We are indebted to Dr. Philip LeCompte for providing us with Figure 3 and to Dr. Herbert Sise for information about Case 6.

REFERENCES

SPECIAL ARTICLE
ETHICS AND CLINICAL RESEARCH*
HENRY K. BREACHER, M.D.†

HUMAN experimentation since World War II has created some difficult problems with the increasing employment of patients as experimental subjects when it must be apparent that they would not have been available if they had been truly aware of the uses that would be made of them. Evidence is at hand that many of the patients in the examples to follow never had the risk satisfactorily explained to them, and it seems obvious that further hundreds have not known that they were the subjects of an experiment although grave consequences have been suffered as a direct result of experiments described here. There is a belief prevalent in some sophisticated circles that attention to these matters would "block progress." But, according to Pope Pius XII, "... science is not the highest value to which all other orders of values... should be subordinated."

I am aware that these are troubling charges. They have grown out of troubling practices. They can be documented, as I propose to do, by examples from leading medical schools, university hospitals, private hospitals, governmental military departments (the Army, the Navy and the Air Force), governmental institutes (the National Institutes of Health), Veterans Administration hospitals and industry. The basis for the charges is broad.‡

I should like to affirm that American medicine is sound, and most progress in it soundly attained. There is, however, a reason for concern in certain areas, and I believe the type of activities to be mentioned will do great harm to medicine unless soon corrected. It will certainly be charged that any mention of these matters does a disservice to medicine, but not one so great, I believe, as a continuation of the practices to be cited.

Experimentation in man takes place in several areas: in self-experimentation; in patient volunteers and normal subjects; in therapy; and in the different areas of experimentation on a patient not for his benefit but for that, at least in theory, of patients in general. The present study is limited to this last category.

REASONS FOR URGENCY OF STUDY

Ethical errors are increasing not only in numbers but in variety — for example, in the recently added problems arising in transplantation of organs.

‡At the Brook Lodge Conference on "Problems and Complexities of Clinical Research" I commented that "what seem to be breaches of ethical conduct in experiment are for no means rare, but are almost, one fears, universal." I thought it was obvious that I was not referring to the fact that examples could easily be found in all categories where research in man takes place to any significant extent. Judging by press comments, that was not obvious hence, this note.

*From the Anesthesia Laboratory of the Harvard Medical School at the Massachusetts General Hospital.
†Dor Professor of Research in Anesthesia, Harvard Medical School.
There are a number of reasons why serious attention to the general problem is urgent. Of transcendent importance is the enormous and continuing increase in available funds, as shown below.

<table>
<thead>
<tr>
<th>Year</th>
<th>Massachusetts General Hospital</th>
<th>National Institutes of Health</th>
</tr>
</thead>
<tbody>
<tr>
<td>1945</td>
<td>$500,000</td>
<td>$701,800</td>
</tr>
<tr>
<td>1955</td>
<td>2,292,916</td>
<td>36,063,200</td>
</tr>
<tr>
<td>1965</td>
<td>8,384,582</td>
<td>436,600,000</td>
</tr>
</tbody>
</table>

*National Institutes of Health figures based upon decade averages, excluding funds for construction, kindly supplied by Dr. John Sherman, National Institutes of Health.

Appropriate, supplied by Mr. David C. Crockett, Massachusetts General Hospital.

Since World War II the annual expenditure for research (in large part in man) in the Massachusetts General Hospital has increased a remarkable 17-fold. At the National Institutes of Health, the increase has been a gigantic 624-fold. This "national" rate of increase is over 36 times that of the Massachusetts General Hospital. These data, rough as they are, illustrate vast opportunities and concomitantly expanded responsibilities.

Taking into account the sound and increasing emphasis of recent years that experimentation in man must precede general application of new procedures in therapy, plus the great sums of money available, there is reason to fear that these requirements and these resources may be greater than the supply of responsible investigators. All this heightens the problems under discussion.

Medical schools and university hospitals are increasingly dominated by investigators. Every young man knows that he will never be promoted to a tenure post, to a professorship in a major medical school, unless he has proved himself as an investigator. If the ready availability of money for conducting research is added to this fact, one can see how great the pressures are on ambitious young physicians.

Implementation of the recommendations of the President's Commission on Heart Disease, Cancer and Stroke means that further astronomical sums of money will become available for research in man.

In addition to the foregoing three practical points there are others that Sir Robert Platt has pointed out: a general awakening of social conscience; greater power for good or harm in new remedies, new operations and new investigative procedures than was formerly the case; new methods of preventive treatment with their advantages and dangers that are now applied to communities as a whole as well as to individuals, with multiplication of the possibilities for injury; medical science has shown how valuable human experimentation can be in solving problems of disease and its treatment; one can therefore anticipate an increase in experimentation; and the newly developed concept of clinical research as a profession (for example, clinical pharmacology) - and this, of course, can lead to unfortunate separation between the interests of science and the interests of the patient.

**FREQUENCY OF UNETHICAL OR QUESTIONABLY ETHICAL PROCEDURES**

Nearly everyone agrees that ethical violations do occur. The practical question is, how often? A preliminary examination of the matter was based on 17 examples, which were easily increased to 50. These 50 studies contained references to 186 further likely examples, on the average 3.7 leads per study; they at times overlapped from paper to paper, but this figure indicates how conveniently one can proceed in a search for such material. The data are suggestive of widespread problems, but there is need for another kind of information, which was obtained by examination of 100 consecutive human studies published in 1964, in an excellent journal; 12 of these seemed to be unethical. If only one quarter of them is truly unethical, this still indicates the existence of a serious situation. Pappworth, in England, has collected, he says, more than 500 papers based upon unethical experimentation. It is evident from such observations that unethical or questionably ethical procedures are not uncommon.

**THE PROBLEM OF CONSENT**

All so-called codes are based on the bland assumption that meaningful or informed consent is readily available for the asking. As pointed out elsewhere,* this is very often not the case. Consent in any fully informed sense may not be obtainable. Nevertheless, except, possibly, in the most trivial situations, it remains a goal toward which one must strive for sociologic, ethical and clear-cut legal reasons. There is no choice in the matter.

If suitably approached, patients will accede, on the basis of trust, to about any request their physician may make. At the same time, every experienced clinician investigator knows that patients will often submit to inconvenience and some discomfort, if they do not last very long, but the usual patient will never agree to jeopardize seriously his health or his life for the sake of "science."

In only 2 of the 50 examples originally compiled for this study was consent mentioned. Actually, it should be emphasized in all cases for obvious moral and legal reasons, but it would be unrealistic to place much dependence on it. In any precise sense statements regarding consent are meaningless unless one knows how fully the patient was informed of all risks, and if these are not known, that fact should also be made clear. A far more dependable safeguard than consent is the presence of a truly responsible investigator.

**EXAMPLES OF UNETHICAL OR QUESTIONABLY ETHICAL STUDIES**

These examples are not cited for the condemna-

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*Reduced here to 22 for reasons of space.
tion of individuals; they are recorded to call attention to a variety of ethical problems found in experimental medicine, for it is hoped that calling attention to them will help to correct abuses present. During ten years of study of these matters it has become apparent that thoughtlessness and carelessness, not a willful disregard of the patient's rights, account for most of the cases encountered. Nonetheless, it is evident that in many of the examples presented, the investigators have risked the health or the life of their subjects. No attempt has been made to present the "worst" possible examples; rather, the aim has been to show the variety of problems encountered.

References to the examples presented are not given, for there is no intention of pointing to individuals, but rather, a wish to call attention to widespread practices. All, however, are documented to the satisfaction of the editors of the Journal.

**Known Effective Treatment Withheld**

*Example 1.* It is known that rheumatic fever can usually be prevented by adequate treatment of streptococcal respiratory infections by the parenteral administration of penicillin. Nevertheless, definitive treatment was withheld, and placebos were given to a group of 109 men in service, while benzathine penicillin G was given to others.

The therapy that each patient received was determined automatically by his military serial number arranged so that more men received penicillin than received placebo. In the small group of patients studied 2 cases of acute rheumatic fever and 1 of acute nephritis developed in the control patients, whereas these complications did not occur among those who received the benzathine penicillin G.

*Example 2.* The sulphonamides were for many years the only antibacterial drugs effective in shortening the duration of acute streptococcal pharyngitis and in reducing its supplicative complications. The investigators in this study undertook to determine if the occurrence of the serious nonsuppurative complications, rheumatic fever and acute glomerulonephritis, would be reduced by this treatment. This study was made despite the general experience that certain antibiotics, including penicillin, will prevent the development of rheumatic fever.

The subjects were a large group of hospital patients; a control group of approximately the same size, also with exudative Group A streptococcus, was included. The latter group received only nonspecific therapy (no sulfadiazine). The total group denied the effective penicillin comprised over 500 men.

Rheumatic fever was diagnosed in 5.4 per cent of those treated with sulfadiazine. In the control group rheumatic fever developed in 4.2 per cent.

In reference to this study a medical officer stated in writing that the subjects were not informed, did not consent and were not aware that they had been involved in an experiment, and yet admittedly 25 acquired rheumatic fever. According to this same medical officer more than 70 who had had known definitive treatment withheld were on the wards with rheumatic fever when he was there.

*Example 3.* This involved a study of the relapse rate in typhoid fever treated in two ways. In an earlier study by the present investigators chloramphenicol had been recognized as an effective treatment for typhoid fever, being attended by half the mortality that was experienced when this agent was not used. Others had made the same observations, indicating that to withhold this effective remedy can be a life-or-death decision. The present study was carried out to determine the relapse rate under the two methods of treatment; of 408 charity patients 251 were treated with chloramphenicol, of whom 20, or 7.97 per cent, died. Symptomatic treatment was given, but chloramphenicol was withheld in 157, of whom 36, or 22.9 per cent, died. According to the data presented, 23 patients died in the course of this study who would not have been expected to succumb if they had received specific therapy.

**Study of Therapy**

*Example 4.* TriA (triacetyloleandomycin) was originally introduced for the treatment of infection with gram-positive organisms. Spotty evidence of hepatic dysfunction emerged, especially in children, and so the present study was undertaken on 50 patients, including mental defective or juvenile delinquents who were inmates of a children's center. No disease other than acne was present; the drug was given for treatment of this. The ages of the subjects ranged from thirteen to thirty-nine years. "By the time half the patients had received the drug for four weeks, the high incidence of significant hepatic dysfunction . . . led to the discontinuation of administration to the remainder of the group at three weeks." (However, only two weeks after the start of the administration of the drug, 54 per cent of the patients showed abnormal excretion of bromsulphalein.) Eight patients with marked hepatic dysfunction were transferred to the hospital "for more intensive study." Liver biopsy was carried out in these 8 patients and repeated in 4 of them. Liver damage was evident. Four of these hospitalized patients, after their liver-function tests returned to normal limits, received a "challenge" dose of the drug. Within two days hepatic dysfunction was evident in 3 of the 4 patients. In 1 patient a second challenge dose was given after the first challenge and again led to evidence of abnormal liver function. Flocculation tests remained abnormal in some patients as long as five weeks after discontinuance of the drug.

**Physiologic Studies**

*Example 5.* In this controlled, double-blind study of the hematologic toxicity of chloramphenicol, it was recognized that chloramphenicol is "well known as a cause of aplastic anemia" and that there
is a "prolonged morbidity and high mortality of aplastic anemia" and that "... chloramphenicol-induced aplastic anemia can be related to dose ...". The aim of the study was "further definition of the toxicity of the drug ...".

Forty-one randomly chosen patients were given either 2 or 6 gm. of chloramphenicol per day; 12 control patients were used. "Toxic bone-marrow depression, predominantly affecting erythropoiesis, developed in 2 of 20 patients given 2.0 gm. and in 18 of 21 given 6 gm. of chloramphenicol daily." The smaller dose is recommended for routine use.

**Example 6.** In a study of the effect of thymectomy on the survival of skin homografts, 123 children, three and a half months to eighteen years of age, about to undergo surgery for congenital heart disease, were selected. Eleven were to have total thymectomy as part of the operation, and 7 were to serve as controls. As part of the experiment, full-thickness skin homografts from an unrelated adult donor were sutured to the chest wall in each case. (Total thymectomy is occasionally, although not usually part of the primary cardiovascular surgery involved, and whereas it may not greatly add to the hazards of the necessary operation, its eventual effects in children are not known.) This work was proposed as part of a long-range study of "the growth and development of these children over the years." No difference in the survival of the skin homograft was observed in the 2 groups.

**Example 7.** This study of cyclopropane anesthesia and cardiac arrhythmias consisted of 31 patients. The average duration of the study was 3 hours, ranging from two to four and a half hours. "Minor surgical procedures" were carried out in all but 1 subject. Moderate to deep anesthesia, with endotracheal intubation and controlled respiration, was used. Carbon dioxide was injected into the closed respiratory system until cardiac arrhythmias appeared. Toxic levels of carbon dioxide were achieved and maintained for considerable periods. During the cyclopropane anesthesia a variety of pathologic cardiac arrhythmias occurred. When the carbon dioxide tension was elevated above normal, ventricular extrasystoles were more numerous than when the carbon dioxide tension was normal, ventricular arrhythmias being continuous in 1 subject for ninety minutes. (This can lead to fatal fibrillation.)

**Example 8.** Since the minimum blood-flow requirements of the cerebral circulation are not accurately known, this study was carried out to determine "cerebral hemodynamic and metabolic changes ... before and during acute reductions in arterial pressure induced by drug administration and/or postural adjustments." Forty-four patients whose ages varied from the second to the tenth decade were involved. They included normotensive subjects, those with essential hypertension and finally a group with malignant hypertension. Fifteen had abnormal electrocardiograms. Few details about the reasons for hospitalization are given.

Signs of cerebral circulatory insufficiency, which were easily recognized, included confusion and in some cases a nonresponsive state. By alteration of the tilt of the patient "the clinical state of the subject could be changed in a matter of seconds from one of alertness to confusion, and for the remainder of the flow, the subject was maintained in the latter state." The femoral arteries were cannulated in all subjects, and the internal jugular veins in 14.

The mean arterial pressure fell in 37 subjects from 109 to 48 mm. of mercury, with signs of cerebral ischemia. "With the onset of collapse, cardiac output and right ventricular pressures decreased sharply.

Since signs of cerebral insufficiency developed without evidence of coronary insufficiency the authors concluded that "the brain may be more sensitive to acute hypotension than is the heart."

**Example 9.** This is a study of the adverse circulatory responses elicited by intra-abdominal maneuvers:

When the peritoneal cavity was entered, a deliberate series of maneuvers was carried out (in 68 patients) to ascertain the effective stimuli and the areas responsible for development of the expected circulatory changes. According, the surgeon rubbed localized areas of the parietal and visceral peritoneum with a small ball sponge as discreetly as possible. Traction on the mesenteries, pressure in the area of the celiac plexus, traction on the gallbladder and stomach, and occlusion of the portal and caval veins were the other stimuli applied.

Thirty-four of the patients were sixty years of age or older; 11 were seventy or older. In 44 patients the hypotension produced by the deliberate stimulation was "moderate to marked." The maximum fall produced by manipulation was from 200 systolic, 105 diastolic, to 42 systolic, 20 diastolic; the average fall in mean pressure in 26 patients was 53 mm. of mercury.

Of the 50 patients studied, 17 showed either atrioventricular dissociation with nodal rhythm or nodal rhythm alone. A decrease in the amplitude of the T wave and elevation or depression of the ST segment were noted in 25 cases in association with manipulation and hypotension or, at other times, in the course of anesthesia and operation. In only 1 case was the change pronounced enough to suggest myocardial ischemia. No case of myocardial infarction was noted in the group studied although routine electrocardiograms were not taken after operation to detect silent infarcts. Two cases in which electrocardiograms were taken after operation showed T-wave and ST-segment changes that had not been present before.

These authors refer to a similar study in which more alarming electrocardiographic changes were observed. Four patients in the series sustained silent myocardial infarctions; most of their patients were undergoing gallbladder surgery because of
associated heart disease. It can be added further that in the 34 patients referred to above as being sixty years of age or older, some doubtless had heart disease that could have made risky the maneuvers carried out. In any event, this possibility might have been a deterrent.

Example 10. Starling’s law — “that the heart output per beat is directly proportional to the diastolic filling” — was studied in 30 adult patients with atrial fibrillation and mitral stenosis sufficiently severe to require valvulotomy. “Continuous alterations of the length of a segment of left ventricular muscle were recorded simultaneously in 13 of these patients by means of a mercury-filled resistance gauge sutured to the surface of the left ventricle.” Pressures in the left ventricle were determined by direct puncture simultaneously with the segment length in 13 patients and without the segment length in an additional 13 patients. Four similar anesthetized patients were studied through catheterization of the left side of the heart transseptally. In all 30 patients arterial pressure was measured through the catheterized brachial artery.

Example 11. To study the sequence of ventricular contraction in human bundle-branch block, simultaneous catheterization of both ventricles was performed in 22 subjects; catheterization of the right side of the heart was carried out in the usual manner; the left side was catheterized transbrachially. Extrasystoles were produced by tapping on the epicardium in subjects with normal myocardium while they were undergoing thoracotomy. Simultaneous pressures were measured in both ventricles through needle puncture in this group.

The purpose of this study was to gain increased insight into the physiology involved.

Example 12. This investigation was carried out to examine the possible effect of vagal stimulation on cardiac arrest. The authors had in recent years transsected the homolateral vagus nerve immediately below the origin of the recurrent laryngeal nerve as palliation against cough and pain in bronchogenic carcinoma. Having been impressed with the number of reports of cardiac arrest that seemed to follow vagal stimulation, they tested the effects of intrathoracic vagal stimulation during 30 of their surgical procedures, concluding, from these observations in patients under satisfactory anesthesia, that cardiac irregularities and cardiac arrest due to vagovagal reflex were less common than had previously been supposed.

Example 13. This study presented a technic for determining portal circulation time and hepatic blood flow. It involved the transcruinate injection of the spleen and catheterization of the hepatic vein. This was carried out in 43 subjects, of whom 14 were normal; 16 had cirrhosis (varying degrees), 9 acute hepatitis, and 4 hemolytic anemia.

No mention is made of what information was divulged to the subjects, some of whom were seriously ill. This study consisted in the development of a technic, not of therapy, in the 14 normal subjects.

Studies to Improve the Understanding of Disease

Example 14. In this study of the syndrome of impending hepatic coma in patients with cirrhosis of the liver certain nitrogenous substances were administered to 9 patients with chronic alcoholism and advanced cirrhosis: ammonium chloride, di-ammonium citrate, urea or dietary protein. In all patients a reaction that included mental disturbances, a “flapping” tremor” and electroencephalographic changes developed. Similar signs had occurred in only 1 of the patients before these substances were administered:

The first sign noted was usually clouding of the consciousness. Three patients had a second or a third course of administration of a nitrogenous substance with the same results. It was concluded that marked resemblance between this reaction and impending hepatic coma, implied that the administration of these [nitrogenous] substances to patients with cirrhosis may be hazardous.

Example 15. The relation of the effects of ingested ammonia to liver disease was investigated in 11 normal subjects, 6 with acute virus hepatitis, 26 with cirrhosis, and 8 miscellaneous patients. Ten of these patients had neurologic changes associated with either hepatitis or cirrhosis.

The hepatic and renal veins were cannulated. Ammonium chloride was administered by mouth. After this, a tremor lasted for three days developed in 1 patient. When ammonium chloride was ingested by 4 cirrhotic patients with tremor and mental confusion the symptoms were exaggerated during the test. The same thing was true of a fifth patient in another group.

Example 16. This study was directed toward determining the period of infectivity of infectious hepatitis. Artificial induction of hepatitis was carried out in an institution for mentally defective children in which a mild form of hepatitis was endemic. The parents gave consent for the intramuscular injection or oral administration of the virus, but nothing is said regarding what was told them concerning the appreciable hazards involved.

A resolution adopted by the World Medical Association states explicitly: "Under no circumstances is a doctor permitted to do anything which would weaken the physical or mental resistance of a human being except from strict therapeutic or prophylactic indications imposed in the interest of the patient." There is no right to risk an injury to 1 person for the benefit of others.

Example 17. Liver cancer cells were injected into 22 human subjects as part of a study of immunity to cancer. According to a recent review, the subjects (hospitalized patients) were "merely told they would be receiving 'some cells'" — "... the word cancer was entirely omitted."

Example 18. Melanoma was transplanted from a
Technical Study of Disease

Example 19. During bronchoscopy a special needle was inserted through a bronchus into the left atrium of the heart. This was done in an unspecified number of subjects, both with cardiac disease and with normal hearts.

The technique was a new approach whose hazards were at the beginning quite unknown. The subjects with normal hearts were not for their possible benefit but for that of patients in general.

Example 20. The percutaneous method of catheterization of the left side of the heart has, it is reported, led to 8 deaths (1.09 per cent death rate) and other serious accidents in 732 cases. There was, therefore, need for another method, the transbrachial approach, which was carried out in the present study more than 500 cases, with no deaths.

Granted that a delicate problem arises regarding how much should be discussed with the patients involved in the use of a new method, nevertheless where the method is employed in a given patient for his benefit, the ethical problems are far less than when this potentially extremely dangerous method is used "in 15 patients with normal hearts, undergoing bronchoscopy for other reasons." Nothing was said about what was told any of the subjects, and nothing was said about the granting of permission, which was certainly indicated in the 15 normal subjects used.

Example 21. This was a study of the effect of exercise on cardiac output and pulmonary-artery pressure in 8 "normal" persons (that is, patients whose diseases were not related to the cardiovascular system), in 8 with congestive heart failure severe enough to have recently required complete bed rest in 6 with hypertension, in 2 with aortic insufficiency, in 7 with mitral stenosis and in 5 with pulmonary emphysema.

Intracardiac catheterization was carried out, and the catheter then inserted into the right or left main branch of the pulmonary artery. The brachial artery was usually catheterized; sometimes, the radial or femoral arteries were catheterized. The subjects exercised in a supine position by pushing their feet against weighted pedals. "The ability of these patients to carry on sustained work was severely limited by weakness and dyspnea." Several were in severe failure. This was not a therapeutic attempt but rather a physiologic study.

Bizarre Study

Example 22. There is a question whether ureteral reflux can occur in the normal bladder. With this in mind, vesicoourethrogramraphy was carried out on 25 normal babies less than forty-eight hours old. The infants were exposed to x-rays while the bladder was filling and during voiding. Multiple spot films were made to record the presence or absence of ureteral reflux. None was found in this group, and fortunately no infection followed the catheterization. What the results of the extensive x-ray exposure may be, no one can yet say.

COMMENT ON DEATH RATES

In the foregoing examples a number of procedures, some with their own demonstrated death rates, were carried out. The following data were provided by 3 distinguished investigators in the field and represent widely held views.

Cardiac catheterization: right side of the heart, about 1 death per 1000 cases; left side, 5 deaths per 1000 cases. "Probably considerably higher in some places, depending on the portal of entry." (One investigator had 15 deaths in his first 150 cases.) It is possible that catheterization of a hepatic vein or the renal vein would have a lower death rate than that of catheterization of the right side of the heart, for if it is properly carried out, only the atrium is entered en route to the liver or the kidney, not the right ventricle, which can lead to serious cardiac irregularities. There is always the possibility, however, that the ventricle will be entered inadvertently. This occurs in at least half the cases, according to 1 expert — "but if properly done is too transient to be of importance."

Liver biopsy: the death rate here is estimated at 2 to 3 per 1000, depending in considerable part on the condition of the subject.

Anesthesia: the anesthesia death rate can be placed in general at about 1 death per 2000 cases. The hazard is doubtless higher when certain practices such as deliberate evocation of ventricular extrasystoles under cyclopropane are involved.

PUBLICATION

In the view of the British Medical Research Council it is not enough to ensure that all investigation is carried out in an ethical manner: it must be made unmistakably clear in the publications that the properties have been observed. This implies editorial responsibility in addition to the investiga-
MEDICAL PROGRESS

IDIOPATHIC THROMBOCYTOPENIC PURPURA (Concluded)*

MARIO BALDINI, M.D.+1

PROVIDENCE, RHODE ISLAND

SYMPTOMATIC IMMUNOLOGIC THROMBOCYTOPENIC PURPURA

Association with Virus Disorders

Probably only chronic thrombocytopenic purpura is truly idiopathic. The acute form is often preceded by a "viral" infection, particularly the exanthematosus infections of children, and may therefore have a clear etiology.

Viruses have been associated with thrombocytopenia in various ways. Recent studies, including those of me and my co-workers,1,2 have shown that human blood platelets contain large amounts of sialic acid (assumed to be the virus receptor) and that myxoviruses are adsorbed to and eluted from blood platelets. In this process of adsorption and elution blood platelets undergo severe morphologic changes and become agglutinated. These and other experiments strongly suggest that blood platelets may serve as carriers of viruses in the circulation and that, in the process, they may become damaged and partially destroyed. The thrombocytopenia that, on occasion, is observed during the acute phase of viral infection could be related to the viremia itself and to the capacity of the virus to alter the circulating platelets. It is also possible that production of platelets is altered in these circumstances since viruses

*As far as principle goes, a parallel can be seen in the recent Mapp decision by the United States Supreme Court. It was stated there that evidence unconstitutionally obtained cannot be used in any judicial decision, no matter how important the evidence is to the ends of justice.

†Supported by a United States Atomic Energy Commission contract (49-1-3596).

‡Director, Division of Hematologic Research, Pawtucket Memorial Hospital and Brown University Institute for Health Sciences.