elevated ALT (Table 1). This rise was further accelerated by intake of a single ketoconazole dose (200 mg) 48 hours before studies were done on day 86. At that time, icterus was present along with marked malaise. Serum bilirubin, alkaline phosphatase, and lactic dehydrogenase, in addition to ALT, were all markedly elevated. Viral hepatitis, types A and B, was excluded by serologic studies. Ultrasonic and computed tomographic scanning of the liver and pancreas showed no abnormalities. The patient refused a liver biopsy. Abnormal laboratory findings gradually subsided and findings were within normal limits 2 months after the episode. At no time during the course of the hepatitis was there a significant change in hematologic values or sedimentation rate.

Hepatic damage associated with ketoconazole therapy has been reported in only a few cases (1, 3, 4) and is probably an idiosyncratic reaction. The incidence has been estimated at between 0.1% and 1%, and many cases appear to be subclinical, detected only by routine liver function studies (5). It currently seems advisable to have liver function tests done before treatment and monthly or more frequently during ketoconazole therapy.

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The Causative Organism in Fort Bragg Fever

TO THE EDITOR: Recent articles on legionella diseases state or imply that Fort Bragg fever was shown to be caused by the gram-negative bacterium bearing my name, now classified as a *Legionella* species. I am writing to correct this mistake, which is becoming fixed in the literature. This mistake is due to speculation by Hébert and colleagues at the Centers for Disease Control in a recent article in *Annals of Internal Medicine* (1).

The scientific evidence showed to my satisfaction that Fort Bragg fever was caused by *Leptospira autumnalis* and had nothing to do with *Legionella.* My reasons for stating this have been outlined in detail in the Readers' Forum section of a new journal, *Infection Control* (2). Unfortunately, even in this article, the Editor's note implies that the rickettsia-like organism, now *Legionella,* was the cause of Fort Bragg fever, a theory rejected in my article. Even Dr. Weinstein's editorial "The New Pneumonias: The Doctor's Dilemma" (3) states that Fort Bragg fever was found to be due to the gram-negative bacterium, another spin-off from the original speculation by Hébert and colleagues.

The well-established fact that the causative organism in Fort Bragg fever was proved to be leptospiral has almost disappeared from the literature since early 1980 and this freak strain of *Legionella* bearing my name, isolated in 1943 at Fort Bragg, has replaced it. Before this error becomes fixed and permanent in the literature on *Legionella,* I hope that subsequent writers on the subject of the various strains of *Legionella* will not include Fort Bragg fever and Bushy Creek fever as examples.

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In response: We concur with Dr. Tatlock's attempt to clarify the evidence for the causative agent in Fort Bragg fever, or pretibial fever. The only serologic evidence available from the outbreak suggests that *Leptospira interrogans* serotype *autumnalis* was involved in a substantial portion of the cases (1). Dr. Tatlock also recounts human transmission experiments with *L. interrogans* serotype *autumnalis* that reproduced the unique pretibial rash (2). These data make it reasonable to assume that *L. interrogans* serotype *autumnalis* was a causative agent of that syndrome at Fort Bragg.

Because detailed clinical information is not available on the patient from whose blood the TATLOCK agent was isolated, one can only speculate as to its importance as a cause of disease in 1943. Possibly the original patient presented with fever alone, and the blood sample was obtained on that basis. It seems probable that one or more cases of legionellosis occurred during the outbreak and were studied as possibly related to the outbreak. Subsequently, the TATLOCK agent has been classified as a new species of bacteria, *Legionella micdadei,* which has been reported as a cause of pneumonia but not of pretibial rash (3). A case of *Legionella pneumophila* pneumonia, however, has been reported in a patient who developed a pretibial rash on the fifth day of illness (4). We hope that Dr. Tatlock's clarification will correct any misperce-

tions about the evidence regarding the cause of Fort Bragg fever.

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Disseminated Histoplasmosis and Asplenia

TO THE EDITOR: We read with interest the article by Wheat and associates concluding that age greater than 54 years and immunosuppression were the only risk factors for disseminated or fatal histoplasmosis (1). In view of the increased risk of overwhelming bacterial disease in asplenic patients (2-5), we question whether asplenism may contribute also to dissemination of fungal disease. Recently we cared for a surgically asplenic but otherwise healthy man who presented with a perplexing long-term fever of undetermined origin until *Histoplasma capsulatum* was isolated from bone marrow and blood cultures.

On 24 September 1980, a 29-year-old truckdriver sustained minor head trauma when in Indianapolis, Indiana. From 24 to 28 September he was hospitalized in that city. On 4 October 1980, he presented to our hospital approximately 500 miles away with a temperature of 40.6 °C. A left upper quadrant scar from splenectomy done 6 years before for an endocarditis-related splenic abscess was present. Leukocyte count was 20 700/mm³ with 61% lymphocytes. Throughout the patient's 6 weeks of hospitalization and follow-up he remained febrile and had a persistent lymphocytosis. Two chest roentgenograms were normal. A work-up for a fever of undetermined origin including studies for infectious mononucleosis, cytomegalovirus, and toxoplasmosis was negative. A bone marrow isolate and a blood culture eventually grew *H. capsulatum.* In the sixth week of illness his fever resolved spontaneously but the lymphocytosis persisted. One month after discharge the patient was asymptomatic.

Perhaps disseminated histoplasmosis should be added to the list of potential pathogens that cause disease in the asplenic patient, especially if the patient has been in an endemic area as was this patient. Of note was the lymphocytosis persisting throughout this patient's illness. Furthermore, this case re-emphasizes the importance of a travel history in a patient with a fever of undetermined origin. Because this patient was admitted to a hospital geographically removed from the region where histoplasmosis is endemic, disseminated histoplasmosis was not highly ranked in the initial differential diagnosis. Recognition that this patient had been both injured and hospitalized in Indianapolis, an area shown by Wheat and colleagues to be in the midst of a histoplasmosis epidemic (1), may have led to an earlier diagnosis.

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Unwitting Heparin Abuse in a Drug Addict

TO THE EDITOR: There have been frequent reports on oral anticoagulant abuse. Less common is the surreptitious use of heparin by patients (1, 2). We report here a case of unwitting heparin abuse.

A 23-year-old woman was hospitalized because of fever and progressive swelling and tenderness of the right foot after attempts to inject heroin through a pedal vein. She was a thin woman and did not appear acutely ill. Physical examination was normal except she had a temperature of 38.3 °C and her right foot was swollen and erythematous. No ecchymoses were present.

Laboratory data included a hemoglobin of 11.9 g/dL and a leukocyte count of 11 200/dL with 54% polymorphonuclear leukocytes, 5% band forms, and 35% lymphocytes. Prothrombin time was 12.3 seconds with a control of 11.6 seconds, and partial thromboplastin time was 63.6 seconds with a control of 25.3 seconds. A partial thromboplastin time done on the patient's plasma mixed with control plasma in a 1:1 ratio (mixing partial thromboplastin time) gave a clotting time of 32.4 seconds as compared with that of a 1:1 combination of saline and control plasma, which was 27.4 seconds.

The initial blood sample had a thrombin time (Parke-Davis, Avon, Connecticut) of greater than 4 minutes, with a clottable fibrinogen (Sigma Fibrinogen Kit, St. Louis, Missouri) of 350 mg/dL and negative fibrin split products (Thrombo-Wellcotest, Greenville, North Carolina). A reptilase time (Abbott Laboratories, Chicago, Illinois) was 18 seconds, with a control of 19 seconds. The protamine sulfate test for heparin was positive and heparin assay (via protamine sulfate titration) showed a heparin level of 833 mg/dL. On a blood sample obtained the next day, all clotting tests were normal.

We suspected from these studies that the patient's illicit drugs were prepared with heparin or a heparin-like substance. The patient denied having any knowledge of this information although she did know that quinine and lactulose were involved in the dilution of the drugs.

Heparin is shown to act at different levels in the coagulation cascade (3). This patient presented with an elevated partial thromboplastin time, an elevated thrombin time, and a mixing partial thromboplastin time that did not correct, showing that anticoagulant was present. Normal clottable fibrinogen and negative fibrin split products supported the evidence for increased antithrombin activity. The normal reptilase time indicated correction of the prolonged fibrin polymerization time. A protamine sulfate test was positive, thereby leading us to do a specific heparin assay by protamine sulfate titration. This test confirmed the presence of a heparin-like substance. Although patients with chronic liver disease can have abnormal thrombin times with negative fibrin split products and normal serum fibrinogen levels, these findings are thought to be due to a delay in polymerization (4, 5) and such patients usually will have a prolonged reptilase time without a positive protamine titration. Also, these abnormal tests do not correct in 1 day because they result from permanent hepatic injury.

We presume that the heroin the patient was using was being cut with heparin. This supposition is supported by the partial thromboplastin time returning to normal on all subsequent tests; the heparin half-life is only about 4 hours. We feel that heparin or heparin-like substances should be considered as a cause for prolonged partial thromboplastin times in patients who are intravenous drug abusers.

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Plasma Exchange or Leukapheresis in the Hypereosinophilic Syndrome

TO THE EDITOR: After reports of the successful treatment of the hypereosinophilic syndrome with leukapheresis (1, 2) we did plasma exchange, leukapheresis, or both on four patients with the hypereosinophilic syndrome. A comparison was made between the fall in eosinophil counts obtained by leukapheresis with those found after plasma exchange.

We were surprised to find that on each occasion plasma exchange produced a larger percent fall in three patients (90%, 83%, and 35%) in the eosinophil count than did leukapheresis in the same three patients (38%, 27%, and 35%). Similar results were obtained after daily plasma exchanges on two other patients with the hypereosinophilic syndrome, one of whom had three serial exchanges (Figure 1). On each occasion there was a marked fall in blood eosinophil counts during and up to 7 hours after the serial exchanges. In all patients the eosinophil count had returned to the previous high level after a period of between 7 and 18 hours.

Plasma exchange and leukapheresis were carried out with a continuous flow celltrifuge blood separator. For plasma exchange, 2.5 to 4.0 L of plasma were exchanged for an equal volume of purified protein fraction of plasma. For leukapheresis, 200 mL of packed buffy coat cells was removed. Both these procedures were done under identical conditions, so that the effects of both procedures on blood eosinophil counts could be compared. This unexpected result suggests that an unidentified factor circulating in the plasma may be contributing to retention of eosinophils in the circulation. Similar results have been shown in two patients with eosinophilia due to filariasis, suggesting that this effect of plasma exchange is not seen only in patients with eosinophilia due to the hypereosinophilic syndrome.

In the hyperoeosinophilic syndrome very high circulating eosinophil counts can be associated with evidence of acute tissue injury, and it has been suggested that acutely lowering high counts may result in clinical improvement (1, 2). However, none of our patients showed clinical improvement after either leukapheresis or plasma exchange. For this reason we cannot recommend these procedures for the treatment of the hyperosinophilc syndrome. But when it may be necessary to reduce the eosinophil count rapidly, plasma exchange may be a more effective procedure than leukapheresis.

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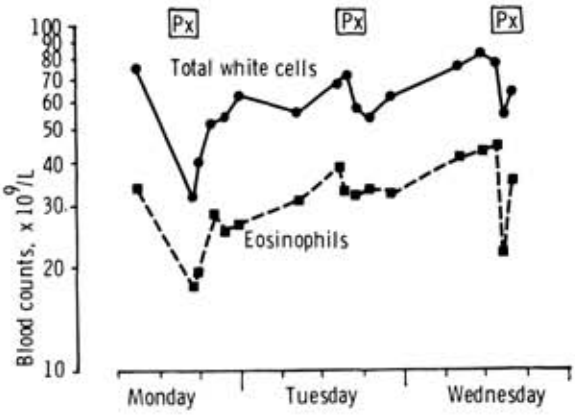

Figure 1. The effects of three sequential plasma exchanges in Patient 2. Px = plasma exchange.

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Thrombotic Thrombocytopenic Purpura

TO THE EDITOR: The report by Rosove and colleagues (1) on the ineffectiveness of aspirin and dipyridamole in the treatment of thrombotic thrombocytopenic purpura underscores the difficulty in determining a therapeutic rationale for a condition of unknown cause, uncertain pathogenesis, and disputed definition (2, 3). The situation is further complicated by the widely differing degrees of severity manifested by this syndrome, which may follow a fulminant and rapidly fatal course, may be subacute and relatively mild (4), or even chronic and relapsing (5). Finally, reporting of treatment has not been standardized and it is often difficult, when perusing a case report, to comprehend what treatment the patient has been given; an example is Table 2 of the article by Rosove and colleagues (1), which does not indicate the time over which the plasma exchanges were carried out.

Confronted with a patient who is comatose, or has seizures, paralysis, high fever, jaundice, a hemorrhagic diathesis, or renal failure, the physician cannot be criticized for using any means at his disposal to bring about a remission. On the other hand, where these features are lacking, a more deliberate approach seems indicated and it may then be possible to distinguish between the effects of different therapies.

One such case, reported recently (4), led to the following observations. Low-dose plasma exchange (10 mL/kg body weight · d) was associated with a reduction in the reticulocyte count from 15% to 4.2%, and a transient decline in lactic dehydrogenase to within the normal range. The plasma exchange had no apparent effect on the thrombocyte count or the patient's neurologic status. The administration of intravenous hydrocortisone, 1 g/d, on the third day of plasma exchange was associated with a rapid amelioration of headache, restlessness, obtundation, and fluctuating neurologic signs, but thrombocytopenia (20 000/mm³) persisted and lactic dehydrogenase levels rose again. At the end of 2 days of combined treatment there was no further improvement and high-dose exchange was begun (25 mL/kg body weight · d), and steroidal treatment was continued. At the end of 5 more days the thrombocyte count was 118 000/mm³ and lactic dehydrogenase was normal. Steroids were tapered over the next 3 weeks and the patient has remained in complete hematologic and clinical remission for 26 months.

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In response: To clarify Table 2 of our report (1), a course of plasma or whole blood manipulation consisted of a period during which treatment was given continually on at least a daily basis. Plasmapheresis or whole blood exchange ranged from 40 to 80 mL/kg body weight · d. A course was considered to have ended if more than 36 hours elapsed without treatment. Improvement was indicated only if it occurred during the treatment course. When there was subsequent deterioration, it occurred after the treatment was discontinued. We appreciate Dr. Herman's request for clarification.

Although it is difficult to draw any definitive conclusion from the case Dr. Herman mentions, he has suggested a reasonable approach to the patient who has mild clinical manifestations. Treatment modalities may be tried one at a time; perhaps it would then be possible to assess their individual value. Such an approach would be best suited to patients with a chronic or subacute form of illness, when active disease is known to be fairly stable. Regarding the acute form, a patient may appear deceivingly well initially, only to deteriorate markedly in a matter of hours or a few days, if not minutes. The principal concern over single-modality treatment in this latter group is that a treatment that may be capable of preventing or attenuating a downhill course may be omitted. Using more than one therapeutic modality is advisable for most patients with illness of acute onset who have any severe disease manifestations.

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REFERENCE

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Paroxysmal Nocturnal Hemoglobinuria and the Myeloproliferative Syndrome

To the editor: Because paroxysmal nocturnal hemoglobinuria has been associated with primary myelofibrosis and myeloid metaplasia, has occurred concomitantly with erythroleukemia, and has terminated in acute myeloblastic leukemia (1) and acute myelomonoblastic leukemia (2), it has been considered a "candidate" myeloproliferative disorder (3).

However, only three studies have been reported in which the paroxysmal-nocturnal-hemoglobinuria-like defect has been systematically sought in a series of patients with any form of myeloproliferative syndrome, and results have been variable. Of 50 patients with polycythemia vera, primary myelofibrosis and myeloid metaplasia, and the subtypes of acute myeloblastic leukemia reported by Catovsky and associates (4), none had a positive Ham's test, although one with chronic myelogenous leukemia and one with the myeloblastic phase of erythroleukemia had positive sucrose lysis tests of 5% or greater. Results of Ham's test, sucrose lysis test, or both were found to be positive by Hansen and Killmann (5) in five of their 10 patients with primary myelofibrosis and myeloid metaplasia and by Kuo and associates (1) in 13 of 22 patients.

To provide further information on the incidence of a defect similar to paroxysmal nocturnal hemoglobinuria in all forms of the myeloproliferative syndrome, 44 successive patients with clinical, laboratory, and marrow biopsy evidence of any form of the myeloproliferative syndrome were evaluated. Twelve of the patients had polycythemia vera; six, primary myelofibrosis and myeloid metaplasia; seven, chronic myelogenous leukemia; seven, thrombocythemia; five, acute myeloblastic leukemia; four, acute myelomonoblastic leukemia; and three, acute promyelocytic leukemia. Laboratory studies done in all cases included hemoglobin, hematocrit, reticulocyte count, Ham's and sucrose hemolysis tests, serum haptoglobin, leukocyte alkaline phosphatase, and urinary hemosiderin. Patients whose test results were suggestive of hemolysis were completely retested at least once every six months for 1 year.

No patients were found to have positive results of sucrose lysis or Ham's tests, including those who had repeat testing. Laboratory evidence suggestive, but not diagnostic, of hemolysis was detected in two of 12 patients with polycythemia vera; three of six with primary myelofibrosis and myeloid metaplasia; one of seven with chronic myeloblastic leukemia; none of seven with thrombocythemia; none of five with acute myeloblastic leukemia; one of four with acute myelomonoblastic leukemia; and none of three patients with acute promyelocytic leukemia. One patient with polycythemia vera, two with primary myelofibrosis and myeloid metaplasia, one with chronic myelogenous leukemia, and one patient with acute myelomonoblastic leukemia had repeatedly low serum haptoglobin levels (less than 50 mg/dL) in the absence of abnormal liver function tests. One other patient with primary myelofibrosis and myeloid metaplasia had a consistently elevated absolute reticulocyte count, and one other patient with polycythemia vera without evidence of cardiac disease or hemochromatosis had persistent hemosiderinuria only.

Possibly except for patients with primary myelofibrosis and myeloid metaplasia, it appears from this study that routine testing for a defect similar to paroxysmal nocturnal hemoglobinuria in patients with myeloproliferative disorders is unlikely to yield positive results.

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Zomepirac and Renal Failure

TO THE EDITOR: Zomepirac sodium, a recently introduced nonsteroidal anti-inflammatory drug, has been heavily promoted for use as an analgesic (1). I report a case of acute renal failure that was likely due to the use of zomepirac sodium.

A previously healthy 26-year-old male physician who was taking no prescribed or over-the-counter medications took one 50-mg tablet of zomepirac sodium for relief of a simple headache. He awoke the next morning (approximately 12 hours after ingestion) feeling nauseated and weak but went to work. During the day nausea persisted, diffuse abdominal and flank pains developed, and weakness progressed, forcing him to return home. The symptoms continued to worsen through the next morning; fluid intake was well maintained and no urinary symptoms were noted. He returned to the hospital and had routine laboratory tests done, suspecting hepatitis. Results showed serum urea nitrogen and creatinine of 38 and 3.9 mg/dL, respectively, and he referred himself to a nephrologist. Medical history was unremarkable as were the results of general physical examination. Urinalysis showed each high-power field loaded with leukocytes and erythrocytes. Some granular and hyaline casts were seen as were rare cellular casts; Wright stain of the urinary sediment did not show eosinophils. Cultures of urine and oropharynx were negative as was a chest roentgenogram. Serum automated reagin test, antistreptolysin O, and hepatitis antigen and antibody were negative; antinuclear antibodies were absent and serum complement was in the high-normal range. The erythrocyte sedimentation rate (Wintrobe) was 5 mm/h. Liver function tests were normal. A 24-hour urinary collection showed a creatinine clearance of 40 mL/min and proteinuria of 184 mg/d. Renal ultrasound showed slightly echoluscent kidneys consistent with an acute injury, but was otherwise normal. Over the next 10 days serum urea nitrogen and creatinine gradually returned to normal, with symptomatic improvement parallel with their fall. Repeat urinalysis was normal and 24-hour collection of urine showed a creatinine clearance of 107 mL/min and proteinuria of 25 mg/d. Renal function remains normal 7 months later.

Previous reports (2-4) have shown allergic interstitial nephritis as a consequence of nonsteroidal anti-inflammatory drug administration as well as a reversible rise in urea nitrogen and creatinine; the latter is seen not infrequently in patients with cirrhosis of the liver and congestive heart failure in whom inhibition of renal prostaglandin synthesis may permit renal vasoconstrictive hormonal influences to predominate. This case is probably an example of an idiosyncratic reaction to zomepirac sodium, namely acute renal failure. In view of the unknown incidence and potentially serious nature of such an adverse reaction, physicians should exercise caution in prescribing this medication and consider the use of better studied and more familiar drugs.

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Granulocytosis and a Sulindac Overdose

TO THE EDITOR: Sulindac (Clinoril; Merck, Sharp & Dohme, West Point, Pennsylvania) is a nonsteroidal anti-inflammatory indene derivative that has gained increasing acceptance in the treatment of rheumatoid arthritis and other inflammatory conditions since its introduction in 1977 (1). Bone marrow aplasia and secondary cytopenias have been associated with the use of sulindac (1-2) but granulocytosis associated with this drug has not been reported. We present the following case of acute, extreme, and rapidly reversible granulocytosis associated with an overdose of sulindac.

A 16-year-old boy was admitted to the hospital on 14 February 1982 for observation and treatment for an episode of scanty hematemesis after he ingested approximately 60 200-mg tablets of sulindac. He had a history of minimal brain dysfunction and drank a six-pack of beer per day. A previous evaluation for abdominal pain in 1980 had shown a normal leukocyte count and differential.

The patient was alert, not acutely ill, and afebrile with minimal orthostatic hypotension (blood pressure supine, 124/82 mm Hg; blood pressure seated, 116/70 mm Hg; pulse supine, 110; pulse seated, 120). There were no purpura or other skin rash and no evidence of lymphadenopathy or hepatosplenomegaly. Findings on neurologic examination and mental status were normal. Blood counts are shown in Table 1. The peripheral blood smear showed normal erythrocyte, leukocyte and platelet structure. No immature granulocytes or nucleated erythrocytes were seen. The only laboratory abnormality was a serum potassium of 2.2 meq/L. Liver function studies remained normal throughout the hospitalization. The patient's intravascular volume depletion and hypokalemia were promptly corrected and he remained asymptomatic without futher gastrointestinal bleeding during the 4 days in the hospital.

Granulocytosis has been reported with the use of several of the older nonsteroidal anti-inflammatory drugs, in particular indomethacin and phenylbutazone (3). According to the few case reports, granulocytosis in most of these patients was associated with a severe systemic reaction to the drug. Associated signs included anemia, purpura, exfoliative dermatitis, fever, glomerulonephritis adenopathy, and hepatosplenomegaly, often associated with liver function abnormalities. The cause of the granulocytosis is not elucidated in the case reports.

Poisoning by various drugs such as lead may result in granulocytosis attributed to tissue necrosis or to a hypersensitivity reaction induced by the drug. Acute hemorrhage has been associated with granulocytosis by a mechanism related to local inflammation or, in some instances, to trauma-induced pain with release of endogenous

Table 1. Granulocytosis Associated with Sulindac Overdose

	Date					
	2/14	2/14	2/14	2/15	2/16	2/17
Leukocyte count, × 10^9/L	36.2	37.1	40.6	28.7	13.5	9.3
Volume of packed erythrocytes, L/L	49.1	46.5	44.9	37.8	34.6	35.5
Platelets, × 10^9/L	...	454	...	...	260	...
Leukocyte differential, %						
Segmented neutrophils	55	52	65	56	74	...
Band neutrophils	33	40	28	29	2	...
Lymphocytes	2	1	4	11	23	...
Monocytes	10	7	3	4	1	...

corticosteroids, epinephrine, or both. A maximal value of 31 000 leukocytes was reported with the massive hemorrhage of a splenic rupture (4).

This case of neutorophilia after sulindac ingestion is remarkable for the absence of systemic illness. Without tissue necrosis, inflammation, or significant hemorrhage, all of which induce granulocytosis through modulation or endogenous corticosteroids or epinephrine, other mechanisms of drug-induced granulocytosis must be considered. It is possible, for example, that sulindac has a direct stimulatory effect on the granulocyte stem cell that could lead to a true increase in the total body granulocyte pool. This is plausible because neither epinephrine (through demarginization or granulocytes) nor corticosteroids (by early release of granulocytes from the bone marrow and diminished egress of granulocytes from the circulation [5]) have been reported to cause the level of granulocytosis reported here.

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Residency Training

TO THE EDITOR: The editorial by Frame (1) in the March issue offers many valuable guidelines for the organization and content of management and teaching rounds for internal medicine residents. Also, his suggestion for further discussion and evaluation of this subject by those organizations most involved is very appropriate. However, there are other recommendations that would clearly not be applicable to many teaching programs. Specifically, I would refer to community-based residencies where physicians in private practice teach on a voluntary basis.

Maintaining a "home floor" is impracticable and unnecessary in many institutions. A "home service" composed of a group of attending physicians provides a superior educational base in the setting mentioned above. Communication among house staff, nursing personnel, and attending physicians is not necessarily hampered in such a system. I feel that the size of the institution and teaching program is a critical factor in this regard.

Assignment of an attending physician to conduct teaching rounds for a given service over a significant period of time is an important concept. To suggest that the other attending staff members of a service would contribute only peripherally to patient care and avoid contact with the house staff is not acceptable in a service-based system. The attending physician who has admitted a patient should retain full responsibility for the care of that patient and supervision of the house staff's management. Communication between house staff and attending physicians regarding individual patients provides a management-rounds type of experience that can be equally valuable to that provided by more formal encounters. Teaching rounds should provide a chance to explore in more detail the issues involved in understanding and caring for selected patients on the service.

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REFERENCE

1. FRAME B. Interaction between house staff and attending physicians [Editorial]. *Ann Intern Med.* 1982;**96**:372-3.

TO THE EDITOR: In recent years residency programs in internal medicine have come to depend on private patients for the education of residents. There are many natural points of intersection whereby residents may relate to senior staff in the clinical care of patients, such as at the time of admission, in decisions regarding ongoing work-up, when significant changes occur in a patient's condition, and at discharge, to cite but a few. Also, the logistics of patient management rounds may facilitate a close working relationship between the attending physician and resident staff, and preserve the mutual communication between a physician and his patient.

These rounds are conducted daily by the intern and senior resident team, are in the early morning, last 2 to 2½ hours, and may include medical students and nursing personnel. At least three mornings each week, these are followed by the more formal and structured patient education rounds that are under the direction of a single teaching attending physician. In the former instance the resident team visits each assigned patient. The identification of new problems, the resolution of others, and fundamental decisions regarding diagnosis and therapy are the central issues considered. Because time is limited, only specific details of clinical care should be addressed. This is not the place for a review of the admission data base. This effort must be completed at another time, preferably within a few hours of admission, and should include a meeting between the responsible attending physician and resident staff, at the patient's bedside to confirm the clinical data and formulate initial plans for diagnosis and care.

The model proposed by Dr. Frame would seriously compromise these important interactions, and infringe on the mutual and stable physician-patient relationship. In the suggested model, a senior teaching attending physician interacts with the resident staff in decision making and provision of care. Private attending physicians communicate their wishes through written notes. This procedure conflicts with a basic tenet of the specialty of internal medicine—that is, a mutual personal commitment between physician and patient that is stable over time and whereby a physician serves as the patient's advocate and accepts responsibility for all of the patient's health needs. This concept was precisely defined by the American Board of Internal Medicine in its description of an ideal internist (1). It is a fundamental attitude of the specialty of internal medicine, and must be constantly illustrated to students and residents in training.

Patient management and patient education rounds are both important in the education of internal medicine residents. Each serves a different set of objectives and goals. I strongly support this coexistence, the continued collaborative interactions between private attending physicians and resident staff, and the continued use of private patients in the education of students and residents in a wide variety of assignments. In my view interested, well-informed, emotionally stable, and motivated senior staff find it challenging and gratifying to work with highly motivated medical students and residents. The interactions that result should be collegial and cooperative, in which trust and a sharing in the responsibility for care of the patient prevail.

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General Internal Medicine in the Medical School

To the editor: As major contributors to the functions and governance of an academic general internal medicine division that has entered its 21st year we write to offer comments on the editorial on this topic by Tarlov (1). Subspecialty divisions emerged and enlarged as research became one of the missions of departments of medicine. The emergence of general internal medicine divisions has been based primarily on the need for teachers and clinicians with broad backgrounds to fulfill the other two of the three major missions of departments of medicine: education and service (2).

In this period of limited financial resources an efficient structure must be provided for a department of medicine to organize its administrators, clincians, teachers, and researchers. Divisions are one component of such a structure. Circumstances unique to each institution and the talents of individual faculty members will result in subspecialty and general internal medicine divisions that are unbalanced in their contributions to the three classic departmental missions.

Our general internal medicine division published three textbooks and innumerable articles in the past year. Although research is our smallest time commitment we have been involved in projects ranging from study of the doctor-patient relationship to clonidine for alcohol withdrawal. However, our main reason for existing is teaching entwined with patient care and educational administration. Our teaching ranges from ambulatory to critical care and from human values to ethical decision making (3). Current administrative roles held by division faculty include Chairman of the Department of Medicine and Directors of the General Internal Medicine Division, the Residency Program, and Medical Director of the Physician Assistants Program.

Rather than assume that any division is deficient in research activities it may be more productive to examine outcome data of the department. What is the quantity and quality of its administration, service, education, and research?

It is often a paradox that quality teaching, service, and administration are not fully recognized as academic excellence even when delivered in quantity. Simultaneously, research and publication are often weighed as academic excellence when delivered in quantity even without quality.

Let us not lose sight of the historical roots of divisions of general internal medicine as noted above. An expectation that these divisions model themselves after subspecialty divisions will simply spawn a series of new subspecialties and once again we will lose the broad-based general internist who is needed as an educational administrator, clinician, teacher, and role model.

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Joe McCarthys in Medicine

To the editor: Having read Dr. Fitzgerald's note, "From Galen to Xerox: The Authoritarian Reference in Medicine" in the February 1982 issue (1), I should like to add the Joe McCarthy syndrome.

This acquired syndrome is manifested by a propensity to cite literature out of context. The reference is generally accurate in terms of either journal, year, or content—but never quite right in all these respects. The reference is usually, but not always, related to the clinical problem or subject matter under discussion, but is not specifically pertinent.

Just as Senator Joseph McCarthy attempted to buttress his views by waving sheets of meaningless white paper as he spoke on the floor of the Senate, there is a tendency among house staff and attending physicians to quote the literature in a cavalier fashion. Unless a member of the decision-making team has read an article critically, the patient may be subject to unneeded diagnostic measures as well as inappropriate therapy.

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Correction: Hurst's "The Heart"

The annotation on *The Heart* (5th edition, J. Willis Hurst, editor-in-chief, Harper and Row Publishers) that appears in "A Library for Internists IV" in our March issue (*Ann Intern Med.* 1982;**6**:390) was based on the 4th edition. The 5th edition was listed for accuracy in the interests of readers ordering a copy.

The comment in the annotation, "limited discussion of laboratory studies," may not be accurate for the 5th edition. Dr. Hurst has pointed out in a letter that "electrocardiography and chest x-ray are covered early in the book. Part 6 of the book deals with specialized diagnostic techniques and therapeutic procedures in addition to electrocardiography and the chest x-ray. In fact, there are 228 pages devoted to techniques in addition to the pages on electrocardiography and chest x-ray."—*The Editor.*

Correction: Review of "Textbook of Endocrinology"

A word was deleted from a sentence in the penultimate paragraph of Dr. Christy's review of *Textbook of Endocrinology* in the April issue (*Ann Intern Med.* 1982;**96**:539). The sentence should have read, "What audience is the author aiming at?"