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

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SPECIAL ARTICLE

ETHICS AND CLINICAL RESEARCH*

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BOSTON

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,[1] ". . . 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... basis for the charges is broad.‡

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

Experimentation in man takes place in ... areas: in self-experimentation; in patient vol... and normal subjects; in therapy; and in the d... areas of *experimentation on a patient not for h... fit but for that, at least in theory, of pati... general.* The present study is limited to th... category.

REASONS FOR URGENCY OF STUDY

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

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

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.

MONEY AVAILABLE FOR RESEARCH EACH YEAR

	MASSACHUSETTS GENERAL HOSPITAL	NATIONAL INSTITUTES OF HEALTH*
1945	$ 500,000†	$ 701,800
1955	2,222,816	36,063,200
1965	8,384,342	436,600,000

*National Institutes of Health figures based upon decade averages, including funds for construction, kindly supplied by Dr. John Sherman, of National Institutes of Health.
†Approximation, supplied by Mr. David C. Crockett, of 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 future 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[2] 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 in the 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,[3] 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,[4] 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-

*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 sulfonamides were for many years the only antibacterial drugs effective in shortening the duration of acute streptococcal pharyngitis and in reducing its suppurative 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 ward 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 the present study was undertaken on 50 patients including mental defectives 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 on 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 the

prolonged morbidity and high mortality of ic anemia" and that ". . . chloramphenicol-ed aplastic anemia can be related to dose . . ." im of the study was "further definition of the logy of the drug. . . ."

y-one randomly chosen patients were given 2 or 6 gm. of chloramphenicol per day; 12 l patients were used. "Toxic bone-marrow ssion, predominantly affecting erythropoiesis, loped in 2 of 20 patients given 2.0 gm. and in 21 given 6 gm. of chloramphenicol daily." The dose is recommended for routine use.

mple 6. In a study of the effect of thymectomy survival of skin homografts 18 children, three half months to eighteen years of age, about to go surgery for congenital heart disease, were ed. Eleven were to have total thymectomy as of the operation, and 7 were to serve as con- As part of the experiment, full-thickness skin rafts from an unrelated adult donor were su- to the chest wall in each case. (Total thymec- s occasionally, although not usually part of mary cardiovascular surgery involved, and as it may not greatly add to the hazards of the ary operation, its eventual effects in children known.) This work was proposed as part of a nge study of "the growth and development of children over the years." No difference in the l of the skin homograft was observed in the 2

mple 7. This study of cyclopropane anesthesia ardiac arrhythmias consisted of 31 patients. verage duration of the study was three hours, ng from two to four and a half hours. "Minor al procedures" were carried out in all but 1 ct. Moderate to deep anesthesia, with endotra- intubation and controlled respiration, was Carbon dioxide was injected into the closed atory system until cardiac arrhythmias ap- Toxic levels of carbon dioxide were ed and maintained for considerable periods. the cyclopropane anesthesia a variety of ogic cardiac arrhythmias occurred. When the dioxide tension was elevated above normal, icular extrasystoles were more numerous than the carbon dioxide tension was normal, ven- ar arrhythmias being continuous in 1 subject inety minutes. (This can lead to fatal fibrilla-

mple 8. Since the minimum blood-flow re- ments of the cerebral circulation are not accu- known, this study was carried out to de- "cerebral hemodynamic and metabolic ges . . . before and during acute reductions in al pressure induced by drug administration or postural adjustments." Forty-four patients erages varied from the second to the tenth were involved. They included normotensive ts, those with essential hypertension and fi- 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 in 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. Accordingly, the surgeon rubbed localized areas of the parietal and visceral peritoneum with a small ball sponge as discretely 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 unanesthetized patients were studied through catheterization of the left side of the heart transeptally. 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 transbronchially. 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 transected 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 transcutaneous 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 technic, not of therapy, in the 14 normal subjec

Studies to Improve the Understanding of Disease

Example 14. In this study of the syndrom impending hepatic coma in patients with cir of the liver certain nitrogenous substances administered to 9 patients with chronic alcoh and advanced cirrhosis: ammonium chloride, monium citrate, urea or dietary protein. In al tients a reaction that included mental disturba a "flapping tremor" and electroencephalogr changes developed. Similar signs had occurr only 1 of the patients before these substance administered:

> The first sign noted was usually clouding of th sciousness. Three patients had a second or a third of administration of a nitrogenous substance wa same results. It was concluded that marked resem between this reaction and impending hepatic coma plied that the administration of these [nitrogenou stances to patients with cirrhosis may be hazardous

Example 15. The relation of the effects of ed ammonia to liver disease was investigated normal subjects, 6 with acute virus hepatiti with cirrhosis, and 8 miscellaneous patients these patients had neurologic changes w with either hepatitis or cirrhosis.

The hepatic and renal veins were ca Ammonium chloride was administered b After this, a tremor that lasted for three da oped in 1 patient. When ammonium chlo ingested by 4 cirrhotic patients with tra mental confusion the symptoms were exa during the test. The same thing was true o patient in another group.

Example 16. This study was directed tow termining the period of infectivity of infectio atitis. Artificial induction of hepatitis was c out in an institution for mentally defective chi in which a mild form of hepatitis was endem parents gave consent for the intramuscular i or oral administration of the virus, but not said regarding what was told them concern appreciable hazards involved.

A resolution adopted by the World Medic ciation states explicitly: "Under no circumst a doctor permitted to do anything which weaken the physical or mental resistance man being except from strictly therapeuti phylactic indications imposed in the interes patient." There is no right to risk an inj person for the benefit of others.

Example 17. Live cancer cells were inject 22 human subjects as part of a study of immu cancer. According to a recent review, the (hospitalized patients) were "merely sta would be receiving 'some cells'" — ". . . cancer was entirely omitted. . . ."

Example 18. Melanoma was transplanted

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nter to her volunteering and informed mother, the hope of gaining a little better understanding ancer immunity and in the hope that the pro- ion of tumor antibodies might be helpful in the ment of the cancer patient." Since the daughter on the day after the transplantation of the tu- into her mother, the hope expressed seems to been more theoretical than practical, and the hter's condition was described as "terminal" at time the mother volunteered to be a recipient. primary implant was widely excised on the ty-fourth day after it had been placed in the her. She died from metastatic melanoma on the hundred and fifty-first day after transplantation. evidence that this patient died of diffuse mela- that metastasized from a small piece of trans- ted tumor was considered conclusive.

chnical Study of Disease

ample 19. During bronchoscopy a special nee- was inserted through a bronchus into the left m of the heart. This was done in an unspecified ber of subjects, both with cardiac disease and normal hearts.

e technic was a new approach whose hazards at the beginning quite unknown. The subjects normal hearts were used, not for their possible fit but for that of patients in general.

ample 20. The percutaneous method of cathe- tion of the left side of the heart has it is re- led to 8 deaths (1.09 per cent death rate) other serious accidents in 732 cases. There was, efore, need for another method, the trans- chial approach, which was carried out in the ent study in more than 500 cases, with no ths.

anted that a delicate problem arises regarding much should be discussed with the patients lved in the use of a new method, nevertheless e the method is employed in a given patient is benefit, the ethical problems are far less than this potentially extremely dangerous method ed "in 15 patients with normal hearts, under- bronchoscopy for other reasons." Nothing was about what was told any of the subjects, and ing was said about the granting of permission, uch was certainly indicated in the 15 normal sub- used.

ample 21. This was a study of the effect of ise on cardiac output and pulmonary-artery sure in 8 "normal" persons (that is, patients diseases were not related to the cardiovascu- ystem), in 8 with congestive heart failure severe gh to have recently required complete bed rest, with hypertension, in 2 with aortic insuffi- y, in 7 with mitral stenosis and in 5 with pul- ary emphysema.

racardiac catheterization was carried out, and atheter then inserted into the right or left main ch 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, vesicourethrography was carried out on 26 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[5] 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 proprieties have been observed. This implies editorial responsibility in addition to the investiga-

tor's. The question rises, then, about valuable data that have been improperly obtained.* It is my view that such material should not be published.[5] There is a practical aspect to the matter: failure to obtain publication would discourage unethical experimentation. How many would carry out such experimentation if they *knew* its results would never be published? Even though suppression of such data (by not publishing it) would constitute a loss to medicine, in a specific localized sense, this loss, it seems, would be less important than the far reaching moral loss to medicine if the data thus obtained were to be published. Admittedly, there is room for debate. Others believe that such data, because of their intrinsic value, obtained at a cost of great risk or damage to the subjects, should not be wasted but should be published with stern editorial comment. This would have to be done with exceptional skill, to avoid an odor of hypocrisy.

Summary and Conclusions

The ethical approach to experimentation in man has several components; two are more important than the others, the first being informed consent. The difficulty of obtaining this is discussed in detail. But it is absolutely essential to *strive* for it for moral, sociologic and legal reasons. The statement that consent has been obtained has little meaning unless the subject or his guardian is capable of understanding what is to be undertaken and unless all hazards are made clear. If these are not known, [illegible] too, should be stated. In such a situation the sub[illegible] at least knows that he is to be a participant in [illegible] experiment. Secondly, there is the more reli[illegible] safeguard provided by the presence of an in[illegible] gent, informed, conscientious, compassionate [illegible] sponsible investigator.

Ordinary patients will not knowingly risk [illegible] health or their life for the sake of "science." E[illegible] experienced clinician investigator knows this. W[illegible] such risks are taken and a considerable numbe[illegible] patients are involved, it may be assumed tha[illegible] formed consent has not been obtained in all c[illegible]

The gain anticipated from an experiment m[illegible] commensurate with the risk involved.

An experiment is ethical or not at its inceptio[illegible] does not become ethical *post hoc* — ends d[illegible] justify means. There is no ethical distinction [illegible] tween ends and means.

In the publication of experimental results it [illegible] be made unmistakably clear that the propo[illegible] have been observed. It is debatable whether [illegible] obtained unethically should be published even [illegible] stern editorial comment.

References

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*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.

MEDICAL PROGRESS

IDIOPATHIC THROMBOCYTOPENIC PURPURA (Concluded)*

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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 exanthematous 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,[10,78] have shown that human blood platelets contain large amo[illegible] sialic acid (assumed to be the virus recept[illegible] that myxoviruses are adsorbed to and elut[illegible] blood platelets. In this process of adsor[illegible] elution blood platelets undergo severe mor[illegible] changes and become agglutinated. These an[illegible] experiments[79,80] strongly suggest that blood [illegible] may serve as carrier of viruses in the circula[illegible] that, in the process, they may become dama[illegible] partially destroyed. The thrombocytopenia [illegible] occasion, is observed during the acute phase [illegible] infection could be related to the viremia [illegible] to the capacity of the virus to alter the [illegible] platelets. It is also possible that production [illegible] lets is altered in these circumstances since

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