

IN HOUSE CORRESPOND (MEMOS)
To PV OCT 1986 - APR 1987

City and County of San Francisco



Department of Public Health

San Francisco General Hospital
Medical Center

October 15, 1986

TO: ✓ Paul Volberding, M.D., Director AIDS Activities Division
Lawrence Kaplan, M.D., Ward 86 Medical Director

FROM: Gayling Gee, RN, Head Nurse, Ward 86 *GG*

RE: Administrative Nurse I

Thank you for participating in the interview process for the Administrative Nurse I position. As you know, it is a vital position to me and the clinic in strengthening the delivery of nursing care on Ward 86. Per our discussions about the various applicants, I have selected and offered the position to Mr. William A. Nelson. Bill graduated from Seattle University with a bachelor's degree in nursing in 1975. He comes to us with a comprehensive nursing background that includes 11 years of medical and surgical critical care, coronary care, post-operative, and nursing education experience. Bill has also worked on the 5A-5B AIDS inpatient unit since 1983, with both acting head nurse and charge nurse responsibilities and has demonstrated great skills in his clinical care. He is also enrolled in the Masters of Nursing program at San Francisco State University.

Bill has accepted the AN I position and will officially begin his duties on November 3, 1986. I know Bill will prove to be a valuable addition to the nursing staff. I look forward to working with him. Please join me in welcoming him to the staff.

cc: C. Wofsy, M.D.
D. Abrams, M.D.
R. Wilson, Adm. Analyst

City and County of San Francisco

Department of
Public Health

San Francisco General Hospital
Medical Center



October 15, 1986

TO: Chris Christenson, Personnel
FROM: Gayling Gee, RN, Head Nurse, Ward 86 *ggee*
RE: Administrative Nurse I

Per our discussion, I have selected Mr. William Nelson for the Administrative Nurse I position. I am requesting consideration for Mr. Nelson to be offered the AN I position beginning at Step 4 for the following reasons:

1. Mr. Nelson is a 1975 graduate of Seattle University with a BS in Nursing. He has had over eleven years of nursing experience, including medical and surgical critical care, post-operative and coronary care nursing.
2. He has supervisory experience that includes charge nurse, evening nursing supervisory and acting head nurse responsibilities.
3. Mr. Nelson has also had the unique experience of three years of inpatient AIDS nursing on Ward 5A-5B at San Francisco General Hospital. His clinical skills and knowledge background in AIDS is excellent; he would be able to step directly into his administrative role without requiring additional time for orientation to AIDS nursing care.

I feel that Mr. Nelson is uniquely qualified for this position and that a Step 4 is very appropriate to his experience and abilities.

Thank you for your assistance.

cc: R. Wilson, Adm. Analyst
P. Volberding, M.D.



October 17, 1986

TO: All Sub-Specialty Clinic Chiefs

FROM: Dick Fine, M.D. *DF*
Chief, Adult Medical Center

RE: Residents and Fellows from Outside U.C. System.

Many of you have recruited housestaff from other institutions to see patients in your specialty clinics. Some of these residents have not gone through the Hospital Training Staff Appointment process. All residents from non-U.C. institutions must have a Hospital Training Staff appointment in advance in order to comply with Hospital and University regulations. This is a liability and malpractice insurance issue, as well as documentation that the outside trainee did an official rotation with us. Completion of this process will also result in the trainee being assigned an ID number so that pharmacy, lab and X-Ray requisitions can be processed correctly. These forms are available from the School of Medicine/Dean's Office, U.C., Box 0410 (Tel: 476-4561).

Your cooperation is appreciated.

DF:ee

cc: Kaplan

Gee

B. Woodruff

Bobbi

10-31

DEPARTMENT OF MEDICINE
SAN FRANCISCO GENERAL HOSPITAL

MEMORANDUM

DATE: October 15, 1986

TO: Clinical Faculty and Ward Attendings Dr. Paul Volberding

FROM: Chris Forsmark, M.D.
Chuck Daley, M.D.
Chief Medical Residents

RE: Ward Attending Coverage

During their stay here, each first and second year resident is assigned one day off per month. When the interns are off, the resident is responsible for caring for the team. When the resident is off, the interns are present and the ward attending is responsible for rounding with the interns. If for some reason you are unable to round with your team when your resident is off, the Chief Residents may be able to cover for you under special circumstances. We would appreciate it, however, if you would ask us to do this before the day that your resident is off as we have frequently made plans to round with some other team or are frequently tied up with generalized trouble-shooting on the weekend. In addition, if you need to be absent during your stint as ward attending, please arrange attending coverage for your team before you leave.

Attached please find copies of the Day Off and the Ward On-Call Schedules. Thank you very much.

RESIDENT: Larry Epstein, MD

INTERNS: Cameron Ashbaugh, MD
Colleen Riley, MD

4TH YEAR STUDENT: Rebecca Bicker

WARD: 5D

THE MEDICAL SERVICE
SAN FRANCISCO GENERAL HOSPITAL

DAY OFF SCHEDULE
NOVEMBER 1986

	<u>RESIDENT</u>	<u>INTERNS</u>
Sat. Nov 1		
Sun. Nov 2		Chesnutt, Berry
Sat. Nov 8		McLamb, Arredondo
Sun. Nov 9	Krieger	Freye, Lusher
Sat. Nov 15	Regan	Ashbaugh, Riley
Sun. Nov 16	Mashal	Fraser, McCartney
	Oken	
Sat. Nov 22	Epstein	Sellers, Tishman
Sun. Nov 23	Welsh	Chang, Hambleton
Sat. Nov 29	Kuhn	

THE MEDICAL SERVICE
SAN FRANCISCO GENERAL HOSPITAL
WARD ON-CALL SCHEDULE
NOVEMBER 1986

		<u>RESIDENT</u>	<u>INTERNS</u>	<u>RESIDENT</u>	<u>INTERNS</u>
Sat	1	Mashal	Freya, Lusher	Epstein	Ashbaugh, Riley
Sun	2	Welsh	Fraser, McCartney	Kuhn	Chang, Hambleton
Mon	3	Krieger	Chesnutt, Berry	Regan	McLamb, Arredondo
Tue	4	Mashal	Freya, Lusher	Epstein	Ashbaugh, Riley
Wed	5	Welsh	Fraser, McCartney	Oken	Sellers, Tishman
Thur	6	Krieger	Chesnutt, Berry	Regan	McLamb, Arredondo
Fri	7	Mashal	Freya, Lusher	Epstein	Ashbaugh, Riley
Sat	8	Welsh	Fraser, McCartney	Oken	Sellers, Tishman
Sun	9	Kuhn	Chang, Hambleton	Regan	McLamb, Arredondo
Mon	10	Mashal	Freya, Lusher	Epstein	Ashbaugh, Riley
Tue	11	Welsh	Fraser, McCartney	Oken	Sellers, Tishman
Wed	12	Kuhn	Chang, Hambleton	Krieger	Chesnutt, Berry
Thur	13	Mashal	Freya, Lusher	Epstein	Ashbaugh, Riley
Fri	14	Welsh	Fraser, McCartney	Oken	Sellers, Tishman
Sat	15	Kuhn	Chang, Hambleton	Krieger	Chesnutt, Berry
Sun	16	Regan	McLamb, Arredondo	Epstein	Ashbaugh, Riley
Mon	17	Welsh	Fraser, McCartney	Oken	Sellers, Tishman
Tue	18	Kuhn	Chang, Hambleton	Krieger	Chesnutt, Berry
Wed	19	Regan	McLamb, Arredondo	Mashal	Freya, Lusher
Thur	20	Welsh	Fraser, McCartney	Oken	Sellers, Tishman
Fri	21	Kuhn	Chang, Hambleton	Krieger	Chesnutt, Berry
Sat	22	Regan	McLamb, Arredondo	Mashal	Freya, Lusher
Sun	23	Epstein	Ashbaugh, Riley	Oken	Sellers, Tishman
Mon	24	Kuhn	Chang, TBA	Krieger	Chesnutt, TBA
Tue	25	Regan	Arredondo, TBA	Mashal	Lusher, Freya
Wed	26	Epstein	Ashbaugh, TBA	Welsh	McCartney, TBA
Thur	27	Kuhn	Chang, TBA	Krieger	Chesnutt, TBA
Fri	28	Regan	Arredondo, TBA	Mashal	Lusher, Freya
Sat	29	Epstein	Ashbaugh, TBA	Welsh	McCartney, TBA
Sun	30	Oken	Tishman, TBA	Krieger	Chesnutt, TBA

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SANTA BARBARA • SANTA CRUZ

SCHOOL OF MEDICINE

Department of Anatomic Pathology

Please address reply to the undersigned at

UNIVERSITY OF CALIFORNIA
SAN FRANCISCO GENERAL HOSPITAL
SAN FRANCISCO, CALIFORNIA 94110

October 30, 1986

To: Paul Volberding, M.D.
Oncology
Bldg. 80, Ward 84

From: David Abis, M.D.
Chief Resident
Anatomic Pathology

Edward L. Howes, Jr., M.D.
Professor of Pathology
Chief of Service
Anatomic Pathology

*PLEASE REVIEW ?
try to improve
our support for
pathology.*

*Thanks -
PR*

We are writing this letter to enlist your help in improving our autopsy percentage. For many years, until July 1, 1986, it has been approximately 50%. It has suddenly fallen to 30%. With all the interesting cases that come under your care; with all the new therapeutic agents being used on these patients and with the danger of recrudescence of disease for which we have means of prevention and treatment; we regard autopsies as making an important contribution to the knowledge necessary to maintain the general health of our community, the teaching programs of the University and the final result of certain chemotherapeutic agents.

We are enclosing a copy of an article from a recent American Journal of Medicine on the subject and hope that you will take a few moments to read it because of its completeness and persuasive character.

If you have any questions about permissions, notification of the coroner, or the availability of material from autopsies for teaching, anatomic or surgical therapeutic studies, research or medical publication, please feel free to call us at any time, extension 8215.

DA/ELH:amz
Encl. 1

Autopsy: Moribund Art or Vital Science?

STEPHEN J. MCPHEE, M.D.
KENT BOTTLES, M.D.
San Francisco, California

The autopsy rate in the United States has fallen dramatically in the past 40 years. Factors contributing to its decline include diagnostic over-confidence among clinicians, competing demands upon pathologists, difficulties obtaining consent from families, and its costs. The benefits of autopsy are clear: confirmation, clarification, and correction of antemortem diagnoses; discovery and definition of new diseases; evaluation of new diagnostic tests, new surgical techniques, and new drugs; investigation of environmental and occupational diseases; reassurance of family members; and contributions to medical and epidemiologic research. Proposals to revive the autopsy are reviewed, including altering the method of obtaining consent, altering autopsy procedures, structuring teaching around the autopsy, training autopsy pathologists in anatomic subspecialties, reinstating minimal autopsy requirements for hospital accreditation, providing financial support, and educating the public and the medical profession about its values. Accomplishing these changes quickly will prevent loss of its many benefits to the clinician, family, hospital, and society.

To investigate the causes of death, to examine carefully the condition of organs, after such changes have gone on in them as to render existence impossible and to apply knowledge to the prevention and treatment of disease, is one of the highest objects of the Physician

William Osler

The autopsy is in decline: the autopsy rate in the United States has fallen from 50 percent of deaths in the 1940s to 15 percent today [1]. There is disagreement, however, about whether this decline should be applauded, ignored, or deplored.

Criticism and apathy toward the autopsy is not new. In the 17th century, Sydenham wrote: "Some physicians pompously and speciously prosecute the promotion of medicine by search into the bowels of the dead." More recently, autopsy has come under attack from several directions [2]. Clinicians maintain that the autopsy is inefficient, irrelevant, and unnecessary because of sophisticated new diagnostic tests. Pathologists complain it is time-consuming, disagreeable, thankless, and totally ineffective in changing the behavior of clinicians. Some families find an autopsy disagreeable. Hospital administrators complain about the costs.

There are many consequences of the declining rate of autopsy in the United States. First, clinicians who err may continue to do so. Second, vital statistics based upon death certificates become increasingly inaccurate. Third, undiagnosed contagious diseases are

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missed. Fourth, accidental deaths, suicides, and homicides go undetected. Fifth, new environmental hazards and iatrogenic diseases may go unrecognized. Sixth, the clinical training of medical and pathology students may be hampered. Finally, assessments of the quality of medical care are impaired.

When the history and benefits of the autopsy are reviewed, the seriousness of its decline becomes obvious. We suggest effective plans to revitalize this important procedure.

THE PROCEDURE

The word autopsy derives from the Greek for "seeing for oneself." After examination for exterior abnormalities, including growths, wounds, and surgical scars, a surgical incision is made to allow gross inspection of the internal organs. The brain and spinal cord are then removed. The removed organs are weighed, measured, and examined, and incisions are made in each to identify fine details. Next, tissue samples are obtained for light and electron microscopy, cultures, and toxicologic analysis. After autopsy, the skin incisions are sewn up and the body released to the mortuary for burial. Actual dissection takes two to four hours depending on whether the autopsy is total or limited, but the final report is often not finished for months. About three quarters of the autopsies performed in the United States are total [1,3].

HISTORY OF THE AUTOPSY

The roots of the autopsy can be traced back some 3,500 years to the Babylonians [4]. They attempted to foretell the future by examining the liver or entrails of sacrificed animals. In ancient Egypt, the art of embalming became highly developed. Hippocrates considered autopsy "an unpleasant, if not cruel, task." Erasistratus, who did autopsies in Alexandria, first described cirrhosis, noting that "the liver of a man who died from dropsy was hard as a stone, but in a man who died of snakebite, the liver was soft" [5]. Galen observed wounded men and examined two human skeletons obtained by chance, one washed out of a grave during a flood and one of an unburied robber picked clean by vultures. The ancient Jews examined slaughtered animals for signs of disease. In 100 A.D., students of Rabbi Ismael obtained the body of a young prostitute who had been executed. They boiled it in order to count the number of bones and found 252.

The general attitude of early Church leaders toward autopsy was unfavorable. However, when Pope Alexander died suddenly in 1410, an autopsy was performed. Pope Sixtus IV issued a bill permitting autopsy by students at Padua and Bologna. In the late 15th century, Benivieni published a book entitled "On Some Remarkable Hidden Causes of Diseases and of Cures" based upon his clinical experiences; autopsy had been

carried out in many of the cases. In 1679, Bonetus published a collection of more than 3,000 autopsy reports by some 450 physicians, ranging from Galen to the outstanding physicians of the late 17th century, including Bartholin, Fallopius, Harvey, Malpighi, Vesalius, and Willis. In the 18th century, Morgagni began to correlate clinical observations with autopsy findings. Bichat, even before the microscope was developed, stressed the importance of examining tissues obtained from the organs. In the late 19th century, Rokitsansky is alleged to have performed 30,000 autopsies. Only at the end of his career, however, was the microscope available. Virchow, 17 years younger, grew up with the microscope; he published a book on autopsy technique [4].

Early in the 20th century, many outstanding clinicians spent considerable time in the autopsy room. They were frequently good pathologists. Osler epitomized the best of the era. He believed it important for the clinician to conduct his own postmortem examinations. He amassed an extensive experience with almost 1,000 autopsies over a 13-year span in Montreal and Philadelphia. He published monographs based on 105 autopsies in patients with lobar pneumonia and 56 autopsies in patients who had typhoid; his 1885 Gouldstonian lecture on valvular endocarditis was based upon his pathologic and clinical observations [6].

DECLINE OF AUTOPSY IN THE UNITED STATES

The autopsy rate in the United States has fallen dramatically from about 50 percent of deaths after World War II to a mere 15 percent today. In general, autopsy rates are higher in teaching hospitals than in community hospitals and are higher in larger than in smaller hospitals. In the 330-bed Peter Bent Brigham Hospital, autopsy rates were 75 percent in 1960, 71 percent in 1970, and 38 percent in 1980 [7]. In the 560-bed Moffitt Hospital of the University of California at San Francisco, autopsy rates were 57 percent in 1962, 46 percent in 1982, and 39 percent in 1983 [8]. Autopsy rates are lower for women and are much lower for the elderly. Peak autopsy rates of 50 to 80 percent occur in the third decade of life; the nadir occurs with a 2 percent rate by age 90 [9]. Unfortunately, the number of clinically "missed" diagnoses discovered at autopsy is higher in older patients [10,11].

Autopsy rates are much lower for certain fatal conditions, such as stroke [9]. Geller [1] illustrated the skewed pattern of autopsy rates by diagnosis. Of the 69 categories for causes of death in the 1977 U.S. Vital Statistics, autopsy was performed in more than 50 percent of cases for only six: homicide, abortion, other complications of pregnancy, meningococcal infections, bacillary dysentery and amebiasis, and other external causes of death. These six conditions accounted for fewer than 2 percent of U.S. deaths in 1977. By con-

trast, the autopsy rate for cardiovascular deaths was only 10 percent and for cancer, only 11 percent.

Autopsy rates can vary considerably on the different services of a single hospital. In 1983 at Moffitt Hospital (UCSF), the rates varied between 7 percent in the emergency department and 66 percent in the obstetrics and gynecology wards [8].

REASONS FOR DECLINE OF AUTOPSY

Several factors have contributed to the declining autopsy rate [12,13]. First, pathologists have many other responsibilities and demands upon their time. Surgical pathology and clinical laboratory pathology serve living patients and are considered more important than autopsy. Thus, the technicians cut the paraffin blocks of autopsy material last, the staff pathologists assign a low priority to "signing out" autopsies, and the secretaries type the autopsy reports last [12]. These delays mean that clinicians and families may not receive autopsy results for months and discourage physicians from seeking permission for future autopsies.

Second, autopsy is often relegated to the most junior members of pathology departments, who often lack the clinicopathologic experience of their senior colleagues. In addition, unlike surgical or experimental pathology, autopsy does not serve as a basis for professional recognition and advancement. These factors contribute to the poor image of many autopsy pathologists [12].

Third, clinicians are requesting fewer autopsies. Greater diagnostic confidence has led many clinicians to believe that the autopsy is no longer necessary. In addition, many physicians regard death as a failure to be quickly forgotten. Thus, they do not request or attend postmortem examinations of their patients [14]. Some physicians may fear that autopsy findings will increase malpractice risks [15].

Fourth, the process of obtaining consent for autopsy is cumbersome. Generally, the surviving spouse or next of kin may authorize or prohibit autopsy. In California, a person may authorize postmortem examination prior to death through his or her will. Otherwise, a written authorization signed by the next of kin or a telegram is required. The consent can limit the extent of the autopsy to be performed [16]. The coroner or medical examiner may order an autopsy even without the consent of the next of kin to determine the cause and manner of death in some cases. In addition, the negative attitudes of morticians, who object to delays in embalming, are often transmitted to families. The "red tape" of the consent forms may interfere.

Fifth, family members who must request or consent to autopsy are in emotional turmoil. They frequently say that their loved one has "suffered enough," perceiving the procedure as a further injury or indignity [17]. They may fear disfigurement of the body not realizing that the

pathologist's surgical incisions are inapparent to mourners viewing an open casket. In other cases, families may raise religious or cultural objections to autopsy [18]. The relatives of the dying patient may be too grief-stricken to request an autopsy or to understand its utility. They may resent not having been told of autopsy results for other family members in the past. Poor rapport with hospital staff caregivers previously unknown to family members may decrease the likelihood that they will grant autopsy permission.

Sixth, in 1971, the Joint Commission on Accreditation of Hospitals eliminated the required 20 percent autopsy rate for hospital accreditation. The intent of the JCAH was to emphasize the quality and interpretation of autopsy findings more than the number performed [19]. However, since then, the number of autopsies in the United States has declined dramatically.

Finally, autopsies are expensive and their costs generally non-reimbursable. In 1820, Sir Isaac Cooper paid two men 13 pounds to steal the body of a man whose iliac artery he had ligated some 24 years before. The money was used to pay the gravediggers, guards, porter, and coach and carriage [20]. Today, autopsy expenses are much greater. In academic centers, each autopsy now costs as much as \$900 to \$1,100 [21,22]. Costs of autopsies required by the medical examiner or coroner are supported by the state or county. The Veterans Administration hospital system finances its autopsies through Congressional appropriations as a part of the hospital's general operating expenses. Community hospitals generally allocate autopsy costs to other income-producing departments. University hospitals generally budget the autopsy service as a hospital service rather than as a medical school cost. The American Hospital Association considers the cost of autopsy an overhead cost of the hospital. Third-party payers do not recognize autopsy as a direct medical service to a patient (a cadaver is not considered a patient). They support autopsies only through reimbursement of charges from income-producing departments [20]. Medicare does recognize the hospital's overhead costs incurred by autopsy services as administrative and quality control activities under its Part A, and plans have been developed to include these costs in the hospital's base under prospective reimbursement schemes [19]. Undoubtedly, however, the advent of prospective reimbursement will put even greater financial pressures on autopsy services [23,24].

BENEFITS OF AUTOPSY

The decline in autopsy rates has not gone unnoticed. In analyzing the consequences of this decline, many authors have clearly defined the benefits of autopsy. Although some physicians argue that the autopsy is no longer needed because of new diagnostic tests, many

TABLE I Published Studies Comparing Autopsy Findings with Clinical Diagnosis

Reference	Number of Cases	Percent with Missed Major Diagnoses of Clinical Relevance*	Comments
[64]	3,000	5.0	
[65]	600	8.0	
[66]	1,000	11.0	
[67]	1,106	6.0	
[68]	265	7.0	
[69]	200	8.0	
[28]	2,734	40.0	Overall, 26 percent had clinically undiagnosed cancer
[10]	383	7.3	
[70]	252	6.0	Overall, 11.7 percent showed major discrepancies
[71]	1,096	18.7	
[29]	154	15.0	Increasing the necropsy rate produced a higher rate of confirmation of clinical diagnoses
[61]	1,076	9.0	
[47]	1,152	39.0	Diagnostic accuracy did not improve with length of time in hospital
[72]	200	11.0	9.5 percent disagreement about cause of death 1.5 percent disagreement about major underlying diagnosis
[13]	286	11.0	
[49]	1,405	27.0	Tumor undiagnosed in 27 percent; diagnostic accuracy inversely proportional to age of patient
[55]	100	13.0	In 24 percent, cause of death was not in clinical diagnosis
[73]	272	4.0	Includes coroner's cases; overall, 29 percent showed major disagreement about cause of death
[7]	300	10.3	An additional 11.8 percent showed important discrepancies without definite impact upon survival
[4]	2,537	10.2	Overall, 61 percent showed important unexpected postmortem findings

* Includes only major diagnoses missed clinically and discovered at postmortem examination with potential impact on patient survival.

studies demonstrate its importance in confirming, clarifying, and correcting antemortem diagnoses [25,26]. For example, Lundberg and Voigt [27] found that a presumptive diagnosis of coronary artery disease in sudden, unexpected death in adults was often unreliable. At autopsy, they found that 51 percent of 100 such deaths were due to non-coronary conditions, such as pulmonary emboli, intoxication, or hemorrhage.

Even when clinicians are "certain" of major diagnoses, they are wrong in 5 to 40 percent of cases at autopsy (Table I). For example, in a series of 2,734 autopsies in patients who had cancer there was a 40 percent rate of serious clinical diagnostic errors. In 26 percent of the cases, cancer had not been diagnosed before death [28]. In another series, in 15 percent of autopsies, readily diagnosable and treatable conditions (such as miliary tuberculosis) had been missed clinically [29]. Goldman et al [7] retrospectively analyzed 100 randomly selected autopsies from 1960, 1970, and 1980 at the Peter Bent Brigham Hospital. In all three eras, eight to 12 percent of the autopsies revealed major "missed" diagnoses that, with antemortem identification and treatment, might have prolonged survival. These included pulmonary emboli, myocardial infarction, systemic infection, tumor, and hemorrhage. Another 12 percent of the autopsies showed clinically

missed major diagnoses for which treatment would not have changed the outcome. Over-reliance on radionuclide scanning, ultrasonography and computed tomography in several cases contributed directly to the failure to identify the major diagnosis. Gambino [30] found a 4.4 percent rate of incorrect major diagnoses directly attributable to the incorrect results of diagnostic tests.

Autopsy also aids in the discovery and definition of new diseases such as Legionnaire's disease, the toxic shock syndrome, and the acquired immune deficiency syndrome [31]. Angrist [32] presented a list of 73 entities revealed and elucidated in recent years by autopsy findings.

Autopsy is critically important to the evaluation of new diagnostic tests, new surgical techniques, new implantable mechanical devices [33], and new drugs [34]. For example, autopsy studies elucidated doxorubicin (Adriamycin) cardiotoxicity [1]. In addition, autopsy supplies organs for transplantation. Finally, autopsy studies may reveal the influence of environmental factors on disease—for example, the development of hepatic angiosarcomas in vinyl chloride factory workers [35]. Investigation of environmental and occupational diseases by autopsy allows compensation of victims, complements and validates epi-

demologic studies, and is the most likely evidence to result in adoption of preventive measures [35].

Autopsy also offers many benefits to the families of dying patients [36]. Especially in the death of children, the findings at autopsy may help to alleviate guilt feelings of family members. In a recent case in our hospital, chemotherapy in a 14-year-old girl with leukemia was interrupted because of major family problems. When she died unexpectedly, her mother was convinced that the family difficulties had led to recurrent leukemia. Autopsy, however, showed no leukemia. Death had occurred, instead, from widespread infection. Knowing the cause of death relieved the mother's guilt and helped her to accept her daughter's death.

Certainty about the cause of death may reassure family members. Sometimes, a criminal charge such as child abuse or manslaughter may be dropped on the basis of autopsy findings [37]. Autopsy may uncover contagious diseases such as tuberculosis, allowing screening and early treatment of affected family members. Similarly, autopsy may benefit family members by discovery of hereditary disorders, allowing genetic counseling and prophylactic treatment [38]. Autopsy may establish the accidental nature of a death and may substantially increase the insurance benefits accruing to family members [25]. Finally, by allowing the extension of medical knowledge and the donation of organs and tissues for transplantation, autopsy can provide consolation that the death has helped someone else to live [17].

Autopsy enables hospitals to monitor the quality of care (including outcomes from new surgical and chemotherapeutic techniques), to detect contagious diseases, to discover nosocomial infections, and to investigate iatrogenic illness. Derman [39] has argued that autopsy is the ultimate "outcome" measure of medical care quality, far better than "process" measures such as length of stay or per diem cost. It is far more important, he says, to show that there are too many pulmonary emboli in a hospital than to show that the length of stay for pulmonary embolism is too long. Autopsy, by providing reassurance to families, by eliminating suspicion, by substituting fact for conjecture, and by improving quality of care may also reduce the number of malpractice claims and allow the construction of better defenses to meet such claims [15].

Autopsies performed for forensic purposes attempt to establish the cause, time, and manner of death, and the circumstances preceding and surrounding death [40]. Forensic autopsies are also used for insurance claims, for documentation of industrial accidents, and for identification of bodies.

Autopsy also aids medical research, in such areas as basic cellular pathology, carcinogenesis, and atherogenesis [41-43], and medical education in both

anatomy and pathology [40,44,45]. In addition, mortality statistics based upon autopsy findings are far more accurate than vital statistics based upon death certificate data alone [46-49]. By aiding epidemiologic research in the early detection of communicable diseases and in generating accurate mortality statistics, autopsy helps health policy-makers to establish priorities and allocate resources [50].

REVIVING THE AUTOPSY

What, then, can be done to revive the autopsy? First, United States hospitals might alter the method of obtaining consent for autopsy. In Scandinavia, hospitals obtain permission at the time of admission for routine autopsy in all hospital deaths unless the family signs a form refusing postmortem examination within 12 hours [12]. This has resulted in an autopsy rate of more than 90 percent. Brown [17] has also suggested that teaching hospitals support autopsy advocates who are trained in approaching the newly bereaved to obtain permission for autopsy. In an articulate, sensitive, and informative fashion, such persons could stress the importance of the autopsy, emphasizing its benefits for the family.

Second, pathologists might alter autopsy procedures. A limited autopsy may answer questions about the cause of death at much less expense than that of a complete autopsy [51]. Selection for microscopic investigation might be based upon the gross findings [52]. Saladino and Dailey [53] have proposed the "problem-oriented" autopsy. Goodale [54] recommended that autopsies be tailored to answer specific objectives, and that cases may be selected for autopsy: (1) when the clinical diagnosis is unknown or uncertain; (2) to provide a random sample of the hospital's population; (3) to meet educational and investigational needs; and (4) to monitor the effects of new drugs.

Third, hospitals might structure more teaching activities around the autopsy, such as autopsy grand rounds [55], clinicopathological conferences, and teaching of gross and microscopic anatomy and pathology.

Fourth, Roberts [12] has proposed that pathologists be trained in anatomic pathology "subspecialties." This specialization may improve the image of autopsy pathologists and provide more expert analysis.

Fifth, communication between pathologists, clinicians, and families might be improved. This may be done by altering the autopsy report format or substance, by ensuring speedy reporting of results, by identifying the major clinical questions to be answered, and by encouraging pathologists to report their autopsy findings directly to the patients' families. Interventions to improve communications with attending and resident staffs, to issue initial postmortem diagnoses promptly,

and to forward appropriate findings to quality-of-care committees have resulted in improved autopsy rates [56]. Pathologists who have held post-autopsy conferences for families to provide information on the cause of death and its meaning have found them to be greatly appreciated [57,58].

Sixth, the JCAH might reinstate minimal autopsy requirements, perhaps differing for each hospital or class of hospitals appropriate to its patient profile [59]. Clinicians who obtain high autopsy rates might be rewarded with discounts on their professional liability premiums [60].

Seventh, several financing mechanisms to support autopsy costs have been proposed. Some believe that medical schools should share these costs with university hospitals. Clark [61] has proposed that hospital and physician malpractice insurers share autopsy costs with hospitals. Orsini [62] suggested that employers and unions should include autopsy in their fringe benefit programs. Physicians performing research using autopsy materials may seek grant support for autopsy costs.

Eighth, both the public and the medical profession must be educated about the values of autopsy. Such public education is probably most readily accomplished through the media at times other than the time of death. To attempt such education for the grief-stricken families of deceased patients is often both unrewarding and unfair to clinicians and families [17]. For hospital personnel, education about the purpose and potential value of autopsy has been accomplished through the use of

videotapes designed to dispel misconceptions and improve attitudes among nurses, social workers, clergy, hospital administrators, and physicians [56].

Finally, Carter has proposed the development of a computerized National Autopsy Data Bank [63]. This would incorporate pathologic, biomedical, demographic and epidemiologic information from all autopsies performed in the United States and would allow more accurate mortality statistics. It would also allow new diseases to be identified and research questions to be answered more easily. By demonstrating the benefits of autopsy to clinicians, the data bank might encourage physicians to work harder to obtain permission for autopsy.

CONCLUSIONS

The reasons for the recent dramatic decline in the autopsy rate in the United States are clear. Clear, too, are the serious consequences of that decline. For those who examine the whole picture, the benefits of autopsy far outweigh the drawbacks. The challenge will be to revive the autopsy in an age of shrinking health care dollars. The changes outlined herein should be accomplished quickly to prevent the loss of its many benefits to the clinician, family, hospital, and society.

ACKNOWLEDGMENT

Bernard Lo, M.D., Robert Steinbrook, M.D., and Glenn Saika, M.A., provided help in revising the manuscript, and Mary McLean provided secretarial support.

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from Alice - please review & comment

Paul Volberding

The face is friendly, the voice soft, and the words carefully chosen.

As he has done in scores of televised interviews over the past six years, Paul Volberding turns to the camera to answer yet another

emic that has transformed his career and his always comforting, it is clear he is taking small accomplishment in times of public panic.

AIDS "answer man" was slow to develop and a bench researcher working in the relative atory at UCSF--and uncomfortable with the 37-year-old Minnesota native has seen f of oncology at SFGH change as the AIDS ctor of AIDS Activities at SFGH and ne at UCSF, he oversees a staff of about 50 successfully integrated clinical research . The rest of his time is divided between tees, responding to almost daily media in clinic. It is there, in one-on-one

sessions with patients that he has earned a reputation as a compassionate, concerned and knowledgeable physician. It is also there that Volberding had to face his own anxiety about a disease that in the early days, had no name, no cause and no bounds.

"I saw my first Kaposi's sarcoma patient the day I started at SFGH in 1981, which was just one day after the CDC issued its report on KS and pneumocystis carinii pneumonia cases in New York and Los Angeles.

TV -

Please Change
or not ASAP

Alice

OK PV

from Alice - please review & comment

Paul Volberding

The face is friendly, the voice soft, and the words carefully chosen. As he has done in scores of televised interviews over the past six years, Paul Volberding turns to the camera to answer yet another question about the AIDS epidemic that has transformed his career and his life. If his message is not always comforting, it is clear he is taking pains to make it accurate--no small accomplishment in times of public misinformation and borderline panic.

Volberding's role as the AIDS "answer man" was slow to develop and impossible to predict. Once a bench researcher working in the relative anonymity of Jay Levy's laboratory at UCSF--and uncomfortable with public speaking of any kind--the 37-year-old Minnesota native has seen his original position of chief of oncology at SFGH change as the AIDS epidemic has grown. Now Director of AIDS Activities at SFGH and associate professor of medicine at UCSF, he oversees a staff of about 50 and a model program that has successfully integrated clinical research into a system of patient care. The rest of his time is divided between serving on various AIDS committees, responding to almost daily media inquiries and seeing patients in clinic. It is there, in one-on-one sessions with patients that he has earned a reputation as a compassionate, concerned and knowledgeable physician. It is also there that Volberding had to face his own anxiety about a disease that in the early days, had no name, no cause and no bounds.

"I saw my first Kaposi's sarcoma patient the day I started at SFGH in 1981, which was just one day after the CDC issued its report on KS and pneumocystis carinii pneumonia cases in New York and Los Angeles.

We had almost no clues about AIDS then." For the next three years, Volberding and his colleagues lived, first in ignorance and then in fear, as it became clear that AIDS was a transmissible disease. "1983 was a year of great personal anxiety for me." Bothered by constant nightmares, this "nice, level-headed guy" and father of two young sons, stopped discussing AIDS at home with his SFGH physician wife, Molly. It was only in 1984, after taking the AIDS antibody test, that everyone could relax.

Relaxation can be a very relative term, however. The disease itself remains such a gripping medical and human problem that Volberding admits, "It is impossible for me to imagine myself not being involved with it. You just can't walk away."

That explains Volberding's eagerness to talk to the media and almost any group willing to listen. "Short of a vaccine, the only way to stop the epidemic is through public education of how AIDS does and doesn't spread. Without that knowledge, it's going to get a lot worse."

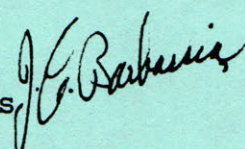
Being on television and in print so often with that message has made him well known, well liked and respected both inside and outside the usual medical and academic circles.

But Volberding remains far from a self-serving celebrity. "It's wonderful to be on TV, but when it comes right down to it, it doesn't help you deal with your patients or staff. The real world of AIDS is on Ward 5A (the world's first inpatient ward for AIDS patients which Volberding originally proposed) and the outpatient clinic on Ward 86." For all of Volberding's notoriety, it is something he never forgets.--
A.B.

March 9, 1987

TO: Members of the Academic Senate
San Francisco Division

FROM: J. C. Barbaccia, Chair
Committee on Committees



Preference for Committee Service, 1987-88

Participation in faculty governance through service to the many committees of the Academic Senate is one of the responsibilities and obligations of the members of the Academic Senate. Attached are the forms used by the Committee on Committees in its annual survey of members willing to serve on these committees.

Please check the appropriate boxes on the two forms. The **first** form shows School and Departmental affiliation; the **second** is designed so that you may show a first, second, and third choice for committee service. If you are to be on sabbatical leave or leave of absence during 1987-88, please so indicate in the spaces provided at the top of the second form. If you do not respond, you may nevertheless be asked to serve on a committee.

Please return to the

Committee on Committees
Academic Senate Office
Bx 0764, U 100-H

by THURSDAY, MARCH 26, 1987.

attachment

COPY

PREFERENCE FOR COMMITTEE SERVICE, 1987-88

NAME: Last, first, initial

Example: /D/o/e/./J/o/h/n/P/./NOELBER/DINIG, IPANIL, A. / / / / / / / / / /
1-25

TITLE:

Prof. Assoc. Prof. Asst. Prof. Instructor Senior Lecturer) with security of
Lecturer) employment

26-1
26-2
26-3
26-4
27-1

DEPARTMENT OR DIVISION (Mark one principal affiliation only)

29-30

DENTISTRY

- ☐ Growth & Development
☐ Stomatology
☐ Dental Public Health
and Hygiene
☐ Restorative Dentistry

NURSING

- ☐ Physiological Nursing
☐ Social & Behav. Sci.
☐ Family Hlth Care Nsg.
☐ Mental Health & Com.
Nursing

PHARMACY

- ☐ Pharmaceutical Chem.
☐ Pharmacy
☐ Clinical Pharmacy

MEDICINE

- ☐ Anatomy
☐ Anesthesia
☐ Biochem.&Biophysics
☐ Dermatology
☐ Epidemiology &
Internat'l Hlth
☐ Family & Com. Med.
☐ Forensic Pathology
& Medicine
☐ History & Phil. of
Health Sciences
☐ Laboratory Medicine
☒ Medicine
☐ Microbiology &
Immunology
☐ Neurological Surg.
☐ Neurology

- ☐ Ob/Gyn & Reproductive
Sciences
☐ Ophthalmology
☐ Orthopaedic Surgery
☐ Otolaryngology
☐ Pathology
☐ Pediatrics
☐ Pharmacology & Exper'l
Therapeutics
☐ Physiology
☐ Psychiatry
☐ Radiology
☐ Radiation Oncology
☐ Surgery
☐ Urology

INDICATE QUARTER(S) ON SABBATICAL LEAVE OR LEAVE OF ABSENCE DURING 1987-88

FALL

WINTER

SPRING

SUMMER

ALL YEAR

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INDICATE ONE - FIRST, SECOND, AND THIRD CHOICE FOR COMMITTEE SERVICE BY MARKING THE APPROPRIATE BOXES

COMMITTEE

PREFERENCE

36-37 38-39 40-41

1st 2nd 3rd

Academic Freedom	☐	☐	☐
*Academic Personnel	☐	☐	☐
*Academic Planning & Budget	☐	☐	☐
Courses of Instruction	☐	☐	☐
Educational Policy	☐	☐	☐
Equal Opportunity	☐	☐	☒
Graduate Council	☐	☐	☐
Honors, Graduate Professional & Undergrad. Scholarships	☐	☐	☐
Library	☐	☐	☐
Privilege and Tenure	☒	☐	☐
Research	☐	☐	☐
Rules and Jurisdiction	☐	☐	☐
Schedule and Space	☐	☒	☐
University Welfare & Memoriae	☐	☐	☐

* Senior faculty

City and County of San Francisco



Department of Public Health

San Francisco General Hospital
Medical Center

MEMORANDUM

DATE: November 7, 1986

TO: Chris Christensen, Personnel

FROM: Gayling Gee, RN, Head Nurse, Ward 86

RE: Waiver of Recruitment and Salary Justification
Clinical Nurse II at Ward 86

As you know, we have recently recruited and hired for a Clinical Nurse II position for Ward 86. We have also generated a second requisition for a CNII (Emp. Req. No. E-47441). Since we went through such a recent recruitment and interview process, I am requesting a waiver for recruitment for this position.

I have interviewed Mr. Edward Kimberly Withrow and find him to be an excellent applicant with over ten years of nursing experience that includes two years of inpatient nursing care on the AIDS unit at San Francisco General Hospital. I would like to recommend him for this position and to request a start date of November 17, 1986.

Additionally, I would like to request consideration for Mr. Withrow to be offered the CNII position beginning at Step 5 for the following reasons:

1. Mr. Withrow is a 1976 graduate of the University of Texas with a BS in Nursing. He has had over ten years of nursing experience, including intensive and coronary care, psychiatry and forensic nursing care.
2. Mr. Withrow has also had over a years' experience of caring for AIDS patients on Ward 5A-5B, the inpatient AIDS unit at San Francisco General Hospital. His clinical nursing skills and background knowledge in AIDS is excellent. He will be able to step directly into his clinical role with minimum orientation time.
3. Mr. Withrow presently makes a yearly salary of \$37,000 per year as a City and County employee at SFGH. He is willing to take a salary reduction to work on Ward 86; however, he feels that the CNII Step 5 is the only acceptable salary range for him as a condition of employment.
4. My initial choice for this position was also a staff nurse employed at SFGH; she, too, refused the position due to the salary that she would have incurred due to accepting our position with the University. I feel that unless we are able to offer Mr. Withrow the Step 5 salary, we would lose a highly competent and "AIDS-experienced" nurse to our Clinic.

I feel that Mr. Withrow is a highly qualified nurse for this position and that a Step 5 is appropriate to his experience and abilities.

Thank you for your assistance.

cc: Barbara Woodruff, Admin. Analyst
Paul Volberding, MD, Director, AIDS Activities

Pat

MEMORANDUM

DATE: December 3, 1986

TO: Cliff Morrison, Pat Franks, Mary Pittman-Lindeman, Dave Feigel, Diane Miller-Brazas, Michael Johnson

FROM: Jenny White *JW*

RE: Meeting, Monday Dec. 8, 3:30 p.m.
Conference Room, San Francisco AIDS Foundation
333 Valencia, 4th fl., San Francisco

Enclosed are a revised draft of cohort study procedures, and draft data forms, for discussion at the Monday meeting.

JW/ef

Enc.

I. ENTRY INTO THE COHORT STUDY.

A. From SFGH Ward 86

EITHER

1. Cliff and Jenny will select every fifth patient from the Ward 86 Patient Care List (Patient Roster), up to a total of 30.
2. C/J will send a letter to these patients explaining the study to them, and informing them that C/J would like to ask them to join the cohort when they come in for their next visit, and ^{to} be interviewed. They will be asked to call C/J if they have any questions, or if they know in advance they don't want to participate. Refusals will be tallied, by sex.
3. C/J will go to Ward 86 and check the Appointment List, noting down dates and times of appointments for all cohort clients. This will be continued until 30 appointments are identified, initially. As patients decline to participate, additional patients will be randomly selected.

OR

4. C/J will go to Ward 86 and randomly select potential cohort members from the Appointment List, selecting every fifth patient. (In this case, patients will know nothing of the study until they are met by the interviewer, thus requiring more interviewing time.)

5. C/J's interviewer will go to Ward 86 at the selected appointment times, and will explain the study, answering any questions; enroll the patient; have him/her sign the informed consent form; ^{assign a cohort number;} and conduct the interview, filling out the client intake form. Refusals will be tallied by sex and ethnicity. Interviewer will "red-flag" cohort member charts.
6. Service utilization data will be collected via the Encounter Form. Physicians and RNs hand the E.F. to the Ward Clerks for processing. Ward Clerks will take the fifth (extra) copy of the E.F. for every patient seen that day and file it in a box labeled "AIDS Home Care Study."
7. At the end of each week, C/J will go to 86, pick up the E.F. box, and staff will go through the box, selecting out cohort member E.F.s. Data from these will be entered into the computer.

B. From SFGH Ward 5A and Spillovers

1. At 4 p.m. the afternoon before, Cliff or Jenny will go to SFGH (where?) and get from the Daily Admission Records, from Alison Moet on 5A, or from Rita Fahrner, the list of AIDS/Severe ARC inpatients who were referred from the Emergency Room and who have not been to Ward 86.
2. Rita Fahrner and Dr. Clements see every PWA in I/P. Either Ms. Fahrner or Dr. Clements, someone they designate, or C/J's interviewer, will enroll the ~~maximized~~ cohort.

The enroller will briefly explain the study, including what it involves for the patient in terms of participation and of confidentiality, and ask the patient if he/she consents to be in the study. If patient consents, enroller will ask the patient to sign the informed consent form. Enroller will "red-flag" the patient's chart, assign a cohort number, and then conduct the interview, filling out the intake form.

If patient refuses, enroller will write "Refused" on the informed consent form. Enroller will then go on to the next patient seen and follow the same procedure. Completed and refused consent forms, and intake forms, will be placed in a box labeled "AIDS Home Support Study" at the Nurse's Station in Ward 5A.

3. At 4 p.m. that day, Cliff or Jenny will pick up the forms and
 - a) add the new patients to the cohort list, including the cohort number,
 - b) tally the number of patients refusing, by ethnicity and sex.
4. The above procedure will continue until about 70 patients are enrolled.
5. As "red-flagged" charts come across his/her desk, the Discharge Planner will notify Cliff and Jenny of dates of discharge, days in hospital, and where patients referred. They'll note this in their patient cohort records, and contact the new agency(ies). Discharge Planner will "red-flag" those Discharge Summaries going to VNA Hospice.

C. Representativeness of the Sample

After approximately 50 patients are enrolled at SFGH, C/J will begin to keep track of how many women and minorities are enrolled. In order to reflect the demographic makeup of the total current AIDS population at SFGH, no more than 87 white males will be enrolled; and there should be two women, eight Blacks, seven Hispanics, one Asian-Pacific Islander, and one Native American in the study.

II. REFERRALS THROUGH THE SYSTEM

a. For Shanti Emotional Support

Shanti Practical Support

1. Cliff and Jenny will notify Volunteer Coordinators of which new clients are in the cohort, and their cohort numbers, and will provide VCs with service unit tally sheets. VCs will "red flag" the cohort clients' charts.
2. Cliff and Jenny will provide Shanti with service unit tally forms which VCs will distribute to each counselor, volunteer or paid. VCs will notify each counselor of which patients/clients are in the cohort. Each counselor will log in service units provided to cohort clients, and will submit to the VCs a summary of total SUs provided during the month by the end of the first week of the following month.

OR

3. At their weekly meeting, VC will ask volunteers how many hours each cohort member was seen that week, and log it into their own tally sheets.
4. At the end of the month, VCs will mail their tally sheets to C/J, who will summarize the data.
5. Charges per unit of service will be available in the budget provided to AAO by the agency; C and J will compute charges per client.
6. Once a week, VCs will submit to C/J a list of any cohort members discharged that week, service unit tallies for the last month, and referrals.

OR

C/J will call the VCs weekly to get the information.

7. If client is being referred to an agency he/she has not been to before, C & J will notify the new agency that the client is in the cohort, and that his/her chart should be "red-flagged." If

client has already been to the new agency, this won't be necessary because the chart will already have been red-flagged (presumably).

B. For AIDS Health Project at Ward 86

Substance Abuse Counselor at ~~Ward 86~~ SFGH

Shanti Emotional Support at Ward 5A and 86

SFAF Social Service Advocacy

1. C and J will provide each counselor with the names of each new cohort client, their study ID number, and tally sheets for service units. Each counselor will log in service units provided and at the end of the month will submit their tallies to C and J.
2. Charges per unit of service will be available in the budget provided to AAO by the agency. C and J will compute charges per client.
3. At discharge, counselors will submit total service units provided during the final, partial month to C & J, along with date of discharge and where they (rather than the hospital) referred the client to, if applicable.

C. For VNA Hospice

1. The Discharge Planner at SFGH Inpatient will see the "red flag" on cohort number charts, and will notify Hospice staff that a cohort member is being referred to them when s/he phones them to make the referral.
2. Administrator will use her/his current Service Record forms to tabulate service units provided to cohort clients. Service Units will be in hours and will be broken down by type of provider (Nurse, Home Health Aide, etc.), Administrator will submit to C/J a summary of service units provided at the end of the month.
3. Charges per unit of service will be available in the budget provided to the AAO by VNA; C/J will complete charges per client.
4. At discharge, Administrator will submit total days provided the client during the final, partial month to C/J, along with date of discharge and where client was referred to, if appropriate.

D. For Shanti Residential

1. C & J will notify administrator of newly admitted clients who are in the cohort, and their case number.
2. Administrator will use her/his current tally sheet for service units (residential days) to summarize days provided to cohort clients. Administrator will submit to C & J a summary of total service units provided to each cohort client at the end of the month.
3. Charges per day will be available in the budget provided to AAO by the agency; C & J will compute charges per client.
4. At discharge, Administrator will submit total days provided the client during the final, partial month to C & J, along with date of discharge and where client was referred to, if appropriate.

E. For readmissions to Ward 5A and spillovers

1. Once a week, C/J will either inspect the Daily Admission Records from the previous week and compare with the updated cohort list, or speak with Alison Moet on 5A or Rita Fahrner; and note down any cohort patients readmitted to 5A and spillovers.

2. C/J will "red flag" chart of cohort patients who have not been admitted to 5A and spillovers before, and log in where these patients were referred from.
3. As "red-flagged" charts come across her desk, the Discharge Planner will notify C/J of the dates of discharge and where patients referred. They'll note this in their patient cohort records, and contact the new agencies.

F. For Public Health Nurses

1. The Public Health Nurse Liaison at SFGH attends the discharge planning meetings for all AIDS patients on 5A and spillovers, arranging referrals to P.H. Nurses at the District Health Centers for appropriate cases.

When a red-flagged cohort client is discharged and referred to Public Health Nursing, the Nurse Liaison will send a Cohort Study reporting form to the Health Center along with the referral form.

2. C/J will notify Virginia Yee of all cohort clients referred to P.H. Nursing who did not come through SFGH. Virginia will then notify nursing staff of these new cohort members, and will send a Cohort Study Data form to the appropriate nurse.

3. C/J will also send Virginia an updated list of all cohort members, so that she can monitor if data is being collected for all members who are being seen by Public Health Nurses.
4. At the end of the month, Nurses will submit their Monthly Reporting Forms to Virginia Yee's office. C/J will pick up the forms, or Virginia will mail them to us.
5. When a patient is discharged, the nurse will immediately send the Monthly Reporting Form to Virginia Yee. C/J will pick up the forms, or Virginia will mail them to us.

--Missing: Garden-Sullivan--

III. SPOT CHECKS

Periodically, C/J will go to each agency and check their client records to make sure a cohort member has not appeared at the program unreferred. If unreferred, the client's chart will not be red-flagged, and service units will not be being tallied. C/J will talk to the

appropriate administrator and arrange to have the chart red-flagged, counselors notified if appropriate, and the backlog of service units tallied.

C/J will at that time check to make sure service units are being tallied for all other cohort members as well.

IV. COHORT SURVEY: SERVICE UTILIZATION AND REFERRALS (See #1.12, p. 5 of
25 of Scope of Work)

At the beginning of each month, C/J will mail to each cohort member a questionnaire to be filled out and returned via a self-addressed stamped envelope. The questionnaire will cover

- a) services utilized at each of the different providers
- b) referrals made by the providers
- c) which referrals the cohort client followed up on

Clients can log in services and referrals throughout the month, and then mail in the questionnaire at the end of the month.

INITIAL CLIENT ENTRY FORM

Client Initials

Date - -
MO Day Yr

X Client Number

Previous Client ☐ Yes ☐ No

Date of First Admission to SFGH: - -
Mo Day Yr

Referred from:

DEMOGRAPHIC INFORMATION

X Date of Birth - -
mo dy yr

Age

APLA Study

X Sex: ☐ M ☐ F

X Ethnicity:

- 1 ☐ Asian/Pacific
2 ☐ Black
3 ☐ Hispanic

- 4 ☐ Wh...
5 ☐ Native American
6 ☐ Other

X Sexual Orientation:

- 1 ☐ Homosexual
2 ☐ Heterosexual
3 ☐ Bisexual

 Decline to state

Trouble collecting this one

Current Intimate Involvement

- ☐ Lover/Spouse living with client
☐ Lover/Spouse living away from client
☐ None

X Current Living Arrangement:

- 1 ☐ Living with lover/spouse
2 ☐ Living with blood relation(s)
3 ☐ Living with friends
4 ☐ Living alone
5 ☐ Living arrangement unstable
(no permanent residence)

Years	Months
<u> </u> <u> </u>	<u> </u> <u> </u>
<u> </u> <u> </u>	<u> </u> <u> </u>
<u> </u> <u> </u>	<u> </u> <u> </u>
<u> </u> <u> </u>	<u> </u> <u> </u>

X Residence:

- ☐ City of West Hollywood ☐ District 1 ☐ District 4
☐ Los Angeles ☐ District 2 ☐ District 5
☐ Other District ☐ District 3 ☐ Outside SF

OR ☐ SF
☐ Bay Area not SF
☐ Calif not Bay Area
☐ US not Calif

Case Manager
Enroller

 - -
Mo Day Yr

Client Initials _____

Date _____
Mo Day Yr

Client Number _____

MEDICAL INFORMATION

Month Day Year

X Date of ARC Dx: _____ [] NA
Date of AIDS Dx: _____ [] NA
Kaposi's Sarcoma: _____ [] NA

Present Karnofsky Scale Status: _____

History of Hemophilia [] Yes [] No

History of IV Infusion of blood products within the last seven years- [] Yes [] No

If yes, how long ago did the last infusion occur? _____ Years _____ Months

History of parent at risk for AIDS (pediatric case only) [] Yes [] No

History of heterosexual contact with person at risk for AIDS [] Yes [] No

X Opportunistic Infections:

	Yes	NO	Unknown
Pneumocystis Carinii Pneumonia (PCP)	[]	[]	[]
Cytomegalovirus (CMV)	[]	[]	[]
Herpes Simplex Virus (HSV)	[]	[]	[]
Mycobacterium Avium-Intracellulare	[]	[]	[]
Candida (Thrush) <i>CAN</i>	[]	[]	[]
Cryptococcus Neoformans <i>CAN</i>	[]	[]	[]
Toxoplasma Gondi	[]	[]	[]
Other _____	[]	[]	[]

X Number of Days Hospitalized (AIDS-Related) to Date _____

Current Symptoms:

	Yes	No
Fatigue	[]	[]
Weight Loss	[]	[]
Persistent Fever	[]	[]
Night Sweats	[]	[]
Diarrhea	[]	[]
Swollen Glands	[]	[]

*Was I ever doing
admitted for?*

Taking AZT: Yes No

Case Manager _____
Enroller _____

Date _____
Mo Day Yr

Client Initials ___ ___

Date ___ - ___ - ___
 Mo Day Yr

Client Number ___ ___ ___

FUNCTIONAL CAPACITY

1. Ambulation

- 1 ☐ Ambulatory without assistance
- 2 ☐ Ambulatory with assistance
- 3 ☐ Bedridden

2. Self-care

	Yes	No
Able to work	☐	☐
Able to cook for self	☐	☐
Able to feed self	☐	☐
Able to wash self	☐	☐
Able to groom self	☐	☐
Able to dress self	☐	☐
Able to change bed linens	☐	☐
Able to do light housekeeping	☐	☐
Able to use bathroom	☐	☐
Able to take prescribed oral medications	☐	☐
Problems with vision or hearing	☐	☐
Impairment of memory	☐	☐
Impairment of mental status	☐	☐

3. Independence in self care:

0%	0-25%	25-50%	50-75%	75-100%
☐	☐	☐	☐	☐
1	2	3	4	5

4. Need for skilled or semi-skilled nursing care:

None	Occasional	Approx 1hr/dy	>1-2 hr/dy
☐	☐	☐	☐

Case Manager _____
Enroller

Date ___ - ___ - ___
 Mo Dy Yr

VISITING NURSE ASSOCIATION AND HOMEMAKERS SERVICE ACUITY SCALE
ADAPTED FROM KARNOFSKY PERFORMANCE STATUS SCALE

Stage I Diagnosis	100	Normal, no complaints, no evidence of disease.
	90	Able to carry on normal activity, minor signs or symptoms of disease.
	80	Normal activity with effort, some signs or symptoms of disease.
Stage II Early Chronic	70	Cares for self. Unable to carry on normal activity or to do active work.
	60	Requires occasional assistance, but is able to care for most of care needs.
Stage III Late Chronic	50	Requires considerable assistance and frequent medical care.
	40	Disabled, requires special care and assistance.
Stage IV Terminal	30	Severely disabled, hospitalization is indicated although death not imminent.
	20	Hospitalization necessary, very sick, active supportive treatment necessary.
	10	Moribund, fatal processes progressing rapidly.
	0	Dead

REFERRAL CODES

Referrals Within the System

- 01 SFGH Inpatient
- 02 SFGH Outpatient - Ward 86
- 03 Garden-Sullivan Subacute
- 04 VNA Hospice Home Care
- 05 Public Health Nurses
- 06 AHP - Mental Health at Ward 86
- 07 AHP - Substance Abuse at ~~Ward 86~~ SFGH
- 08 Shanti - Emotional Support
- 09 Shanti - Emotional Support at SFGH
- 10 Shanti - Practical Support
- 11 Shanti - Long Term Housing
- 12 SFAF - Social Service Advocacy

Referrals Outside the System

- 13 SFGH Emergency Room
- 14 Other Hospital
- 15 Coming Home Hospice
- 16 Private Physician
- 17 Private Therapist
- 18 S.F. Dept. of Social Services
- 19 Social Security Administration
- 20 SFAF Emergency Housing
- 21 Open Hand
- 22 Friend/Lover/Family
- 23 Self
- 24 Other

SFGH Inpatient
Discharge Planners -/0/1/

AIDS COHORT STUDY
DISCHARGE REPORT

Name of Patient _____

Discharge Planner

Initials: / / / /

Patient Initials: / / / /

Patient Number: / / / / (same as hospital number)

Previous Patient? Yes / / No / /

Date of Admission / / / - / / / - / / / /
Mo. Day Yr.

Time: / / / / /

Date of Discharge / / / - / / / - / / / /
Mo. Day Yr.

Time: / / / / /

Deceased / /

Diagnostic Level at Discharge: / /

Referred to: / / / / / / / / / /

Not referred: /

AZT Trial Participant: Yes / / No / /

Reason for no referral:

Appropriate agency full /

Agency refused referral /

No appropriate agency /

Client refused / left /

Referral not indicated /

Other - Specify below /

Garden-Sullivan Subacute /0/3/

AIDS COHORT STUDY
ADMISSION REPORT

Name of Patient _____

R.N. Initials: / / / /

Patient Initials: / / / /

Patient Number: / / / / ~~(same as hospital number)~~

Previous Patient? Yes / / No / /

Date of Admission / / / / / / / / / / / / /
Mo. Day Yr.

Time: / / / / / /

Diagnostic Level at Admission: / / /

Client Initials: / / / /

PROVIDER: /0/3/

Client Number: / / / /

Date: / / / / / / / / /
Mo. Day Yr.

FUNCTIONAL CAPACITY AT ADMISSION

1. Ambulation

- / / Ambulatory without Assistance
 / / Ambulatory with Assistance
 / / Bedridden

2. Self-care

	<u>Yes</u>	<u>No</u>
Able to work	<u> / / </u>	<u> / / </u>
Able to cook for self	<u> / / </u>	<u> / / </u>
Able to feed self	<u> / / </u>	<u> / / </u>
Able to wash self	<u> / / </u>	<u> / / </u>
Able to groom self	<u> / / </u>	<u> / / </u>
Able to dress self	<u> / / </u>	<u> / / </u>
Able to change bed linens	<u> / / </u>	<u> / / </u>
Able to do light housekeeping	<u> / / </u>	<u> / / </u>
Able to use bathroom	<u> / / </u>	<u> / / </u>
Able to take prescribed oral medications	<u> / / </u>	<u> / / </u>
Problems with vision or hearing	<u> / / </u>	<u> / / </u>
Impairment of memory	<u> / / </u>	<u> / / </u>
Impairment of mental status	<u> / / </u>	<u> / / </u>

3. Independence in self care: -% 0-25% 25-50% 50-75% 75-100%
 / / / / / / / / / /

4. Need for skilled or semi- None Occasional Approx. >1-2 hr/dy
skilled nursing care: / / / / 1 hr/dy / /

R.N.

Date: / / / / / / / / /
Mo. Day Yr.

Garden-Sullivan Subacute
Discharge Planners -/0/3/

AIDS COHORT STUDY
DISCHARGE REPORT

Name of Patient _____

Discharge Planner

Initials: / / / /

Patient Initials: / / / /

Patient Number: / / / /

Date of Discharge / / / - / / / - / / / /
Mo. Day Yr.

Time: / / / / /

Deceased / /

Diagnostic Level at Discharge: / / /

Referred to: / / / / / / / / / / / / /

Not referred: / /

AZT Trial Participant: Yes / / No / /

Reason for no referral:

Appropriate agency full: / /

Agency refused referral: / /

No appropriate agency: / /

Client refused/left / /

Ref. not indicated / /

Other - specify below / /

Client Initials: / / / /

PROVIDER: /0/3/

Client Number: / / / /

Date: / / / / / / / / /
Mo. Day Yr.

FUNCTIONAL CAPACITY AT DISCHARGE

1. Ambulation

 / / Ambulatory without Assistance
 / / Ambulatory with Assistance
 / / Bedridden

2. Self-care

	<u>Yes</u>	<u>No</u>
Able to work	<u> / / </u>	<u> / / </u>
Able to cook for self	<u> / / </u>	<u> / / </u>
Able to feed self	<u> / / </u>	<u> / / </u>
Able to wash self	<u> / / </u>	<u> / / </u>
Able to groom self	<u> / / </u>	<u> / / </u>
Able to dress self	<u> / / </u>	<u> / / </u>
Able to change bed linens	<u> / / </u>	<u> / / </u>
Able to do light housekeeping	<u> / / </u>	<u> / / </u>
Able to use bathroom	<u> / / </u>	<u> / / </u>
Able to take prescribed oral medications	<u> / / </u>	<u> / / </u>
Problems with vision or hearing	<u> / / </u>	<u> / / </u>
Impairment of memory	<u> / / </u>	<u> / / </u>
Impairment of mental status	<u> / / </u>	<u> / / </u>

3. Independence in self care: -% 0-25% 25-50% 50-75% 75-100%
 / / / / / / / / / /

4. Need for skilled or semi-skilled nursing care: None Occasional Approx. 1 hr/dy >1-2 hr/dy
 / / / / / / / /

Discharge Planner

Date: / / / / / / / / /
Mo. Day Yr.

AIDS COHORT STUDY
MONTHLY REPORTClient Initials: / / / / Client Number: / / / / * Date of Admission / / / - / / / - / / / Time: / / / / /
Mo. Day Yr.* Referred from: / / / / / / / / (see referral codes on back)
* only fill out for first monthService Hours for the Month of / / / - / / /
Mo. Yr.

Nurse:	<u> / / / </u>
HHA:	<u> / / / </u>
Med SW:	<u> / / / </u>
Ther.:	<u> / / / </u>
LVN:	<u> / / / </u>
Attend.	<u> / / / </u>
Vol.:	<u> / / / </u>
Other:	<u> / / / </u>

Referrals During the Month: / / / / / / / / Client Deceased: / / Date: / / / - / / / - / / /
Mo. Day Yr.Client Discharged: / / If yes, Date of Discharge: / / / - / / / - / / /
Mo. Day Yr.Referred to: / / / / / / / / Not referred:

Reason for no referral:

Appropriate agency full	<u> </u>
Agency refused referral	<u> </u>
No approp. agency	<u> </u>
Client refused/left	<u> </u>
Ref. not indicated	<u> </u>
Other-specify below	<u> </u>

Client Initials: / / /

PROVIDER: /0/4/

Client Number: / / /

Date: / / - / / - / / /
Mo. Day Yr.

FUNCTIONAL CAPACITY AT ADMISSION

1. Ambulation

- / Ambulatory without Assistance
 / Ambulatory with Assistance
 / Bedridden

2. Self-care

	<u>Yes</u>	<u>No</u>
Able to work	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Able to cook for self	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Able to feed self	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Able to wash self	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Able to groom self	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Able to dress self	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Able to change bed linens	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Able to do light housekeeping	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Able to use bathroom	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Able to take prescribed oral medications	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Problems with vision or hearing	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Impairment of memory	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Impairment of mental status	<u> </u> / <u> </u>	<u> </u> / <u> </u>

3. Independence in self care: -% 0-25% 25-50% 50-75% 75-100%
 / / / / /

4. Need for skilled or semi-skilled nursing care: None Occasional Approx. 1 hr/dy >1-2 hr/dy
 / / / /

Enroller

Date: / / - / / - / / /
Mo. Day Yr.

Public Health Nurse /0/5/

AIDS COHORT STUDY
MONTHLY REPORT

Client Initials: / / / /

R.N. Initials: / / / /

Client Number: / / / /

Health Center #: / /

* Date of Admission / / / - / / / - / / / /
Mo. Day Yr.

* Diagnostic Level: / /

* Referred from: / / / / / / / / (see referral codes on back)
* only fill out for first month

(Log in contacts here) ↘

Total Service Units

New Visit: / / /
Home visit: / / /
Revisit: / / /
Phone: / / /
etc.: / / /

Diagnostic Level at End of the Month: / /

Referrals During the Month:
/ / / / / / / / / / / / / / / /

Client Deceased: / / Date: / / / - / / / - / / / /
Mo. Day Yr.

Client Discharged: / /

If yes, Date of Discharge: / / / - / / / - / / / /
Mo. Day Yr.

Referred to: / / / / / / / /

Not referred: ☒

Reason for no referral:

- Appropriate agency full ☒
- Agency refused referral ☒
- No appropriate agency ☒
- Client refused/left ☒
- Ref. not indicated ☒
- Other - specify below ☒

Client Initials: / / / /

PROVIDER: /0/5/

Client Number: / / / /

Date: / / - / / - / / /
Mo. Day Yr.

FUNCTIONAL CAPACITY AT ADMISSION

1. Ambulation

 / / Ambulatory without Assistance
 / / Ambulatory with Assistance
 / / Bedridden

2. Self-care

	<u>Yes</u>	<u>No</u>
Able to work	<u> / / </u>	<u> / / </u>
Able to cook for self	<u> / / </u>	<u> / / </u>
Able to feed self	<u> / / </u>	<u> / / </u>
Able to wash self	<u> / / </u>	<u> / / </u>
Able to groom self	<u> / / </u>	<u> / / </u>
Able to dress self	<u> / / </u>	<u> / / </u>
Able to change bed linens	<u> / / </u>	<u> / / </u>
Able to do light housekeeping	<u> / / </u>	<u> / / </u>
Able to use bathroom	<u> / / </u>	<u> / / </u>
Able to take prescribed oral medications	<u> / / </u>	<u> / / </u>
Problems with vision or hearing	<u> / / </u>	<u> / / </u>
Impairment of memory	<u> / / </u>	<u> / / </u>
Impairment of mental status	<u> / / </u>	<u> / / </u>

3. Independence in self care:

-%	0-25%	25-50%	50-75%	75-100%
<u> / / </u>	<u> / / </u>	<u> / / </u>	<u> / / </u>	<u> / / </u>

4. Need for skilled or semi-skilled nursing care:

None	Occasional	Approx. 1 hr/dy	>1-2 hr/dy
<u> / / </u>	<u> / / </u>	<u> / / </u>	<u> / / </u>

Enroller

Date: / / - / / - / / /
Mo. Day Yr.

AIDS Health Project at Ward 86 /0/6/
Shanti Project at SFGH /0/9/
Substance Abuse Counselor at Ward 86 /0/7/

AIDS COHORT STUDY
MONTHLY REPORT

Client Initials: / / / /

Counselor Initials: / / / /

Client Number: / / / /

AHP at 86: / /

*Previous Client Yes / / No / /

Shanti I/P: / /

*Date of Admission / / / - / / / - / / / /
Mo. Day Yr.

Shanti at 86: / /

ASAS: / /

*Referred from: / / / / / / / / (see referral codes on back)
* only fill out for first month

Service Hours for the Month of / / / - / / / /
Mo. Yr.
(log in hours here) Total Hours

Week 1	/ / /
Week 2	/ / /
Week 3	/ / /
Week 4	/ / /
Week 5	/ / /

Referrals During the Month:

/ / / / / / / / / / / / /

Client Deceased: / /

Date: / / / - / / / - / / / /
Mo. Day Yr.

Client Discharged: / /

If yes, Date of Discharge: / / / - / / / - / / / /
Mo. Day Yr.

Referred to: / / / / / / / /

Not referred ☒

Reason for no referral:

Appropriate agency full ☒

Agency refused referral ☒

No appropriate agency ☒

Client refused/let ☒

Ref. not indicated ☒

Other - specify below ☒

Shanti Project
Emotional Support /0/8/

AIDS COHORT STUDY
MONTHLY REPORT

Client Initials: / / / /

Counselor Initials: / / /

Client Number: / / /

*Previous Client Yes / No /

* Date of Admission / / - / / - / /
Mo. Day Yr.

*Referred from: / / / / / / / / / (see referral codes on back)
* only fill out for first month

Service Hours for the Month of / / - / /
Mo. Yr.

	Individual Counseling	Group Counseling
Week 1	<u> </u> / <u> </u> / <u> </u>	<u> </u> / <u> </u> / <u> </u>
Week 2	<u> </u> / <u> </u> / <u> </u>	<u> </u> / <u> </u> / <u> </u>
Week 3	<u> </u> / <u> </u> / <u> </u>	<u> </u> / <u> </u> / <u> </u>
Week 4	<u> </u> / <u> </u> / <u> </u>	<u> </u> / <u> </u> / <u> </u>
Week 5	<u> </u> / <u> </u> / <u> </u>	<u> </u> / <u> </u> / <u> </u>

Diagnostic Level: /

Referrals During the Month: (see referral codes on back)
 / / / / / / / / / / / / / / / / /

Client Deceased: / Date: / / - / / - / /
Mo. Day Yr.

Client Discharged: /

If yes, Date of Discharge: / / - / / - / /
Mo. Day Yr.

Referred to: / / / / / / / / / Deceased: /

Not referred:

Reason for no referral:

Appropriate agency full

Agency refused referral

No appropriate agency

Client refused/left

Ref. not indicated

0421a-12/03/86

Other - specify below

Client Initials: / / /

PROVIDER: 0/8/

Client Number: / / /

Date: / / - / / - / /
Mo. Day Yr.

FUNCTIONAL CAPACITY AT ADMISSION

1. Ambulation

 / Ambulatory without Assistance
 / Ambulatory with Assistance
 / Bedridden

2. Self-care

	<u>Yes</u>	<u>No</u>
Able to work	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Able to cook for self	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Able to feed self	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Able to wash self	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Able to groom self	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Able to dress self	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Able to change bed linens	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Able to do light housekeeping	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Able to use bathroom	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Able to take prescribed oral medications	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Problems with vision or hearing	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Impairment of memory	<u> </u> / <u> </u>	<u> </u> / <u> </u>
Impairment of mental status	<u> </u> / <u> </u>	<u> </u> / <u> </u>

3. Independence in self care: -% 0-25% 25-50% 50-75% 75-100%
 / / / / /

4. Need for skilled or semi-skilled nursing care: None Occasional Approx. 1 hr/dy >1-2 hr/dy
 / / / /

Counselor

Shanti Project
Practical Support /1/0/

AIDS COHORT STUDY
MONTHLY REPORT

Client Initials: / / / /

Volunteer Initials: / / / /

Client Number: / / / /

*Previous Client Yes / / No / /

*Date of Admission / / / - / / / - / / /
Mo. Day Yr.

*Referred from: / / / / / / / / (see referral codes on back)
* only fill out for first month

Service Hours for the Month of / / / - / / /
Mo. Yr.

Week 1	/ / /
Week 2	/ / /
Week 3	/ / /
Week 4	/ / /
Week 5	/ / /
TOTAL	/ / /

Client Deceased: / /

Date: / / / - / / / - / / /
Mo. Day Yr.

Client Discharged: / /

If yes, Date of Discharge: / / / - / / / - / / /
Mo. Day Yr.

Referred to: / / / / / / / /

Not referred: ☒

Reason for no referral:

Appropriate agency full ☒

Agency refused referral ☒

No appropriate agency ☒

Client refused/left ☒

Ref. not indicated ☒

Other - specify below ☒

Client Initials: / / / /

PROVIDER: /1/0/

Client Number: / / / /

Date: / / - / / - / / /
Mo. Day Yr.

FUNCTIONAL CAPACITY AT ADMISSION

1. Ambulation

- / / Ambulatory without Assistance
 / / Ambulatory with Assistance
 / / Bedridden

2. Self-care

	<u>Yes</u>	<u>No</u>
Able to work	<u> / / </u>	<u> / / </u>
Able to cook for self	<u> / / </u>	<u> / / </u>
Able to feed self	<u> / / </u>	<u> / / </u>
Able to wash self	<u> / / </u>	<u> / / </u>
Able to groom self	<u> / / </u>	<u> / / </u>
Able to dress self	<u> / / </u>	<u> / / </u>
Able to change bed linens	<u> / / </u>	<u> / / </u>
Able to do light housekeeping	<u> / / </u>	<u> / / </u>
Able to use bathroom	<u> / / </u>	<u> / / </u>
Able to take prescribed oral medications	<u> / / </u>	<u> / / </u>
Problems with vision or hearing	<u> / / </u>	<u> / / </u>
Impairment of memory	<u> / / </u>	<u> / / </u>
Impairment of mental status	<u> / / </u>	<u> / / </u>

3. Independence in self care: -% 0-25% 25-50% 50-75% 75-100%
 / / / / / / / / / /

4. Need for skilled or semi-skilled nursing care: None Occasional Approx. 1 hr/dy >1-2 hr/dy
 / / / / / / / /

Volunteer

Date: / / - / / - / / /
Mo. Day Yr.

Shanti Residential /1/1/

AIDS COHORT STUDY
MONTHLY REPORT

Client Initials: / / / /

Client Number: / / / /

* Date of Admission / / / - / / / - / / / /
Mo. Day Yr.

*Referred from: / / / / / / / / (see referral codes on back)
* only fill out for first month

*Previous Client Yes / / No / /

Days Provided During the Month of: / / / - / / / /
Mo. Yr.

Total Days Provided: / /

Client Deceased: / /

Client Discharged: / /

If yes, Date of Discharge: / / / - / / / - / / / /
Mo. Day Yr.

Referred to: / / / / / / / /

Not referred: ☒

Reason for no referral:

Appropriate agency full ☒

Agency refused referral ☒

No appropriate agency ☒

Client refused/left ☒

Ref. not indicated ☒

Other - specify below ☒

Client Initials: / / / /

PROVIDER: /1/1/

Client Number: / / / /

Date: / / - / / - / /
Mo. Day Yr.

FUNCTIONAL CAPACITY AT ADMISSION

1. Ambulation

- / / Ambulatory without Assistance
 / / Ambulatory with Assistance
 / / Bedridden

2. Self-care

	<u>Yes</u>	<u>No</u>
Able to work	<u> / / </u>	<u> / / </u>
Able to cook for self	<u> / / </u>	<u> / / </u>
Able to feed self	<u> / / </u>	<u> / / </u>
Able to wash self	<u> / / </u>	<u> / / </u>
Able to groom self	<u> / / </u>	<u> / / </u>
Able to dress self	<u> / / </u>	<u> / / </u>
Able to change bed linens	<u> / / </u>	<u> / / </u>
Able to do light housekeeping	<u> / / </u>	<u> / / </u>
Able to use bathroom	<u> / / </u>	<u> / / </u>
Able to take prescribed oral medications	<u> / / </u>	<u> / / </u>
Problems with vision or hearing	<u> / / </u>	<u> / / </u>
Impairment of memory	<u> / / </u>	<u> / / </u>
Impairment of mental status	<u> / / </u>	<u> / / </u>

3. Independence in self care: -% 0-25% 25-50% 50-75% 75-100%
 / / / / / / / / / /

4. Need for skilled or semi-skilled nursing care: None Occasional Approx. 1 hr/dy 1-2 hr/dy
 / / / / / / / /

Enroller

SFAF Social Service Advocacy /1/2/

AIDS COHORT STUDY
MONTHLY REPORT

Client Initials: / / / Social Worker Initials: / / /

Client Number: / / /

*Reactivated Case Yes / No /

Date of Admission / / - / / - / / /
Mo. Day Yr.

*Referred from: / / / / / / (see referral codes on back)

*Diagnostic Level: /

* only fill out for first month

Service Hours for the Month of / / - / / /
Mo. Yr.
(log in hours here) Total Hours

Week 1	<u> </u> / <u> </u> / <u> </u> /
Week 2	<u> </u> / <u> </u> / <u> </u> /
Week 3	<u> </u> / <u> </u> / <u> </u> /
Week 4	<u> </u> / <u> </u> / <u> </u> /
Week 5	<u> </u> / <u> </u> / <u> </u> /

Referrals During the Month:
 / / / / / / / /

Case Closed? / / /
Yes No

If yes, Date of Closing: / / - / / - / / /
Mo. Day Yr.

Referred to: / / / / / /

Client Deceased: /

Not referred: /
Reason for no referral:
Appropriate agency fail /
Agency refused referral /
No appropriate agency /
Client refused/left /
Ref. not indicated /
Other - specify below /

Client Initials: / / / /

PROVIDER: /1/2/

Client Number: / / / /

Date: / / / / / / / /
Mo. Day Yr.

FUNCTIONAL CAPACITY AT ADMISSION

1. Ambulation

 / / Ambulatory without Assistance
 / / Ambulatory with Assistance
 / / Bedridden

2. Self-care

	<u>Yes</u>	<u>No</u>
Able to work	<u> / / </u>	<u> / / </u>
Able to cook for self	<u> / / </u>	<u> / / </u>
Able to feed self	<u> / / </u>	<u> / / </u>
Able to wash self	<u> / / </u>	<u> / / </u>
Able to groom self	<u> / / </u>	<u> / / </u>
Able to dress self	<u> / / </u>	<u> / / </u>
Able to change bed linens	<u> / / </u>	<u> / / </u>
Able to do light housekeeping	<u> / / </u>	<u> / / </u>
Able to use bathroom	<u> / / </u>	<u> / / </u>
Able to take prescribed oral medications	<u> / / </u>	<u> / / </u>
Problems with vision or hearing	<u> / / </u>	<u> / / </u>
Impairment of memory	<u> / / </u>	<u> / / </u>
Impairment of mental status	<u> / / </u>	<u> / / </u>

3. Independence in self care: -% 0-25% 25-50% 50-75% 75-100%
 / / / / / / / / / /

4. Need for skilled or semi-skilled nursing care: None Occasional Approx. 1 hr/dy 1-2 hr/dy
 / / / / / / / /

Social Worker

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

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SANTA BARBARA • SANTA CRUZ

MERLE A. SANDE, M.D.

Chief, Medical Service
San Francisco General Hospital

Professor and Vice-Chairman
Department of Medicine

4 December 1986

Paul A. Volberding, M.D.
Chief, Division of Medical Oncology
Director, AIDS Activities
Ward 84, Building 80, SFGH

Dear Paul:

Ellen Feigal came to see me to discuss the possibility of her staying at San Francisco General Hospital as a member of the medical staff after she completes her fellowship training a year from this coming July. Although I haven't spoken directly to Mike about this, it would certainly seem to be a reasonable move for Ellen, and I think that it's something that we should probably discuss at the noon meeting Monday, 8 December.

I told Ellen that she would be an ideal candidate to apply for funding by the Universitywide Task Force on AIDS through an AIDS Postdoctoral Fellowship this year and an AIDS Investigator Award the following year. I encouraged her to request the application information and to consider applying for these awards.

Please think about this, and we'll discuss it Monday.

Thanks, Paul.

Sincerely,

A handwritten signature in dark ink, appearing to read "Merle A. Sande".

Merle A. Sande, M.D.

cc: Michael S. McGrath, M.D., Ph.D.
Carol Roberts, M.S.O.

MAS/rab-f

22 December 1986

Memo to Paul Volberding

From Gifford Leoung 

RE: Toxoplasma antigen/antibody study with Remington

Jack Remington has agreed to run toxoplasma antibody tests on our patients free of charge. This is not an experimental procedure; he is interested in the baseline seropositivity in AIDS patients and in having a pool of patients for a future study (outlined below).

In the past, we have spoken about doing toxo antibodies on all our patients but decided not to because of the cost and having to store all the specimens. This way they would store all the sera for us. Aside from the zero cost except for transporting the sera, another advantage is that, in the future, these patients may be a pool to draw from when antigen test is available (such as for cryptococcus). We are submitting an IRB protocol for that as an experimental procedure.

I have been drawing sera from my patients but would like to draw blood on all the patients to send to Remington. To be systematic, I thought I would fill out a blood draw slip and include it in the registration form packet. Dave Feigal thought it was a good idea and suggested I pass it through you.

Connie and Dick also mentioned that we have sera stored for ourselves in the Ward 86 freezer that would be available for use. They further suggested that if we use these sera, we should assess a handling charge since it does take up time for our personnel to pipette aliquots of sera and prepare the packages.

Please let me know how you feel about these ideas. Ultimately, we expect that those patients who are Ab positive will be evaluated by Remington's antigenemia and parasitemia test and if positive, be considered for therapy before clinical symptoms, as we are doing for cryptococcus. Thanx.

cc: Dave Feigal

Paul -
any suggestions?

will send to
Merle, Flewis,
P Sowa, S Spinelli

we are already in
the budget process,
by the way

JL.

DRAFT

December, 1986

Proposal for an Oncology Nursing Unit, SFGH

I. Rationale

Cancer care is now regarded as a highly specialized branch of nursing, with increasing technical knowledge required in the area of management of chemotherapy and radiation therapy, with increasing sophistication of surgical techniques, and with better understanding of the personal needs and concerns of cancer patients and their families. The Oncology Nursing Society is now a nationally recognized specialty organization, and postgraduate training programs are producing increasing numbers of highly trained graduates.

Oncology nursing units are now the standard of care in hospitals the size of SFGH. All of the hospitals in San Francisco which have more than approximately 200 new cases of cancer per year have inpatient oncology units. Such units are able to provide a high level of technical knowledge and safety to nursing staff, a high level of teaching to nurses as well as housestaff regarding cancer and its associated problems, and a high level of intervention for the social and emotional needs of patients and their families. To reach these standards is the goal of an oncology nursing unit at SFGH.

We are currently seeing in excess of 470 new cases of cancer each year at SFGH, and that number has been steadily rising since 1981. The AIDS epidemic has contributed a large fraction of the increase, with the high local incidence of Kaposi's sarcoma. However, the number of non-AIDS cases has increased also. In 1985, we had 715 non-AIDS-related hospital admissions for cancer, with an average of twenty beds occupied at all times by patients with cancer. While we may increase the number of cancer admissions to the hospital by providing new areas of research and cancer care, we nonetheless must improve the setting for care of the patients we are now seeing.

San Francisco General Hospital's population of cancer patients ranges over a great variety of diseases. We currently provide care for these patients in the hospital in a variety of settings. Continuity of care and adequate followup care have been chronic problems. In order to attempt to consolidate care, a social worker has been appointed to concentrate on cancer patients and a hospice team made available. No other patient or family-oriented services are available. We are currently writing nursing guidelines for the proper administration of chemotherapy, but have not educated the vast majority of the nursing staff in the safe handling and disposal of these agents. We have no provisions for regular nursing education in cancer treatment or cancer nursing care. In addition, we currently do not treat patients with leukemia and certain other acute hematologic problems at SFGH, since adequate nursing support is a prerequisite to care of these patients. Our participation in clinical trials is likewise limited by inpatient nursing care.

II. Physical setting

We propose to provide a minimum of 17 beds on Ward 4C. We may need more than the three isolation beds available on one side of the hall; if

so we may have to use beds on the other side or make fewer beds open for use. We would like to use the solarium as a family gathering area, and to have available conference rooms for the housestaff and nurses. In addition, we would like to use one room for the Oncology fellows and the clinical nurse specialist.

III. Nursing staffing

Since the proposal meshes with other uses of Ward 4C, the head nurse position, while ideally occupied by an individual with oncology nursing training and/or experience, will probably not be so specialized. Therefore, the success of this unit will require the addition of an oncology clinical nurse specialist. This individual must have master's degree level training in oncology nursing. This individual will be responsible for all of the education of the nursing staff on the unit, including chemotherapy handling and safety, and chemotherapy administration training and certification. Additional responsibilities of the clinical nurse specialist would be to teach in oncology clinic and in any other outpatient setting where cancer patients are being regularly followed and nursing education is appropriate. Liaison to the outpatient clinics for continuity of care is another important function of this individual, as well as education of nursing staff on other inpatient units which might temporarily house other patients with cancer (such as psychiatry and the ICU's). Important to the success of a new unit such as this is an attempt at recruitment of some staff with experience in oncology nursing.

Staffing in most oncology units in San Francisco is at a higher acuity level than staffing on general wards; this has occurred because many cancer patients are more ill or require more nursing time than "regular" ward patients. Although other nursing unit acuity ratings systems differ from SFGH's system, we estimate a ratio of 1:3 or 4 is most appropriate. LVN care is practiced in virtually all oncology units, and such staff members often highly motivated and certified for higher levels of care than LVN's on regular wards.

IV. Administration

This oncology unit will be a nursing function, and as such administered by Nursing. Because of its specialized nature, a medical advisory body is necessary to oversee its activities. The Cancer Committee should be the oversight committee, and should appoint a Medical Director to oversee day-to-day activities. The Head Nurse and the clinical nurse specialist should be members of the Cancer Committee.

Policies and procedures for the unit must be created with the advice of the Cancer Committee. Reasonable management of resources and training demands that all chemotherapy patients be on the oncology unit; no specific contraindications to unit admission exist, except the requirement for psychiatric confinement or ICU care.

DRAFT

Study of Inpatient Cancer Care at SFGH, 1985

I. Purpose

- A. Identification of patients hospitalized in 1985 with a cancer diagnosis.
- B. Assess criteria for eligibility for an oncology nursing unit, such as length of stay, ICU or other unit use.
- C. Assess financial resources where possible.
- D. Identify specific areas of need for specialized care
 1. General cancer-related nursing care
 2. Chemotherapy administration and safety
 3. Use of ancillary services

II. Methods

All cases with a coded discharge diagnosis (one of the top eight) of a malignant disease were identified for 1985: there were more than 900 such admissions for the calendar year. All patients having a diagnosis of Kaposi's sarcoma were eliminated by removing those names with specific ICD-9 codes used for Kaposi's sarcoma. The resulting 715 admissions were ranked by ICD-9 diagnosis code and by ethnic group.

From these groupings a representative sample of 100 patients (and 100 admissions) was obtained randomly. These 100 charts were audited by J. Luce, M.D., T. Moran, RN, OCNS, and R. Nichols, R.N. Where charts were unobtainable, others of the same category were selected at random to replace them. Only one case of misassignment was found (no proven cancer), and no patient had a "history of" cancer with inactive disease.

III. Results

The attached appendix outlines the data in detail. Audit criteria were difficult to generate, since this was a retrospective chart review and much of the information we felt ought to be obtained was not available by this method.

The audited 100 patient charts display the same racial and diagnosis distribution as the entire 715 admissions. The average length of hospital stay was the same: 9.85 days for the whole group and 9.71 days for the audited group. This represents an average of 20 patients in the hospital at any time, with roughly half on the medical service and its subspecialties and half on surgery and surgical subspecialties.

Financial data were scarce on the charts. Most of the patients had some source of payment; this is understandable since it is relatively easier for cancer patients to obtain SDI. However, 70% of the patients who were admitted with no recorded means of payment were never seen by social service, at least as judged by notes in the chart. This potential avenue of payment may be being lost.

The distribution of diagnoses at SFGH is rather atypical. Aside from the large population of Kaposi's sarcoma cases, there are unusually few patients with certain very common cancers such as uterine and prostatic carcinomas. Hepatoma is vastly more common in our population than usual. Our patients are also younger than the cancer populations

seen in other San Francisco hospitals. Our average age is 55, whereas 60% of the populations from 5 other S. F. hospitals were over 60 years of age. These patients are also sick, though relatively few of them (only 6%) were in intensive care units. Sixty per cent underwent one or more procedures while in the hospital, with nearly forty per cent having a major surgical procedure.

Only 15 per cent of the audited admissions were for chemotherapy. This number significantly underrepresents the true number of patients receiving chemotherapy because of the manner in which charts were selected. Perhaps as many as 25% of the admissions were actually for chemotherapy, although the precise number is unobtainable.

Relatively few of the patients were receiving radiotherapy, and still fewer were paid for by Medical alone. If Medical continues to refuse to pay for transportation to Moffitt, this will impact on a very small number of patients.

Bed requirements could be assessed from the study. Between 17 and 20 beds could contain all of the admissions in the hospital at a given time. Isolation was used in 20% of the sample, not a surprising finding.

Use of ancillary services was below the level of the standard in the community. Social service and dietary consultations are mandatory in some oncology units in the city, and used more often in most others. Auditing for the necessity of these and other services was difficult, but at least in the case of VNA and Hospice services, the auditors felt that twice as many patients needed services as were seen, and these services cost the hospital nothing. Particularly vexing is the lack of dietary consults on patients on chemotherapy, who virtually all have significant problems with eating and nutrition and for whom skilled advice is very helpful.

Nursing care was below standard for the community also. Chemotherapy patients received very poor care, if the notes and care plans are reflective of the level of knowledge and intervention. The only care plan note which consistently appeared in chemotherapy patients' charts was for hydration, regardless of whether this was appropriate to the particular chemotherapy. Wrong information appeared in four of fifteen charts, and only one reflected some knowledge of the standard of care for a chemotherapy patient.

In general, the level of nursing knowledge and intervention in the vast majority of cancer patients was poor, at least as reflected in the charting and care plans. Major, common diagnoses were often omitted from the nursing notes altogether. Occasionally notes acknowledged "depression" or "fear" as problems, but never was an appropriate plan organized or carried out. Terminal care interventions were appropriately spelled out for only two of the twelve patients who died. Signs and symptoms appropriate to the diagnosis or treatment were not recognized, and our subjective impression was that pain was also managed poorly, though this is difficult to document in a retrospective fashion.

IV. Conclusions

1. We have a significant population of cancer patients already being cared for at SFGH, nearly all of whom are eligible for care on an oncology nursing unit.
2. We need 17-20 beds, with 20% of these being isolation beds.
3. The unit would comprise roughly half medical and half surgical cases.
4. The current level of nursing knowledge, and by extrapolation nursing safety, regarding chemotherapy, is very low. We do not meet current OSHA standards.
5. The current level of nursing knowledge and intervention in cancer cases in general is low; improvements in this area could result in better patient care.
6. Many ancillary services are already available for these patients; evidence suggests that they are being underutilized. The reason for this underutilization is not clear, but with both centralization of patients and better nursing awareness, better use of existing resources may occur.
7. Many underused resources are not costly to the hospital; it is possible that increases in resource use could be covered by better attempts to coordinate social service intervention and obtaining of available financial resources for currently non-paying patients.

Appendix--Raw Data

I. Demographic information

Age: Mean 55 years 18% under 40 years
 Median 57 years 5% over 80 years

Average length of stay: 9.7 days

Payment categories:

Medical or Medicare--55

"Private"--11

MIA-23

Other paying source-2

Not reported-10

II. Admitting service and diagnosis

Admitting Service--entire year

Medicine 44%

Surgery 21%

ENT 9%

Family Practice 8%

Urology 5%

GYN 3%

Neurosurg. 2%

Neurology 2%

Cardiology 2%

Others 3%

(peds, ortho,
 plastics,
 psych)

Admitting service--study group

Medicine 50%

Surgery 15%

ENT 9%

Fam. Practice 4%

Urology 5%

GYN 4%

Neurosurg 1%

Neurology 3%

Cardiology 4%

Others 5%

(GI, plastics,
 ortho)

Diagnosis: study group only (selected to represent overall group)

Lung cancer 15%

Breast 14%

Colorectal 14%

Head/neck 17%

Lymphoma 12%

GYN 8%

Others 20%

III. Procedures

41 patients had no procedures done (requiring consent)

9 radiologic procedures (mainly myelograms, arteriograms)

36 minor surgical procedures (biopsies, GI endoscopy, etc)

37 major surgical procedures (general anesthesia in OR)

7 patients receiving radiation therapy

average number of days on RT was 6.5

2 patients Medical, 2 Medical/Medicare

15 patients received chemotherapy

length of stay, mean 7.4 days; range 2-21 days

4 patients got one drug

8 patients got two drugs

3 patients got three drugs

DRAFT

Appendix (continued)

IV. Physical requirements

12 deaths

16 "do not resuscitate" orders; 16 other charts audited which showed clearly terminal patient on whom no DNR order was written

55 of the 971 hospital days were spent in CCU or ICU (6 patients)

22 patients were placed in isolation room during their stay (not all)

15 patients for usual reasons (primarily infectious)

7 patients for psychosocial reasons (primarily terminal)

V. Use of Ancillary Services

Social Service: 30 patients

of those with no obvious resource for payment at admission, only 30% were seen by a social worker during stay

Dietician: 12 patients

of those on chemotherapy, only one consulted (of 15)

Hospice: consulted 13 times; felt to be appropriate by reviewers in another 9 patients

VNA: consulted 14 times; felt to be appropriate by reviewers in another 18 patients

Other services: OT/PT, stoma care, speech rehab, etc: 13 patients felt by reviewers to be appropriate in another 9 patients

Comment: breast teaching usually was done by Reach for Recovery, wound care instructions were done almost always where appropriate. PT rarely used.

VI. Nursing Care

Chemotherapy patients: see above data

delay in administration:

held entirely--3 patients

≤ 6 hours 4 patients

7-12 hours 3 patients

≥ 12 hours 5 patients

8/15 delayed by more than 6 hours from time of orders

clarification of orders--4 patients, average of 5 phone calls

Nursing notes/care plan: appropriate, correct 1 case
incorrect, inapprop. 4 cases
no notes, "hydrate" 10 cases

All patients:

Nursing care plan reflective of any knowledge of disease, any planned nursing interventions specific to disease, terminal care, etc. --15/100 charts

Nursing care plans, of these 15, up to standards of the community--4

Nursing situations in which irrelevant --3 (ankle fracture in melanoma patient, admit for CT, cardiac case)

Date: December 1, 1986

To: Paul Volberding

From: Mark Jacobson 

RE: AZT + DHPG Combination Therapy outside of the Phase II Study

1. A very small pharmacokinetic study (less than 40 patients total) will be sponsored by the ATEU and will probably be done in early 1987. This will involve UCSD, Rochester, and NYU only.
2. I've discussed DHPG + AZT combination therapy with Donna Cederberg (project manager for DHPG at BW). She hasn't yet heard of any movement in NIH/FDA/BW policy toward allowing open-label AZT patients to receive concomittant DHPG. She, personally, supports the idea of allowing certain ATEU centers (e.g. SFGH) to give combined open-label AZT+DHPG, but is pessimistic about getting approval from the "higher-ups". I plan to discuss this issue with Joan Drucker and/or Danny King in the near future
3. Meanwhile, as you know, rumors are flying that many private practioners in the Bay Area are giving combined AZT+DHPG "illegally". I will try to poll practioners at the next SF Consortium on 12/3/86 to see how prevalent this "illegal" practice is. Donna Cederberg says there is no way BW can police AZT use, even with DHPG obtained from BW, let alone DHPG obtained from Syntex.
4. Several of my CMV Ward 86 patients have applied and received AZT on open-label. We discussed this beforehand and I openly explained why I couldn't treat them with both drugs. They understand and accept this, and have stopped DHPG. It will be very tragic, needless to say, if they lose their sight. I've discussed the issue of AZT vs. DHPG with almost all of my CMV patients. Most are reluctantly deciding to stay on DHPG for now. So far, this hasn't interfered with their trusting me; but I fear that if it becomes public knowledge that private practioners are giving combined therapy, there will be big problems maintaining credibility on Ward 86.
5. Pharmacokinetic studies are prodeeding with the first Phase II patient receiving AZT+DHPG (Robert Palmer). Another Phase II patient, Gary Merle, has developed CMV retinitiis and colitis and wants combined therapy. I will need your signiature on a letter to the CHR in the next few days. Also, I heard in Washington that several Phase II patients at UCSD and Miami have been receiving AZT+DHPG.

Thanks,

December 12, 1986

TO: Ira Goldstein, M.D.
Stephen B. Hulley, M.D.
Paul Volberding, M.D.
John Ziegler, M.D.

FROM: Warren M. Gold, M.D.

The American Thoracic Society - American Lung Association has decided to lobby Congress for additional funds for AIDS for the Lung Division of NHLBI. The Society feels strongly in favor of this position because so many pulmonologists are involved in care of AIDS patients. These funds are to be devoted to prevention through education as well as development of appropriate new drugs (e.g., for atypical mycobacteria). Furthermore, the organization of the Lung Association, with offices and staff even in small communities throughout the country would serve as an excellent base for an educational program.

I have been asked by the Society and its Federal Lung Committee to prepare a proposal for the Pulmonary Diseases Advisory Committee ASAP. Enclosed is a draft copy for your comments, suggestions, etc.

My second task is to suggest participants in an ATS-sponsored workshop on AIDS specifically oriented to the practical goals to be achieved by the Society in the field of education, vaccines, and new drug development, etc. Could you suggest topics and speakers for such a workshop?

Thank you for your help.

Sincerely yours,



Warren M. Gold, M.D.
Professor of Medicine

WMG/rw

PROPOSAL - PULMONARY DISEASES ADVISORY COMMITTEE

Problem

The first cases of Acquired Immunodeficiency Syndrome (AIDS) were reported in 1981 from Los Angeles in five young homosexual men diagnosed with Pneumocystis carinii pneumonia. Since that time, the number of cases in the United States has continued to increase, in epidemic proportions with considerable morbidity, mortality, and enormous costs for medical care and social services. In San Francisco alone, there were 866 new cases in 1985 and 5,900 are projected for 1991. The Center for Disease Control (CDC) predicts that 74,000 new patients will be diagnosed in 1991 and an estimated 70,000 additional patients diagnosed during previous years will also require care during 1991. These projections are conservative since they are based upon cases reported to the CDC. Based on review of death certificates in metropolitan areas of the United States, an additional 10% of diagnosed cases of AIDS are not reported to the CDC. An additional 10% of patients may be seriously ill with other Group IV HTLV-III/LAV infections which do not fit current surveillance criteria. This suggests that the CDC figures may underestimate by 20% or more the future morbidity and mortality due to HTLV-III/LAV infection. Because of the lengthy period between infection with the virus and the diagnosis of AIDS, most of the cases projected to occur in the next five years will be in persons already infected. This means that the majority of cases in 1991 will be in homosexual and bisexual men. It is important to realize, however, that "other heterosexual men and women" are projected to increase to more than 7,000 by 1991 and most of these will occur among those already infected.

In some areas, prevention efforts have been implemented successfully (e.g., among patients with hemophilia and recipients of transfusions) so that the

projections may overestimate cases from these sources. In general, however, no effective vaccine will be available for at least several years, few preventable co-factors have been defined, successful infection-prevention educational efforts have been minimal, and current drug therapy at best extends life for a short period only.

AIDS superimposes an unprecedented clinical burden and research mandate on "business-as-usual" in academic medicine. Barriers to an appropriate response include constraints of physical space and an insufficiency of human resources and collaborations. Medical communities that have attempted to manage the epidemic in-hospital (e.g., New York) rather than on an ambulatory basis (e.g., San Francisco) are already overwhelmed. Although responses at a national, state and local level have improved, our reactions are insufficient given the seriousness of the epidemic and its implications for the health and social structure of the nation.

Recommendations

Extraordinary priority should be given to further promotion of AIDS research, particularly in the area of primary prevention:

- Encourage the growth of new faculty and research projects, and further involvement of existing faculty, in activities that pertain to primary prevention;
- Make space and other resources available to the full extent that they can be employed usefully;
- Promote more collaboration with the Department of Health and community health professionals at the national, state and local level who are working on preventing the spread of the epidemic in high-risk minority populations;

- Encourage research applications in the areas of primary prevention education efforts and their effects and in the investigation of co-factors in high-risk populations involving the latest collaboration with and the latest methods of health education professionals; and
- Encourage more interactions with private enterprise that will enhance the likelihood of vaccine development and implementation.

It is probably not possible to overreact to the AIDS epidemic. History will show our current level of response to be, in fact, an underreaction. We need a set of activities devoted to AIDS that is several times larger than the set envisioned currently; one that ranges from basic science to community education and from treatment to prevention; one that integrates the activities of industry, of public health authorities and of health care providers with those of academia. If an endeavor of appropriate size, diversity and quality can be mounted, it will surely help us achieve success in the goal of controlling the epidemic of AIDS.

December 17, 1986

TO: *Paul Volberding, M.D.*

FROM: Leslie Z. Benet, PhD
Chairman, Committee for Chancellor's
Distinguished Lecture, Public Understanding of Science

We have scheduled appointments to meet with Jon Franklin, the Chancellor's Distinguished Lecturer for the Public Understanding of Science, for the week of January 12-16. As discussed with you, your appointment is marked in red on the attached schedule.

Please let Janet Norton know if this is not convenient for you. She can be reached at 476-2557.

CDL:cdlformltr:vr

12/18/86

SCHEDULE FOR Jon Franklin:

SEVENTH CHANCELLOR'S DISTINGUISHED LECTURER

January 12 - 16, 1987

MONDAY, JANUARY 12, 1987

8:30 am: Pick-up (Les Benet, Committee Chair)

9:00 am - 9:30 am: Meet at S 126 with JRK and MR

9:30 am - 10:45 am

LOCATION: Computer Graphics Laboratory, S 1022 (x62630)
Protein Structure and Drug Design

Robert Langridge, PhD, Professor of Pharmaceutical Chemistry and
Biochemistry
Charles Craik, PhD, Assistant Professor of Pharmaceutical Chemistry
Robert M. Stroud, PhD, Professor of Biochemistry and Biophysics and
Pharmaceutical Chemistry

11:00 am - 12:15 pm

LOCATION: Neuroscience Conference Room, S 865 (x62248)
Neuroscience Group

A.J. Hudspeth, PhD, Professor of Physiology and Otolaryngology
Allen Basbaum, MD, Professor of Anatomy and Physiology
Lily Y. Jan, PhD, Associate Professor of Physiology and Biochemistry

12:30 pm - 1:30 pm: Lunch

LOCATION: Chancellor's Conference Room, S 118 (x62401)
Robert Wood Johnson Clinical Scholars

Wallace V. Epstein, MD, Professor of Medicine and Director of Clinical
Scholars Program
Paul Blanc, MD
Nancy Milliken, MD
Michael Rafferty, MD
Ruth Greenblatt, MD
Joseph Castorina, MD

1:30 pm - 2:00 pm: Drive to SFGH

Michela Reichman
Assistant Chancellor
Communications
San Francisco, CA 94143
415/476 2557

University of California, San Francisco

A Health Sciences Campus

UCSF

am I having
lunch to him?
ask Alice

December 23, 1986

TO: Faculty Meeting with Jon Franklin, the
Chancellor's Distinguished Lecturer,
during the week of January 12, 1987

FROM: Michela Reichman



You might be interested in reading some of the
articles written by Mr. Franklin which won him
the Pulitzer Prize.

no- just
the inter on
12th, 2:00?
above library

INSIDE:

PARANORMAL—OR
SELF-PROMOTER?
A HANDY CHECKLIST

ASNE PANEL RAISES
QUESTIONS ABOUT
MEDIA AND MEDICINE

ALEXANDER REVIEWS
WGBH FELLOWSHIPS

AN OPEN LETTER
TO DR. KEYWORTH

BOFFEY PROPOSES
PROMOTIONAL DRIVE

BEN PATRUSKY WINS
AIP WRITING AWARD

VANNEVAR BUSH
FELLOWS NAMED

DETAILS OF CWO
INSURANCE PROGRAM
FOR FREELANCERS

JUNE 1985

JON FRANKLIN WINS SECOND PULITZER— BY DOING IT HIS WAY

Jon Franklin, a high-school dropout who lives with his computer in a modest bungalow in Glen Burnie, Md., is interested in power—the power of science and the power of literary form.

As a science writer for the Baltimore Evening Sun, he has just won his second Pulitzer prize, a distinction he shares with a handful of other journalists.

He won his first in 1979 for "Terrifying Journey Through Tunnels of the Brain," a dramatic account of an unsuccessful surgical procedure. His second was awarded in April for a seven-part series called "The Mind-Fixers." Before the prize was announced, his paper had received requests for 25,000 reprints.

He is a man of heretical views. "Writing about politics," he says, "would be a waste. Hell, politicians talk about being leaders, but all they do is react to technology."

About his chosen field, he says that science writing is in its adolescence, about where general newswriting was during the period of yellow journalism, and that much of it is terrible.

He does all his writing at home, lounging back in a reclining easy chair, stroking the keyboard of a four-drive word processor. He says that the chair is necessary because of damage to his tailbone from writing 18 hours a day.

The interview with ScienceWriters took place at his home in early May.

Do you think of yourself primarily as a reporter or as a writer?

I've been seriously interested in writing since I was about 13. But I was also interested in science and I was thinking about being a scientist, but the gods weren't really for that. I started out writing science fiction. All ambitious writers try to write about the most important thing going on in their society at the moment and I've always thought that was science.

Writing about politics, it seemed to me, would be a waste. Even as a kid, it was sort of obvious to me that science was the force. Hell, politicians talk about being leaders, but all they do is react to technology. The technology is usually a fait accompli before they even realize it's important. That's happening now with brain research. People are ignoring it because what they're finding doesn't fit their prejudices, but the time will come when it will explode on them like the bomb did.

I always thought of myself as a writer and when I was in the Navy I wrote about science, really military technology, for the last five years of my service.

And then when they passed the GI bill, I went to the University of Maryland, where they would accept you without a high-school diploma, and took a smattering of science courses. When I graduated, I went to the Evening Sun in 1970 and said, "I want to be a science writer."

They told me they didn't need a science writer. So, like everybody else in this business, I learned to keep my mouth shut and go ahead and do it, anyway. If you write three or four science stories and they work, pretty soon you're the science writer because whenever they get a science story, they throw it at you. "Here, Franklin, you do it."

That's one of the advantages of being a science writer: Politically, in the news room, they don't think it's important at all. So nobody really watches you. But it is damned important, and if you can get your finger on that importance, pretty soon you're a star, and nobody ever really sees it coming. They don't know much about what you're doing and have to take your word for things.

Now, by the same token, you can also be a real charlatan, and we both know who they are. There really isn't a tradition of science writing. What there is doesn't go back very far and isn't well developed. So there's all this freedom. C. P. Snow's observation about the chasm of understanding between the two societies is very true; and it seems to me that literary power comes when you take two separate groups of people, both quite ignorant of the other, and you communicate between them, so that what people read of your writing is not only news to them in detail but in perception.

Most people know science is important, but they think they can't understand it. So I sensed a real opportunity for someone interested in the craft of writing to interpret science. If you just report straight news (which I did for a while), the only people who read you are scientists. When I reported straight science, I felt that I was only communicating between one scientific discipline and another. I wanted to reach a mass audience.

Were you trying to reach a political audience?

Not particularly. It's not that I don't want to have an impact on policy; I think that the way to have that impact is by reaching the mass audience, and then let that mass audience have the impact. So I very rarely write about things that have already been politicized. I avoid it. I've had very bad experiences writing about things where the levels of hype and confusion were already so high, everybody had already chosen sides, and nobody really wanted to know what the truth of the matter was.

I teach a course in science writing to a group of students in science at the University of Maryland. I was trying to tell them why science writers behave the way they do. Politicians and reporters have a rapport that goes way back. Science writers really don't because it's so new.

It seems that every discipline has an adolescence and that in the newspaper business it was the era of yellow journalism. I think that science writing is in its era of yellow journalism. A large percentage of what you see of it in any newspaper, including the good ones, is just terrible. Most of it is factual, but anyone who has been in this business for a while knows that fact and truth don't necessarily have any great association. You can choose the facts you want.

I can't really blame science writers for this because their editors want to see a certain kind of story, and, damn, it's hard to fight City Hall all the time. When there was all this hysteria about Agent Orange, I wrote some stories that said the degree of terror is

just not justified by the facts. Nobody else ever picked up those stories. They were an anomaly. In order to run my stories, the editors would have had to rethink their attitudes on the subject, and that's hard to do.

Let's go back to the notion of the adolescence of science writing. What do you think it ought to be when it grows up?

The big thing you have to look at is public ignorance. That was what was behind the more generalized era of yellow journalism at the end of the last century. You have to write for your audience.

Maybe it's a stage you have to go through. People are suspicious of science because of their ignorance. They know it can be abused, but they don't how to tell when that's happening. So there's a market for scare stories and for misinformation. Snake oil is easy to sell to ignorant people, and there's a lot of ignorance about science today. If you tried to give the public that level of hokum about politics, about economics, they would recognize and see what you were doing. You couldn't sell the vast majority of Americans on libertarianism, but you can sell them on vegetarianism and any manner of quack cures and diets.

When I realized that you can do almost anything you want to with scientific facts if the public has no context in which to put those facts, it seemed to me that what I ought to be selling then wasn't detail but pattern, not the facts but the way they're woven. The story of mine that won the first Pulitzer was straight drama. People read that story because it was exciting. They didn't read it to learn anything. But by the time they finished, they knew a lot about brain surgery, what the modern techniques were. It was basically a short story. This latest piece is basically a long essay. I use those two forms, the dramatic form and the essay form. I use literary forms in journalism because only literary forms can demonstrate pattern. When people understand the generalities, they can fit in other things that they see in the newspapers.

There've been a lot of features written about the brain in the last few years, many of them explanatory, but nobody seemed to want to put it all together and say, here is the equivalent of the revolution in physics, only it's more important because it's not about what we can do but who we are.

Actually, I tried to do this series several times, but I ran into some hostility.

NATIONAL ASSOCIATION OF SCIENCE WRITERS, INC.
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Correspondence on editorial matters should be addressed to Barbara J. Culliton, 15 Swaner, 1515 Massachusetts Ave., N.W., Washington, D.C. 20005, or Howard J. Lewis, 7110 Northburn Court, Bethesda, Md. 20817. All articles and columns in the newsletter express the opinions of the authors and do not necessarily reflect the positions of the institutions they represent nor of NASW.

On the paper?

On the paper and some from scientists. I think it must have been that way with evolution in the 1870s. Anyone who really wanted to look at it could see clearly where that was going and what it meant, even though very little of it had been proven. But the pattern was emerging before the details were complete. I think that you find that in most major scientific revolutions. You can see where it's going before you can really prove it's going there.

Where brain chemistry is going conflicts with people's perceptions of themselves. Most people view the mind as something spooky. I think that the idea of the biochemical brain is very disconcerting to people. The paper had to have confidence in me.

Four or five years ago, I decided to see—for myself, not for publication—if I could sit down and write what we knew about how the brain works. It was 30,000 words long. And here is why I think that the future is brightest for the writer, as opposed to the reporter, in the science-writing business. What I did in that 30,000-word piece enabled me to insert all the basic perceptions of the long piece into two pieces of the seven-part series that was eventually published.

What is your arrangement with your editors? Do they assign stories to you?

No, but that's a recent development—after the first Pulitzer. When you have a professional breakthrough like that you figure out how you want to spend it. Do you want more money, a particular assignment, or whatever. What I wanted was the freedom. My managing editor took a gamble. He said, "OK, Franklin, you're your own boss. Please don't make me look like an idiot." Not in so many words, but the message was clear.

So I work at home. I find it very efficient. I do my best work early in the morning. I sort of miss the community of the news room a little bit, but on the other hand you don't have people in Easter-bunny costumes hopping in and out. I have my own library; I get all my telephone messages; I can tape-record telephone interviews, and I don't have any deadlines.

Last year I did seven series. Some were easier than this one, and some of those I had really started in 1983. This year so far I've done a series on the genetics of the brain as a follow-up and I'm now working on a series of stories about a heart transplant that I watched, following a fellow through that. When I finish that, I'll probably go on a leave of absence to finish a book.

You said that there is more power in the use of the right literary form than there is in traditional hard-news journalism. What kind of personal evidence do you have for that statement?

Fans. People who sell writing as opposed to people who sell information have fans, people who will read



anything they write. They create an audience. And they do bring awards.

You can do so much with the literary form; through the use of imagery, metaphor, and suspense, you can communicate so much more information. Science stories are so complex that people are not going to understand them in classical journalistic form.

When you read that first Pulitzer piece on the brain surgery, all you're aware of is that you're reading a story. It doesn't seem complex at all. You're getting some technology but it's in context. The reader has the experience of being in the operating room. There is high information content in that. The reader not only knows about this operation, he really knows what it's like to be in an operating room. All the information is in the context of the feeling and the feeling shades the information.

The reader wouldn't have much trouble empathizing with a doctor or a patient. What do you do about particle physics?

Fortunately, I don't do anything about particle physics. When you write about science in Baltimore,

you write about medicine. But if I had the opportunity to work in physics, I don't think that for the most part I would write about physics. I would write about physicists. Science is a human endeavor, and it very rarely gets presented that way except in terms of human fallibility, accidents, cheating, and all that. The human quest almost never gets into it and when it does, it's so saccharine, it never works.

Whom do you consider to be your models or mentors in literary form?

John Steinbeck (he's the original model). Lawrence Durrell's *Alexandria Quartet* had a great influence on me in the use of stream of consciousness and shifting perspectives. Walter Sullivan (I would love to meet him sometime). . . . In terms of reporting, Joann Rodgers [then a reporter on the *Baltimore News-American*]. She taught me a hell of a lot and kept me out of so much trouble. When I started in she took me aside and warned me about things, like never, never write a cancer-cure story. She saved me an incredible amount of grief. In terms of science literary form, Loren Eiseley. Desmond Morris in terms of how I thought about the human dilemma. I've been encouraged in recent years by Lewis Thomas, the fact that he could actually get on the best-seller list. I would like not only to write books, but also to sell them.

One of the problems that face medical writers is that all too often the reader is left with a feeling of helplessness. Editors sometimes demand that you have to tell the reader there is something he or she can do. Is that a problem in your format?

After I did my first book about people with multiple trauma from highway accidents who can sometimes be saved if you can get them to a shock-trauma unit quickly enough, it was serialized by *Woman's Day*. An editor up there had your complaint: She wanted something about what the reader could do if he came upon the victim of multiple traumas by the side of the highway. I couldn't believe it. I said, "Why don't you print the Lord's Prayer?" I try to leave the reader with a positive feeling that now he can understand what is going on.

A lot of science news writers are going to argue with you that somebody has to cover the hard news. I know that Donald Drake has an arrangement something like yours with the Philadelphia Inquirer, but not many other science writers do. Nor do they seem to want to. Do you feel that they limit themselves to the traditional format without really asking whether the literary approach might not be both possible and more effective?

When you're just getting started in this business, you can't do all the news stories that you want to do, so it doesn't become a question. But over a period of years, there's a tendency for people to think that because they've been forced to do something for a long time, it's therefore correct and it's what they

ought to be doing. I think that not nearly enough people are willing to struggle with the tradition, with their editors, to test the bounds of their profession. They say, my editors won't buy that. Well, my editors didn't want my stuff either, and I paid for it heavily. I think I put in more Saturdays at the *Evening Sun* than any other reporter in its history. It was almost a punishment, like KP. I had to come in early and get all the crappy assignments. So you pay for it.

Donald Drake was something of an inspiration to me in this area. We flew back from some conference together. It must have been in 1978 or so. He was the first person in the news business that I found who actually shared my views. He was a big wheel in NASW at the time, and I have to say that that conversation with him, finding out that he had thought it through more than I had, talked to more people because he was more social than I, sort of gave me the courage to keep at it for as long as I did. I almost never see Don because he doesn't go anywhere and I don't go anywhere; but I wish I did see him more. We're fellow-travelers.

A REPORTER'S CHECKLIST:

PARANORMAL—OR SELF-PROMOTER?

by Kendrick Frazier

We've all seen the stories often enough:

The police find the body of a missing person. The next day the news media report that a local psychic helped lead police to the scene.

A California scientist writes a book on the psychic arms race. He says the government is secretly spending millions to develop psychic weapons before the Soviets do. His experiments show we all have innate psychic powers. The book is widely reported as news throughout the country.

An astrologer is interviewed. She pooh-poohs the horoscope columns in newspapers but says astrological readings done for individual persons are eighty percent accurate and valid science, "documented by numerous scientific studies."

Welcome to the world of news media reporting of the paranormal. Stories like these—and countless others—appear regularly in daily newspapers throughout the United States. Readers could be forgiven for assuming that thoughts can be read at a distance, that the laws of physics are capricious and personal, and that mysterious forces unknown to science are readily apparent.

No doubt such stories can be legitimate news. The

Kendrick Frazier is the editor of *The Skeptical Inquirer*, published by the Committee for the Scientific Investigation of Claims of the Paranormal.

→ TPA → MIL

The Evening Sun

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BALTIMORE, JULY 23, 1984

25 CENTS

The Mind Fixers

First of seven articles

Chemistry opens new vistas for psychiatry

By Jon Franklin
Evening Sun Staff

Since the days of Sigmund Freud the practice of psychiatry has been more art than science. Surrounded by an aura of witchcraft proceeding on impression and hunch, often ineffective, it was the bumbling and sometimes humorous stepchild of modern science.

But for a decade and more, research psychiatrists have been working quietly in laboratories, dissecting the brains of mice and men and teasing out the chemical formulas that unlock the secrets of the mind.

Now, in the 1980s, their work is paying off. They are rapidly identifying the interlocking molecules that produce human thought and emotion. They have devised new scanners that trace the flickering web of personality as it dances through the brain. Armed with those scanners, they are mapping out the terrain of the human psyche.

As a result, psychiatry today stands on the threshold of becoming an exact science, as precise and quantifiable as molecular genetics. Ahead lies an era of psychic engineering, and the development of specialized drugs and therapies to heal sick minds.

But that's only the beginning. The potential of brain chemistry extends far beyond the confines of classic psychiatry.

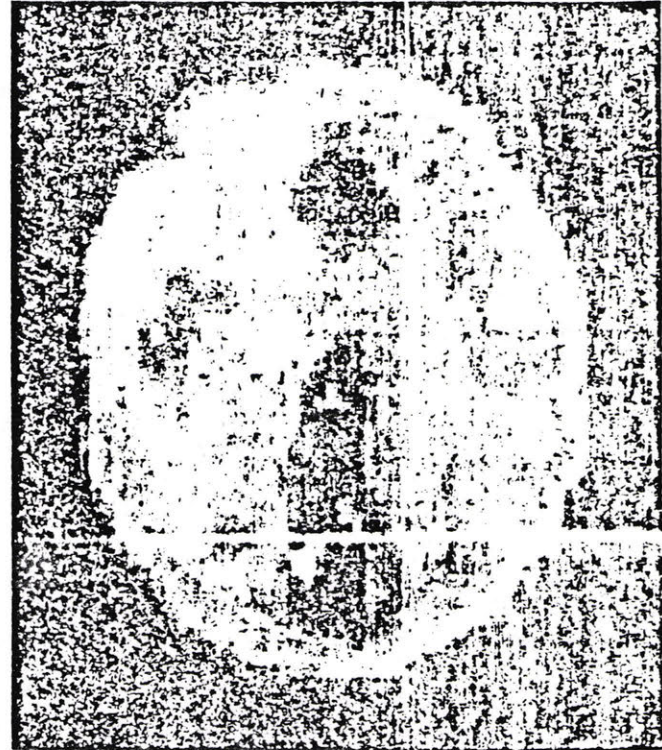
Many molecular psychiatrists, for instance, believe they may soon have the ability to untangle the ancient enigma of violence and criminality.

Further, there is the promise that the current technology will lead to the development of drugs capable of expanding the workings of the normal mind—enhancing memory, heightening creativity and perhaps, one day, even increasing intelligence.

Ultimately, interviews with more than 50 scientists indicate, the revolution may offer us the most important gift of all: a dramatically improved understanding of who we are, why we are that way, and what it means to be human.

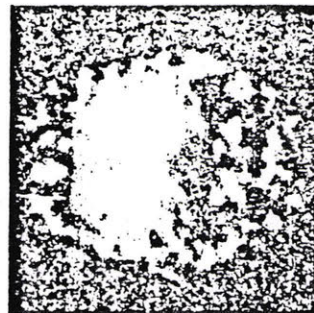
□

Molecular psychiatry, like the new genetics, is based on a chemical interpretation of events



Johns Hopkins University of Texas photon

Aided by computer-generated cross sections of the brain, such as those above and below, scientists are beginning to map the intricate chemistry of thought and emotion.



New scanners
trace the flickering
web of personality
as it dances
through the living
human brain

Coming boon to psychiatry finds herald in chemistry

in and around the living cell. Human perception, feelings and behavior are seen to result from

submicroscopic interactions—the complex interplay of Tinker Toy-like molecules that make up natural substances resembling heroin, Valium and alcohol.

Like molecular genetics, molecular psychiatry possesses the inherent ability to be both precise and quantifiable and, again like genetics, it lends itself to the deliberate process of altering nature, the process called "engineering."

But unlike molecular genetics, which concerns itself only with the physical makeup of the human animal, molecular psychiatry pushes the frontier of science to the eerie and mythical boundary that divides the physical and the mental.

Many philosophers, in recent years, have begun to ask whether that barrier will be breached. But according to most of the scientists involved, the point is moot. The mind-brain barrier has been probed and found not to exist.

They say there is no distinction between mind and

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brain; the one is a direct, mechanistic outgrowth of the other. At least a few philosophers share this view.

"We're out-and-out materialists," says Daniel C. Dennett, professor of philosophy at Tufts University, summing up a Johns Hopkins scientific conference on the issue.

Or, in the blunter words of one neuroanatomist, "The brain is an organ; it produces thoughts the same way the kidney produces urine."

If that attitude outrages some philosophers and priests, the scientists themselves are unperturbed.

A little philosophical discomfort, they say, is a small price to pay for a new science capable of curing the mental diseases that afflict perhaps 20 percent of the population and constitute a major drain on the gross national product.

And scientists like Dr. Candace Pert, a key figure in brain chemistry at the National Institute of Mental Health, say the mechanistic view is in fact the most humanitarian one.

She argues that thinking of the mind as something spooky and apart has historically led to judgmental attitudes toward the insane.

"It's sad, but even today, this far into the 20th century, mental illness is not even totally talked about. It's still considered something ugly, something to hide. People are ostracized."

"But people who act crazy are acting that way because they have too much or too little of some chemicals that are in their brains. It's just physical illness! The brain is a physical thing!"

As molecular psychiatry proceeds in the direction of curing and even improving the function of the brain, it has become a magnet for some of the brightest minds and biggest names in biology.

Francis Crick, the molecular geneticist who won the 1962 Nobel prize for his part in unraveling the secret of DNA, has switched his field of study to molecular psychiatry. Another convert is Gerald M. Edelman, who won the Nobel for studies of the molecular basis of immunity. They are joined by hundreds of top students from the nation's medical schools and graduate programs.

What is this new science? What are its principles? From what promises flow its optimism and appeal?

The flavor is conveyed most dramatically in the words of the scientists themselves as they strive to convey their view of the brain and their hopes for the future:

■ Dr. Michael Kuhar, a brain chemist at the Johns Hopkins Medical School: "The working unit of the brain is the [receptor]. You can think of the receptor as a button. Chemicals come and push that button and make things happen."

"The brain is this complex array of buttons. You give certain drugs which hit certain receptors and certain things happen in the body. It might be an emotional experience, a thought experience—it might be a constriction of blood vessels, or a release of gastric acid. You know, stuff like that."

■ Dr. Marcus Raichle, neurologist and radiologist at Washington University in St. Louis: "This is very seductive stuff . . . for the first time we have the prospect of looking [inside the brains of] living patients with emotional disease, and looking at specific regional changes in their brains."

"I think we are going to find that there is a biological basis for many behavioral disorders."

■ Dr. Paul Mandel, at the Center for Neurochemistry in Strasbourg, France: "People don't realize that psychology is a result of chemical behavior. That's why alcohol changes behavior . . . it acts on the other molecules. A lot of behavior has relatively simple physical causes."

"Specifically, the purpose of my research is to produce drugs for aggression . . ."

"Aggression is like any other disease. It's the lack of inhibitory mechanisms that can be produced by genetics and/or the environment, and there's no reason not to treat it if we can."

■ Dr. A. John Rush, a brain scanner expert at the University of Texas Health Science Center in Dallas: "I would think that within 10 years we'll have at least one or two biotechnologies that will tell us a great deal about the probabilities that someone will in fact develop a [psychiatric] illness. I think we're going to be able to identify people with a reasonable degree of reliability . . . say 70 percent."

□

The technology that underlies the hope for the future is often traced to Baltimore. It was here, in 1973, that Dr. Solomon Snyder and Candace Pert, then a doctoral candidate in Snyder's laboratory at Johns Hopkins,

succeeded in labeling and identifying the submicroscopic chemical sensors that stud the membranes of brain cells—the "buttons" that Kuhar describes.

That discovery opened up psychology as a quantifiable science.

The excitement spread rapidly through brain laboratories around the world as scientists confirmed the Snyder-Pert research and went on to identify, label and map the distribution of other behavior-affecting molecules in the brain.

The technology behind the Snyder-Pert breakthrough also led to an ability to readily create powerful new chemicals capable of literally changing the mind.

Most of the early work, which required dissection of the brain, was performed on animals. But before the 1970s were out, scientists had produced several types of powerful brain scanners capable of monitoring the living chemistry of thought in the human brain itself.

The scanners do for brain scientists what telescopes did for early astronomers. Though the scanner technology is still in its infancy, it has already allowed scientists to peer into the brains of living, thinking human beings—and has produced a variety of findings that tend to bear out the mechanistic view of the mind-brain.

For example:

■ At the University of Texas Health Science Center in Dallas, scientists have discovered that normal people use their brains in very individualistic ways, producing scans so characteristic that they can be likened to "fingerprints." In patients with multiple personalities, shifts in the patterns correlate with changes in persona.

■ At Washington University in St. Louis, where the first of the new generation of brain scanners was developed by a team led by Dr. Michel M. Ter-Pogossian, scientists have produced the first solid proof linking a perceptual disease with a chemical abnormality. The disease involves panic attacks.

■ At Brookhaven National Laboratory in New York, scientists with one of the most modern scanners

"... But people who act crazy are acting that way because they have too much or too little of some chemicals that are in their brains. It's just physical illness! The brain is a physical thing! . . ."

—Dr. Candace Pert

"... People don't realize that psychology is a result of chemical behavior. That's why alcohol changes behavior . . . it acts on the other molecules . . ."

—Dr. Paul Mandel

available seem to be homing in on pinpointing a similar abnormality in the brains of schizophrenics.

■ At Hopkins, researchers led by Dr. Henry Wagner have for the first time labeled and mapped the distribution of receptors in the living human brain. In the process they have uncovered evidence that may explain why males become calmer as they grow older.

The explosive pace of discovery, says Dr. Joseph Coyle at Hopkins, "bodes well for the future."

"It suggests that we're approaching a point when we'll be able to make some coherence out of this wealth of information. I'm optimistic . . . we've gone from ignorance to almost a surfeit of knowledge in only 10 years."

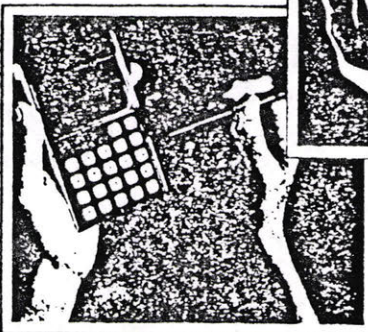
Dr. Fred Goodwin, chief scientist at the National Institute of Mental Health and as such the government's top research psychiatrist, agrees.

"We're being flooded with data," he says. "If you project the rates of growth [of knowledge], you'd have to say it's still accelerating . . . expanding exponentially."

"As we become sophisticated about understanding the biology of behavior, the more potential we get for altering behavior biologically."

He says scientists now understand, for instance, the

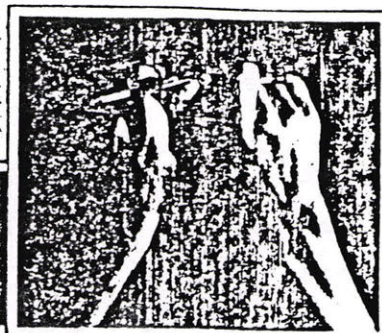
Psychic engineering / its potential



Amplify mental abilities



Curb drug addiction



Alleviate mental illness,
severe stress

Photo Illustrations by Robert E. Hamilton — Evening Sun Staff

chemistry of anxiety. "We now know biologically what anxiety is. We can turn it on and turn it off."

The objective is nothing less than mind control—the therapeutic kind.

In addition to anxiety, the target diseases include the obvious ones: schizophrenia, depression, manic-depressive disease, obsessive-compulsive disease, Huntington's disease and Alzheimer's disease.

But the list goes on to conditions that laymen tend to consider from a moralistic, not medical, point of view.

Many scientists, for instance, suspect that drug addiction may occur because of genetic or environmentally induced defects in the addict's psychological pain centers.

In this view the addict takes drugs in an attempt to alleviate a terrible agony; in his position, any one of us might do the same.

And then there's the subject of criminality.

Dr. Goodwin at NIMH sees the violence-prone criminal as often suffering from one of many physical brain ailments, making him unable to control his actions.

If those ailments could be diagnosed and treated (and there is research to this end), society might be spared a large percentage of its violent crime. The rising costs of the penal system might also be trimmed.

Such research quickly spills over into the political arena.

In France, Dr. Mandel's research on the chemistry of aggression has convinced him that Iran's Ayatollah Khomeini is a sick man, suffering from a chemical imbalance in his brain triggered by religious fanaticism.

In Mandel's theoretical framework, the ayatollah and his followers could "benefit" from the administration of drugs being developed in Mandel's laboratory.

And still, as scientists penetrate farther and farther into forbidden territory, the possibilities unfold.

If the new science could alter the minds of psychotics, criminals and bigots, what might be done to enhance the functioning of the "normal" brain?

Plenty, in the view Goodwin. Already, he says, there is a drug that will improve the memory of normal subjects. And research seems to be pointing toward still another drug, perhaps related to PCP, that will enhance creativity.

Dr. John Lion, an aggression expert at the University of Maryland Medical School, believes such findings put molecular psychiatry at serious odds with the current social and legal systems.

Where does that conflict lead?

According to Dr. Fritz Henn, chief psychiatrist at the State University of New York at Stony Brook, most scientists shy away from thinking about that question. He doesn't think about it much himself.

"It's much more fun," he explains, "to talk about what the next [important neurochemical] is going to be, and how it may be a key to unraveling an illness you're interested in. This [question of conflict] is a much stickier and tougher question. And it's not really a scientific question. It's a political question."

But when the tape recorder is turned off, a few scientists admit that they do think about it—and that they're very concerned.

"We're approaching an historic moment of truth," muses one scientist. "The knowledge that's being produced is rapidly becoming an irresistible force, and it challenges our basic perceptions about who we are... about religion, politics, criminality, right, wrong and free will."

"Historically, society doesn't react very well to challenges like this—especially when they come without warning, out of the sun. And most people are blithely unaware of what's happening. Philosophers, those who get involved at all, put most of their energy into denying the obvious. So there's no preparation, and it's all happening very rapidly."

"Under circumstances like that, society is pretty much an immovable object. It always has been. So there is going to be a collision, and it's going to be of epochal proportions."

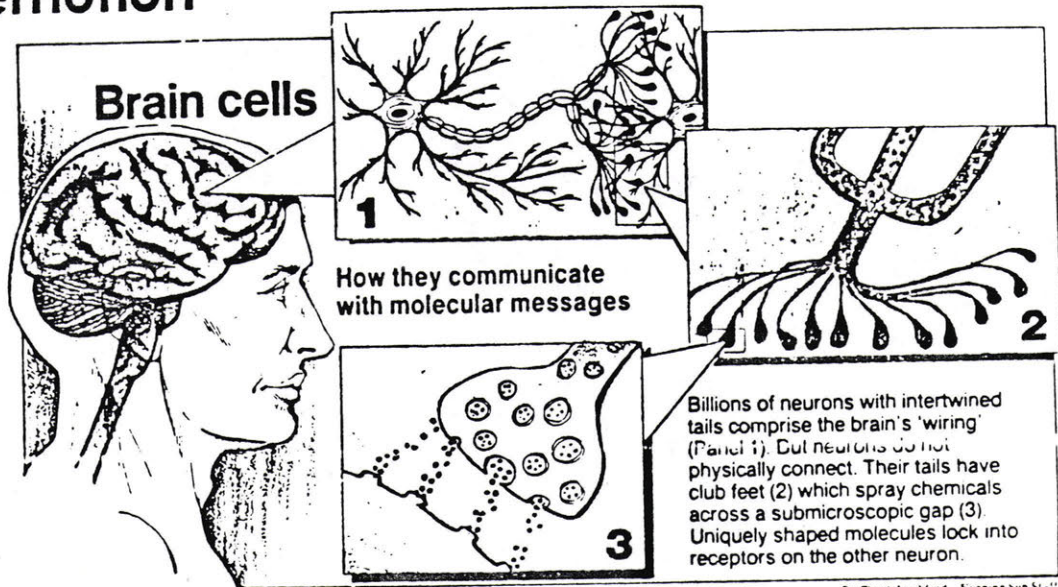
Tomorrow: The molecular marvels of the human psyche.

... As we become sophisticated about understanding the biology of behavior, the more potential we get for altering behavior biologically ...

—Dr. Fred Goodwin

The Mind Fixers/Healing the Human Psyche

Chemical spray is crucial part of thought, emotion



By Chuck Lankford Evening Sun Staff

By Jon Franklin
Evening Sun Staff

Brain scientists have developed a revolutionary new theory of molecular psychology that is catapulting the study of human behavior into the realm of the exact sciences.

That theory, now broadly confirmed by laboratory experiment, reveals that the human mind is controlled by the chemical flux of molecules playing against the surface of brain cells.

Don't be misled by the word "theory." In the world of science the development of a theory is a substantive event, a turning point that often leads rapidly to a technological revolution with broad social impact.

So it was with the theory of relativity, which opened the way to fission and fusion bombs, atomic power, and nuclear medicine. In biology, the more recent development of a theory of molecular genetics during the 1950s and '60s led, in the '70s and '80s, to genetic engineering.

The new body of knowledge about molecular psychology also appears to be leading to a new type of engineering—psychic engineering.

This involves a precise alteration of the chemical activity in the brain in order to correct for, and therefore overcome, mental illness. Prominent researchers also believe such engineering can also be used to enhance the function of the normal mind.

So it is that the new psychology may have medical, social and political consequences at least equal to those flowing out of the theories of relativity and molecular genetics.

To understand why this is so we must focus our attention on the theory itself, and on the once-mystical organ of personality: the human brain.

On the level of the naked eye, the brain is a gray, jelly-like mass that retains its shape only because it's encased in a tough membrane. It weighs an average of 2½ pounds and is so unimposing that, throughout most of the past 2,000 years, anatomists assumed that its function was only marginally important.

It was only with the discovery of the microscope that the incredible complexity of the nondescript gray organ became apparent.

Under the light microscope, the functioning unit of the brain can be seen to be an individual gray cell called a "neuron." There are so many neurons that no one has ever succeeded in counting them; estimates of their numbers in the average brain range from 10 billion to a trillion.

Brain cells come in various sizes and shapes, but each has a long tail called an "axon."

The tail stretches through the brain until, as it nears its destination, it splits into smaller tails. The end of each tail-let lies against the surface of another brain cell.

In the 1800s it was discovered that one of the functions of the neuron was to generate electrical signals and "fire" them down their axons. More modern scientists with delicate probes determined that the neuron idled at about one impulse a second, but could almost instantly increase its frequency to 60 impulses a second.

Though each charge is relatively weak, there are so many firings in any given instant that they average out to produce a measurable magnetic field; that's the

source of the squiggly lines on a neurologist's electroencephalograph, or EEG machine.

By early in this century scientists had begun to understand that the brain was a computer of some sort, the individual elements were apparently the brain cells, and their axons formed the electrical wiring.

The electrical "wiring diagram," though, had one very puzzling aspect. The axons that carried the charge didn't make actual physical contact with their "target" cells.

Instead, the axons terminated in club-like structures that looked like barnacles and were named "boutons." There were so many boutons that they literally covered the brain cells—covered them, but didn't touch them.

That was a real enigma. How did the electrical message get from the bouton to the brain cell? Certainly the electrical charges couldn't jump the gap; there could be no sparks in the wet goo of the brain.

This gap between bouton and brain cell, called the "synapse," came under intense scrutiny when electron microscopes became widely available in the 1950s and '60s.

Finally, from the laboratories of biochemists and electron microscopists, the answer began to emerge. It was a strange one, and it carried scientists of the mind

into the submicroscopic, tinkertoy world of the molecule.

The gray neuron, it turned out, had not one function but two. In addition to producing electrical charges, it manufactured strange, hormone-like chemicals called "neurotransmitters."

What's more, the tail of the gray cell wasn't much like a wire at all. It was a hollow tube. While electrical charges flowed down the outside, neurotransmitters were pumped down the inside and stored in the bouton at the end.

The bouton, as it turned out, was covered with tiny nozzles on its underside. Each time it was hit by an electrical charge, the nozzles opened and chemicals streamed out, spraying onto the surface of the adjacent brain cell.

Somehow, these chemicals transmitted information from the bouton to the underlying cell.

The messages, scientists first surmised and later proved, were coded in the shape of the molecule—as was the case with hormones.

Only one question remained to complete the story of brain cell communication: How did the receiving cell "hear" the messages that were spraying onto its surface?

Scientists guessed that the answer was tiny, shape-sensitive antenna molecules on the cell's surface. Those theoretical "receptor" molecules were likened to locks; the transmitter molecules were keys that snapped into the locks and, by doing so, activated them.

This idea assumed that brain cells were studded with thousands of receptor molecules.

The receptors were probably long molecules that extended from the surface of the cell deep into its

interior, where the "foot" of the receptor was hooked into the cell's metabolic throttle.

The exposed end of the receptor functioned as an antenna, equipped to sense one specific class of neurotransmitter molecule.

Presumably, when a transmitter molecule struck the surface of the receptor, the receptor's shape changed. In the cell's interior, the "foot" of the receptor moved against the throttle and the cell's metabolic engine speed either increased or decreased by one notch.

How many times the receptor's tail twitched each second probably depended upon how many transmitters were bombarding its antenna. Since there were hundreds or thousands of receptors on each cell, and they were all being bombarded by transmitter molecules, the firing rate of the cell depended on the averaged-out signals.

That made sense, but it was guesswork. The proposed receptors were speculation, until they could be found, labeled and isolated for study, this new theory of how the brain worked on a molecular level would remain a subject of debate among specialists.

Then, in 1973, at the Johns Hopkins Medical School, it happened.

The scientists were Dr. Solomon Snyder and a doctoral candidate, Candace Pert. Working together, they devised a sophisticated technique that allowed them to locate and label brain receptors with radioactive chemicals.

Their discovery was published that summer in Science magazine—and it was a bombshell.

The scientific community understood the implications immediately. Cell-to-cell communication was the basis of thought and emotions, and the Snyder-Pert paper

Maryland pioneers



Dr. Solomon Snyder
of Johns Hopkins



Dr. Candace Pert

At Johns Hopkins in 1973, Solomon Snyder and Candace Pert made a breakthrough discovery about cell-to-cell communication in the brain. Dr. Snyder now continues his work in brain chemistry as chief neuroscientist at the Johns Hopkins Medical Institutions and Dr. Pert is a key figure in brain research at the National Institute of Mental Health in Bethesda.

1973: the breakthrough



provided the last chemical link in that chain of communications.

In a matter of months, the receptors were isolated and analyzed, and the whole picture coalesced into sharp focus.

As the tide of transmitters rose and fell in the living brain, and the receptors reacted, the neurons selectively changed their firing rates. As those rates changed, feelings and thoughts wafted through the mind.

In principle, at least, the chemistry of thought was now understood, being understood, it could be specifically manipulated with drugs.

The age of molecular psychology had dawned. Snyder and Pert gained instant worldwide fame in the scientific community; their breakthrough paper became one of the most widely quoted in recent history.

Within a few years Snyder would receive the coveted Lasker Award, assume the leadership of a major new neurosciences department at Hopkins, and become a favorite candidate for a Nobel Prize. He would also become a founding member of a drug research company with stock so hot that he would become a millionaire—at least on paper.

Pert, the junior member of the team, walked into a bright future that would propel her to the head of a major neurosciences laboratory at the National Institute of Mental Health.

They and other scientists, in the meantime, worked feverishly to confirm and elaborate on the theory. As the 1970s drew to a close, the organ of personality emerged as a gizmo—as a computer, no more and no less.

But it is no less wondrous for its mechanistic nature; as an information-processor, the brain puts manmade supercomputers to shame.

The most sophisticated human computers function in classic "digital" fashion: At any instant, a circuit is either off or on. The brain does this too. Any transmitter represents an "on" or "off" command, depending on whether or not it is a "stimulant" or a "depressant."

But while the variables in a manmade computer are confined to that digital code, the digital nature of the human brain represents only its most superficial level.

In the brain, for instance, the cellular "clock" can vary from one cycle per second to 60. Additionally, the efficiency with which the cell can manufacture and transport neurotransmitters down its tail is subject to rapid change. Finally, the receptors on its surface can change from minute to minute, making the cell more or less sensitive to input.

The brain incorporates another neat trick of nature when it uses chemicals instead of electrical impulses as a medium of communication. Electrical impulses are all the same, more or less, but chemicals can differ almost infinitely.

So far, scientists have identified about 50 neurotransmitters; there may be thousands before the full story is known.

Each represents a different way of saying "yes" or "no," and ensures against "crosstalk"—a "yes" message directed at one set of cells can't get mixed up with a different "yes" message directed at another set, because each receptor can "hear" only one molecular shape.

The brain, in other words, is no mere computer. It is hundreds, perhaps thousands, of computers, each superior to anything yet conceived by human engineers.

Yet all those systems and subsystems and sub-subsystems are completely integrated, tying together mood with thought with instinct with observation and summing them all up in something called "personality" and "behavior."

The full complexity of the brain will not be plumbed in this century, and perhaps not ever. But the general theory, as it emerges as a laboratory tool, has immediate applications with direct, practical implications for human society.

The easiest example to understand goes back to that 1973 Snyder-Pert breakthrough.

At the time, their work was financed by the drug abuse arm of the Alcoholism, Drug Abuse and Mental Health Administration. Their specific objective was to discover the chemical mechanism of heroin abuse and addiction.

So it was that the first receptor to be discovered was the one for opiates, the class of chemicals encompassing opium, morphine and heroin. In broad terms, at least, the discovery explained the mechanism of addiction.

Today, 11 years later, the addiction process remains a favorite example for explaining how the physical function of the brain translates into human mood and

consciousness—and how specific drugs can be engineered to affect thought and feeling.

The heroin molecule, it turned out, is addictive because it happens to mimic the shape of a neurotransmitter that was later to be named enkephalin.

Enkephalin is manufactured in the pain centers of the brain—not just the physical pain centers, but the psychological pain centers as well. Both use the same neurotransmitters because, in the course of evolution, the psychological pain centers evolved from the physical ones.

That fact lies behind the world's drug abuse problem, and some of its most serious behavioral problems as well.

In the areas of the brain where physical pain is processed, enkephalin serves a straightforward function.

Pain impulses flow continuously upward from the body, and must be screened. Enkephalin, pumped constantly into those pain centers, suppresses and desensitizes the pain-recognition cells so that they respond only when the pain exceeds a certain level.

In the psychological pain centers, the same transmitter suppresses minute-to-minute psychological pain. But in addition, it serves as a "good-feeling" chemical that rewards us for behaviors that have been programmed into our brain either by genetics or environment (both are apparently of equal importance).

Enkephalin, it appears, is what we feel when Mother smiles at us. Later in life, it rewards us when we achieve something Mother would have classified as "success."

If on the other hand we *don't* have a mother's love, or if we have too little success, we are deprived of enkephalin. The same effect would result, regardless of Mother and her love, from a genetically weak enkephalin system.

Either way, the result is supersensitivity to background psychological pain. That pain is called "depression" and is no less excruciating for its "imaginary" nature.

If we live in a ghetto, and suffer that pain, we may discover a substitute for love and success—a substitute that can be administered by needle. As the heroin floods into our brain, the psychological anguish eases.

It matters not one whit whether our psychological pain is due to socioeconomic deprivation or a genetic malfunction in our enkephalin producers or receptors. The "addictive personality" may in fact be a result of a luckless combination of both.

A similar effect, mediated through different receptors, can be achieved with alcohol, barbiturates, marijuana and other drugs.

The pain-relieving high can even be achieved naturally, by torturing ourselves physically and thus stimulating the natural production of enkephalins.

So it is that the bed of nails is in fact a road to peace, and the "runner's high" is so potent that addicts have been known to run on broken ankles.

More subtle versions of the same thing can be discovered in our individual behaviors. Habits are mediated, in part, by the internal pumping of enkephalin. Depression, both natural and pathological, is profoundly influenced by our enkephalin levels. Love is addicting. Food is addicting. Belief is addicting.

The broad point made by the Snyder-Pert experiments and those that followed was that natural drugs are the basis of human nature and behavior.

It followed, then, that malfunctions in personality such as schizophrenia or violent behavior might be caused by chemical disruptions in the brain.

That being the case, might the new theory of molecular psychology enable scientists to isolate the chemical defect involved?

And might the theory, coupled with the new technology used by scientists like Snyder and Pert, be harnessed to produce new drugs to combat behavioral diseases of the brain?

As for the question of powerful new drugs, the answer seemed to be an emphatic yes!

In one set of experiments, a junior researcher at Hopkins, working alone, was in two years able to produce a caffeine-like drug that was 500,000 times more powerful than the original.

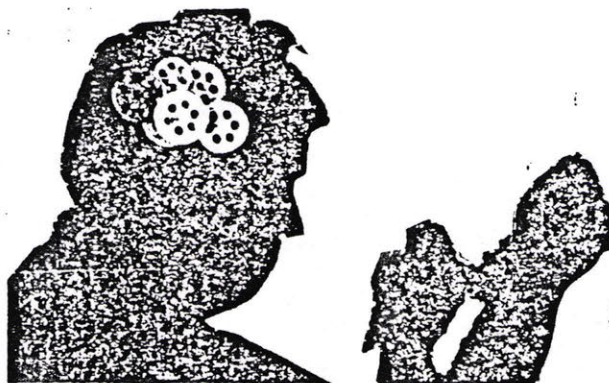
The race was on.

The object: Find the chemical basis of mental disease, and devise ways to correct it.

Whether cast in terms of economics or of human suffering, the stakes were astronomical.

The Mind Fixers/Healing the Human Psyche

Scientists expect cure soon for blue misery of depression



The utter agony of untreated clinical depression may result in suicide . . .

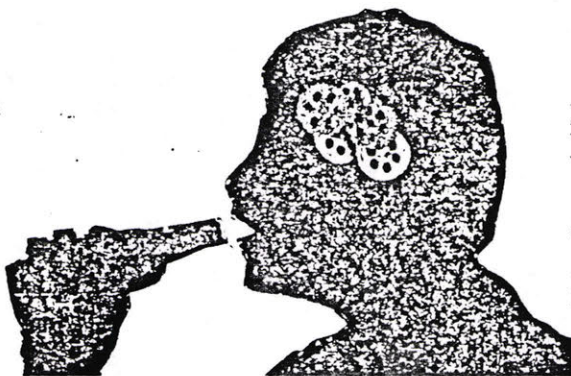


Photo illustrations by Robert K. Hamilton—Evening Sun Staff

. . . or in alcohol and drug abuse, a slower approach to self-destruction

By Jon Franklin
Evening Sun Staff

Perhaps 18 million Americans are victims of clinical depression. They are the "walking wounded" of the high-pressure modern world, and the blue misery that dogs them affects the rest of us as well.

Depression puts a steady drain on national productivity and is a major spoiler of family life and social tranquility. But now scientists are making rapid progress in understanding the disease, and have already managed to trace it to a malfunction in two of the brain's chemical subsystems.

That discovery and a cascade of other findings about the nation's most common mental illness have poured from the new science of molecular psychology during the last few years.

"There have been incredible breakthroughs in the understanding of depression," says Dr. Candace Pert, one of the founders of the new science and a leading researcher at the National Institute of Mental Health in Bethesda. "The prospects for the future have never been so bright."

Pert's enthusiasm echoes that of many neurochemists. And most believe the explosion of knowledge will translate directly into the creation of effective new drugs to combat depression.

Continued on next page

Most mental depression victims unaware of their disorder

Depressive illness is one of the most painful conditions known to medical science. Yet, because of the strange ability of the mind to damp out and transfer pain, many victims aren't even aware that anything's wrong.

"The vast majority of people who are depressed do not know they're depressed," says Dr. Joseph Coyle, a molecular psychiatrist at Johns Hopkins Medical School.

He says that the victims who can feel the psychic pain directly are in some respects the lucky ones. Their pain may compel them to go to a psychiatrist and get treatment.

But the majority of victims, unable to face the situation squarely, are not so fortunate.

With victims unable to accept the psychic pain for what it is, their brains translate the agony into a more readily understandable form of pain—the physical kind.

Or the victims wall it off and treat it with psychic painkillers such as alcohol, heroin or other addictive substances.

That presents a real problem, Coyle says, both for psychiatrists and for family doctors whose waiting rooms are filled with people whose pain, quite literally, is all in their heads.

The Hopkins neurochemist tells a classic story of a team of scientists who were searching for volunteers to help test a new anti-depressant drug.

The researchers advertised in the paper, offering free treatment for depression in return for participation in the drug trials. They got a few takers, but not many.

Then one of the scientists had a brainstorm. The next ad didn't ask outright for depressed volunteers. Instead it included a simple checklist of symptoms: Have you lost interest in sex? Do you feel

... There's a very high tendency for persons with psychic pain to complain of physical pain... many of these people go to their local physician with inscrutable disorders, and with pain that doesn't seem to have any physical basis... The mind plays tricks...

—Dr. Joseph Coyle



hopeless? Do you have trouble with insomnia? Do you often feel that you are a bad person?

The scientists' telephone started ringing as soon as the newspaper hit the streets, and didn't stop for days.

"Many people," says Coyle, "got very upset when they found out they were calling a psychiatric clinic. They didn't perceive that they had a psychiatric problem."

"There's a very high tendency for persons with psychic pain to complain of physical pain... many of these people go to their local physician with inscrutable disorders, and with pain that doesn't seem to have any physical basis."

Pain clinics, including the one at Johns Hopkins, have documented that many people with intractable back pain are in fact suffering from depression and similar disorders.

The traditional psychiatric explanation is that the mental pain gets subconsciously channeled into the physical pain processors in the brain.

A molecular psychiatric explanation, says Coyle, is that in depression the pain threshold is lowered throughout the brain. As a result, otherwise minor pain is translated into unbearable agony.

"The mind plays tricks: Different people do different things. A lot of people don't think psychologically; they don't put all these symptoms together and say, 'Well, I must be depressed.'"

"What you're talking about is this oppressive feeling of hopelessness and lack of energy... I can't sleep, my appetite's lousy... you know, it requires a certain amount of sophistication to tie those things together and see it as a problem with mood."

"We're talking about a rather serious disturbance in brain function that has pervasive effects on the brain and in the body as a whole."

"We call it 'depression' but in fact the prominent symptoms can involve all the fundamental bodily

functions. Individuals often ascribe the mood change, the depression, to the fact that they're physically sick... rather than the other way around."

But if mentally ill patients often end up in treatment for physical ailments, the opposite is also true.

Many patients who seek psychiatric treatment for depression turn out not to have primary depression at all. Instead, the depression is being inadvertently caused by a drug prescribed by their family doctor. Many drugs, including compounds commonly prescribed for heart disease and high blood pressure, can induce depression as a side effect.

But when a patient is in fact clinically depressed, and when that patient gets to a psychiatrist, the treatment can be straightforward.

If the depressed patient is one of those for whom drugs like imipramine are effective, the course of therapy can be relatively brief. The physical symptoms go away first, and are followed by the psychological ones.

"It usually takes somewhere between two and six weeks to respond to treatment with anti-depressants," says Coyle. "Then [patients] feel better. They're able to go back and live their lives."

Often the patient is surprised, even disbelieving, as the symptoms vanish.

"The ones who are psychotically depressed frequently have great difficulty making sense out of what happened," says the Hopkins scientist. Some patients never do quite comprehend that they were the helpless victims of changes in their brain chemistry.

Many deny that the doctor did anything at all. "You just tell them, 'OK,'" sighs Coyle. "You tell them, 'Well, if these things return... come back and see us and we'll make you feel better again.'"

Scientists expect cure soon for blue misery of depression

Continued from preceding page

Though no reputable scientist is willing to make specific predictions, most insiders interviewed by *The Evening Sun* say they would be surprised, even shocked, if such drugs didn't begin to appear within a decade.

More effective drugs for depression would have a dramatic social and economic impact, not just on the victims and their families but also on the nation at large.

The various identifiable types of "clinical depression," as distinguished from the day-to-day depression experienced by normal people in the face of real setbacks, is thought to affect about 8 percent of Americans.

The diagnostic symptom is an overwhelming feeling of helplessness and a conviction that nothing the victim does will make any difference.

Other symptoms include loss of interest in the outside world, malaise, feelings of self-hatred and a delusional expectation of punishment or impending tragedy.

But in the complexity of the human mind, those symptoms may be masked by other responses. What's

more, the symptoms can jump from the mental to the overtly physical as the disease runs its course and the patient, full of self-hatred, fails to practice good hygiene.

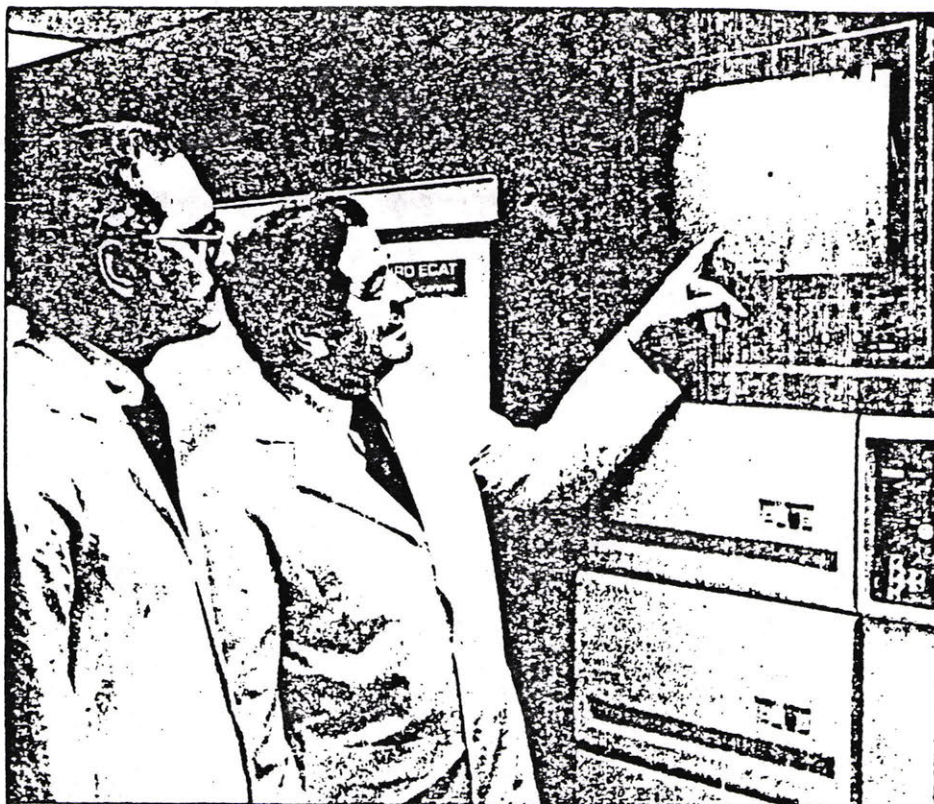
Whatever the manifestations, depression is among the most relentlessly painful of all known illnesses. Patients with overt depression who also have suffered a notably painful physical condition, such as kidney colic, report that the psychic pain is far worse than the physical.

Untreated victims of depression often end their agony with suicide, while others choose a slower form of self-destruction: drugs and alcohol.

Experts believe that much addiction can be attributed to depression; the victim becomes addicted in a desperate quest to numb the psychic pain of an underlying depression.

If this is so, and there is substantial evidence to suggest it is, then the "pure" depressive patient represents only the tip of the iceberg and the disease really affects up to 20 percent of the population.

This leads to an almost desperate need for anti-depressants, but the search for those compounds has



Johns Hopkins Medical Institutions

Johns Hopkins scientists Michael Kuhar, left, and Henry Wagner look at computer-generated image of brain scan. Kuhar says new drugs for depression will have great economic impact.

been severely limited.

For one thing, no one knew the cause of depression. For another, depressive disease was known to exist only in humans, so potentially useful drugs couldn't be screened in animals.

As a result, most of the currently available antidepressant drugs were discovered by accident. Since they can't be readily improved through animal tests they are often ineffective and retain serious, unpredictable and sometimes deadly side effects.

Today the single most effective therapy for severe depression remains electric shock treatment — an alternative that many consider unacceptable.

Consequently millions of citizens with untreated depressive disease continue to function at home and work, but their performance in both arenas is often marginal.

Their listlessness and lack of motivation, coupled with their use of alcohol and drugs, are thought to be a major cause of absenteeism and work accidents, and to constitute a steady drain on productivity.

In addition, by contributing to the deterioration of family structures, depression entails an incalculable social cost.

"As we get new drugs for these things, it's going to have a tremendous economic impact," says Dr. Michael Kuhar, a neurochemist at Johns Hopkins University. "It's fantastic!"

Such effusive optimism from what is traditionally the most conservative quarter of biological science stems from the rapidly accelerating pace of discovery in the field.

Depression, most molecular psychiatrists are now convinced, involves two specific subsystems in the brain.

One of those systems consists of brain cells that communicate with one another via the chemical transmitter "norepinephrine." The other uses "serotonin" to carry its signals.

Both are centrally involved in the limbic system, where mood and emotion are processed.

One of the clues that convince scientists they're on the right track involves the recent discovery of how the anti-depressant drug imipramine works.

Imipramine, despite its side effects and the fact that it is not universally effective, is one of the best antidepressants currently in use. But like other psychotropic, or mind-altering, drugs, it was discovered by accident and no one knew why it worked.

Now molecular psychiatrists have found that it exerts its influence by snapping into a previously unknown receptor in the emotional part of the brain.

Because of its shape, the imipramine molecule activates that natural receptor very much the same way the shape of a morphine molecule activates the receptor for enkephalin, a pain suppressant produced by the brain.

Morphine, of course, directly interferes with a major neurotransmitter system, the normal function of which is to establish a pain threshold. As that threshold rises, the morphine user gets a "high."

Imipramine exerts a much more subtle and specific modulating effect. The receptor it activates apparently controls fine-tuning in the serotonin system, which is responsible in part for the maintenance of mood equilibrium.

The imipramine triggers a metabolic chain reaction that lets the brain become more sensitive to its own serotonin. As it does so, the patient becomes less depressed.

Another recent piece of evidence involves the discovery that imipramine receptors are also present on the surfaces of some blood cells, but there are abnormally fewer of them on the blood cells of depressed patients.

"In conjunction with this," adds Pert, "there are studies that show that there's reduced serotonin in the brain and cerebral spinal fluid of people who die by suicide. So it's all wonderfully consistent. There's obviously something chemical going on."

Scientists are certain that that "something chemical" is, at least in part, genetic.

Studies of identical twins reared in the same household, for instance, have shown that if one twin becomes clinically depressed, the other has more than a 50-50 chance of developing the same illness.

But with fraternal twins, whose genes are not identical, the pattern of shared depression is far less likely to develop.

Significantly, alcoholism tends to run in the same families as depression.

None of this is to say environment does not play a strong role. In fact, most experts believe that depression usually strikes people with a genetic vulnerability and who are also subjected to an environmental stress — the "double hit" theory.

Even so, it has recently been shown that, if the stress

is intense enough, the environment alone is enough to induce depressive disease.

In fact, environmental stress has been used to produce, for the first time, an animal model that can be used in laboratory experiments on depression.

One of the experts in induced depression in animals is Dr. Fritz Henn, chief of psychiatry at the State University of New York at Stony Brook.

On the basis of experimental work done at the University of Pennsylvania and elsewhere, he says, severe depression can now be triggered in any animal, "from rats to goldfish to humans."

The method is simple, and involves what psychologists euphemistically term "exposure to adverse stimuli."

A rat, for instance, might be put in a cage with a metal floor and exposed to occasional, unpredictable electrical shocks to its feet.

But it's not the shocks that induce depression. If there is a ledge the rat can jump onto when the jolts begin, the animal can endure the shock cage for extended periods of time while remaining psychologically normal.

But if the shelf or other escape route is removed, and the rat is totally helpless, the effect is dramatically different.

"When they can't predict when [the shocks] are going to come, and there's nothing they can do to stop them or escape from them . . . when they're waiting all the time to get hit . . . after a while . . . it looks as if [their minds] just shut down."

"They stop even trying to get away. They stop trying to do much of anything."

Like depressed humans, the rats exhibit eating disorders and lose interest in sex. They have trouble sleeping, and it's more difficult for them to learn.

Depressed humans say they feel helpless, without any ability to influence what happens to them. The rats act, at least, as though they feel the same way.

And, once depressed, they don't get over it.

If they are put back in the shock cage, but are now provided with an escape route, they don't use it. They don't even seem to have the will to try; instead, they hunker down and accept the shocks almost as though they deserve them.

"But when you treat them with a drug that's effective clinically [in humans]," Henn says, "something changes. Then they'll use the escape route."

By killing the rats at various stages, dissecting their brains and recording the chemical changes, Henn's group made a remarkable discovery.

As the rats become depressed, predictable alterations occur in their brain receptors. Those changes occur at the same time the behavioral changes are taking place, and affect the brain in exactly those places where anatomists would expect them to.

"We see these changes in certain receptor fields in the [emotional] system. The receptors become more or less dense . . .," Henn says.

The principal alterations, he says, involve a subtype of norepinephrine receptors in one area and serotonin receptors in another.

"And so both receptors seem to play a role," says Henn, "but they do it at different places. And they change as a result of experience . . . and they stay changed."

In itself, the development of an animal model for depression represents a significant breakthrough. As a result, drugs can be engineered specifically to activate or suppress the affected parts of the brain, and can then be tested and improved on live animals.

"I'm very excited about this," says Henn. "[With the rat model] we can really take apart the neurochemical systems and see what's changing, and what's changing in conjunction with the behavioral changes."

"And we can then treat the animal with medications and we can reverse the behaviors. We can look and see what's changing."

The result, he believes, will be to dramatically accelerate the development of new drugs to alleviate the agony and reduce the cost of human depression.

According to Dr. Fred Goodwin, chief scientist at the National Institute of Mental Health, it would be difficult to overestimate the importance of the exponential growth in our knowledge of depression and other mental diseases.

He says a small foretaste of things to come can be found in the success story of lithium treatment for manic-depressive disease.

Manic-depressive disease is a subtype of depression that strikes about 2 percent of the population. It is characterized by dramatic mood swings from profound depression to manic hyperactivity.

During the 1960s it became a target disease for the development of the first rationally engineered psychotropic drug. Though that work predated the revolution in molecular psychology, the scientists were nonetheless successful.

Lithium was introduced in Europe during the late 1960s and proved dramatically effective in smoothing out the mood swings and restoring manic-depressive patients to good mental health. By 1974 it was in wide use in this country.

By 1982 the federal government had computed that the introduction of lithium had saved the taxpayer what Goodwin calls "a very conservative \$18 billion."

That figure, Goodwin emphasizes, does not take into consideration the indirect social costs of the disease, which include diminished work productivity. Also, it did not consider the impact on the families and children of manic-depressive patients.

As molecular psychology becomes an increasingly exact science, Goodwin says, he expects to see the development of new, more specific drugs with fewer side effects to replace currently available anti-depressants.

He also expects to see new drugs that will be effective for the 15 percent of manic-depressive patients who do not respond to lithium, and in the larger group of patients who don't respond at all to current anti-depressant therapy.

Such drugs could dwarf the social and economic savings attributed to lithium.

If the theories that link depression to drug addiction are correct, and new anti-depressant therapy can be translated into better drug treatment, the revolution in molecular psychology will directly affect perhaps 20 percent of the population.

"There's no question," says Henn of Stony Brook, "that addiction is far and away the most serious and most costly mental health problem in the country."

"A study that was just completed at NIH documents that. Just walking away, alcoholism is the single most serious mental health problem we have."

"If we can find out what that is, and do something about it, the impact in terms of savings to the country would just be enormous. Absolutely enormous."

Not since the public health revolution in the 1800s, and the eradication of filth-borne diseases, have the stakes been higher.

And depression research represents but one battlefield in the molecular psychology revolution.

The Mind Fixers/Healing the Human Psyche

Schizophrenia has chemical root in brain

By Jon Franklin
Evening Sun Staff

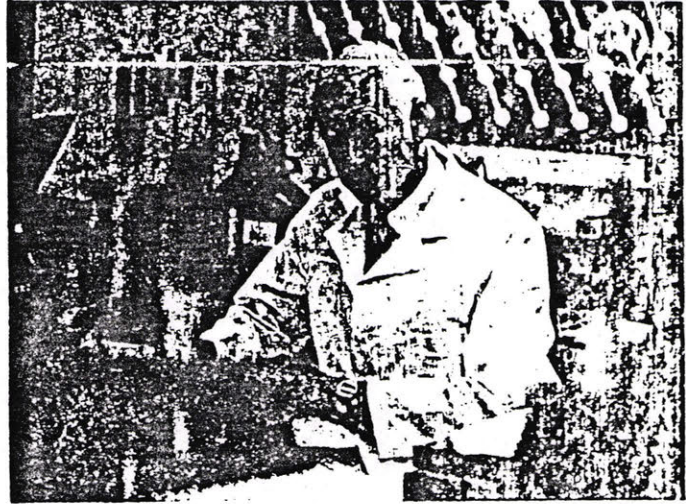
Schizophrenia, the most expensive and devastating of all the common mental illnesses, has been revealed as a physical ailment involving a malfunction in the dopamine system at the base of the brain.

Since 1973, when it became possible to study the brain's chemical communications network in detail, the story of schizophrenia has unfolded so rapidly that scientists are having trouble just keeping track of new discoveries.

Most senior researchers are confident that those discoveries, as they coalesce into new theories of the disease, will eventually result in the creation of specific drugs that will allow victims of the disease to live more normal lives.

Such drugs, which may begin appearing within the next 10 years, would have a dramatic economic and social impact.

Schizophrenia, which strikes about 1 percent of the population and tends to run in families, is the classic example of mental illness.



By Richard Chidress - Evening Sun Staff

Dr. Fred Goodwin, chief scientist at the National Institute of Mental Health, says schizophrenia has a devastating impact on both individuals and the U.S. economy.

Chemical network reveals secrets of schizophrenia

Its victims hear voices, have visual hallucinations, and often become profoundly and even dangerously paranoid. As the disease progresses, patients frequently withdraw and become suicidal.

Schizophrenia is particularly tragic because it generally strikes in the teens and early 20s. The disease is chronic, progressive and incurable, sentencing 80 percent of its victims to lifelong dependency on mental health and social welfare agencies.

According to Dr. Fred Goodwin, chief scientist at the National Institute of Mental Health, these factors combine to make schizophrenia a disproportionately expensive disease.

In 1976 alone, he says, schizophrenia cost the nation at least \$20 billion.

That does not include indirect social and economic costs to the families, nor does it include the expense of crime attributed to schizophrenia.

Though only a tiny minority of schizophrenics commit crimes, those who do are usually responding to paranoid impulses. They are in effect trying desperately to protect themselves from dangers that only they perceive.

As a result, the violent schizophrenic is very unpredictable, and the crimes he commits can be bloody and spectacular.

Until the second half of the 20th century, schizophrenics were warehoused in the back wards of mental hospitals. Most psychiatrists considered the disease to be a psychological one, resulting from a poor family environment.

However, Freudian-based methods were notably unsuccessful in alleviating the symptoms of the disease. The only useful treatments were prefrontal lobotomy and electroconvulsive shock therapy, which sometimes served to make patients slightly more manageable.

Then in 1957 an accidental discovery led to the introduction of the drug thiorazine and foreshadowed the development, a decade and a half later, of the new molecular psychology.

As was common in those days, scientists were using mental patients to test a new drug—in this case an antihistamine designed for the control of allergy symptoms.

The compound, as it turned out, didn't do much for the schizophrenics' runny noses. But, remarkably, the patients' minds seemed to improve; their hallucinations subsided, and they began making contact with reality.

Though termed a "tranquilizer" by a misunderstanding public, thiorazine had very specific effects on the perceptual function of the mind. History's first truly anti-psychotic drug had been discovered.

A whole new generation of scientists, studying the effects of thiorazine, became convinced that schizophrenia must be a physical disease of the brain. That implied that other serious mental illnesses might also have a physical basis.

It was a revolutionary perception. If true, then there was hope to be had from science. If only researchers could develop a chemical theory of the brain, they might design other drugs that would help a wide variety of patients with other "mental" diseases as well.

This proved to be a powerful dream. After a decade of work by visionary scientists, it led directly to the development of the new field of molecular psychology in the '70s and '80s.

Thanks to thiorazine, and to better versions of the same thing that came afterward, the lot of the schizophrenic improved.

The straitjacket and isolation cell faded into memory; shock treatment and prefrontal lobotomy fell into relative disuse. Increasingly, schizophrenics on drug treatment were released from mental institutions.

Despite early claims, however, the patients were by no means cured. Thiorazine relieved the hallucinations, but the "negative" symptoms, including withdrawal and emotional isolation, continued unabated as the disease ran its course.

Most schizophrenics, while no longer confined, remained unable to live normal lives, the vast majority

remained social and economic wards of the state. Many listlessly wandered the streets.

To make things worse, the drugs produced serious side effects. Early in the course of treatment the patient often developed a Parkinson-like slowing of bodily movements and awkward posturing. Sometimes the eyes rolled up into the head.

These early effects could be treated with anti-Parkinsonian drugs. If all else failed, the thiorazine could be withdrawn, of course, and the effects subsided. But a more troubling set of side effects, called "tardive dyskinesia," became permanent.

Tardive dyskinesia was horribly disfiguring. The victim's limbs moved restlessly; his face jerked, his mouth made involuntary chewing movements, and his tongue writhed and darted in and out, snakelike.

Tardive dyskinesia occurred in as many as 40 percent of the cases. It made the schizophrenic repulsive to others, and thus contributed further to his isolation.

On the one hand, the anti-psychotic drugs relieved the hallucinations and delusions of schizophrenia; on the other, the side effects were a powerful incentive for the schizophrenic to avoid taking the stuff.

In the years following the 1957 discovery of thiorazine, the victims of other mental illnesses—most notably manic-depressive disease—benefited dramatically from the discovery that chemical compounds could be used to treat thought disorders.

But schizophrenia, the most profound psychosis of all, remained resistant. While doctors learned to treat the early side effects and could often stave off tardive dyskinesia by a more conservative use of drugs, the "negative" effects of the disease remained untreatable.

The key to better treatment would be found, scientists believed, once the chemical nature of the mind was better understood.

And so it was that in 1973 the discovery of the first brain receptor at Johns Hopkins Medical School by Dr. Solomon Snyder and Candace Pert triggered an explosion of schizophrenia research.

Within a year the search had narrowed to a structure in the base of the brain, "corpus striatum." The striatum was composed of brain cells that communicated with one another via a chemical transmitter called "dopamine."

Significantly, the striatum had two projections, or nerve trunklines, that reached up into the higher brain. One of those projections went to the limbic system, where emotion is processed; the other led to the frontal lobes of the cortex, the seat of consciousness and personality.

These projections were the conduit through which the striatum pumped dopamine into the higher structures. Presumably, the dopamine was the means by which the striatum regulated thought and emotions.

According to Snyder, whose laboratory isolated the dopamine receptor in 1974, it is now known that all drugs effective in schizophrenia work by blocking the action of dopamine.

By blocking dopamine communication, the thiorazine and related compounds reduce the amount of dopamine pumped into the upper brain.

Now that they knew how the anti-psychotic drugs worked, scientists had a whole new appreciation of what schizophrenia was and why the drugs had such terrible side effects.

The most obvious conclusion was that whatever schizophrenia was, it involved the dopamine system. Either there was too much dopamine produced, or the victim's brain cells were for some reason supersensitive to it.

Other, more subtle pieces of the puzzle fell into place as well.

During the 1960s, as the nation's drug culture developed, scientists had observed that abusers of amphetamines (or "speed") often developed hallucinations that emergency room physicians found indistinguishable from schizophrenia. Also, they found, schizophrenics who took amphetamines got a lot worse.

This was explained by the discovery in the mid-'70s that amphetamines increase dopamine production.

As the chemistry of schizophrenia was worked out, scientists also came to understand why prefrontal lobotomy had worked. The surgery severed the trunk lines through which the dopamine system pumped the chemical into the upper brain.

Since lobotomy was also effective in treating severe obsessive-compulsive disorders, the schizophrenia research may have fallout in terms of that disease as well.

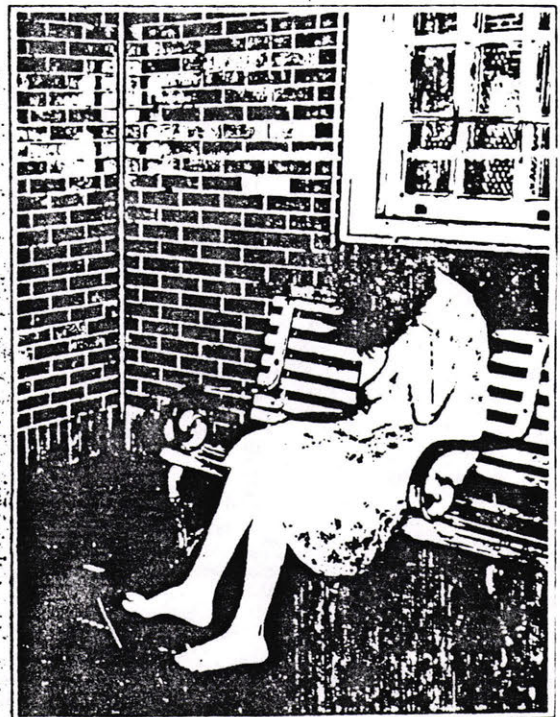
But perhaps most important, the new knowledge explained why thiorazine and the other anti-psychotic drugs had such profound side effects.

"... We're approaching a point when we'll be able to make some coherence out of this wealth of information. ... we've gone from ignorance to almost a surfeit of knowledge in only 10 years ..."

—Dr. Joseph Coyle

Back wards, lost souls

Schizophrenia is the classic example of mental illness. Its victims hear voices, see visions and often become profoundly and even dangerously paranoid. As the disease progresses, patients frequently withdraw and become suicidal. Until the second half of this century, schizophrenics were warehoused in the back wards of mental hospitals. The only useful treatments were prefrontal lobotomy and electro-shock therapy.



place in the motor control centers of the brain, where muscle movement was controlled.

By blocking dopamine, the anti-psychotic drugs suppressed the hallucination-producing striatum, but they also reduced the brain's ability to process movement, eventually, the motor system was permanently damaged.

Once they knew why thiorazine produced its side effects, researchers were in a position to begin the development of drugs free of side effects.

According to Dr. Joseph Coyle, a Johns Hopkins expert on schizophrenia, the first major effort was to look for differences that might exist between the dopamine receptors in the motor system and in the striatum.

Subtle variations are known to exist in other chemical communication systems that are used in more than one part of the brain. Presumably the differences help the brain to avoid "crosstalk" between various brain centers that use the same transmitter.

If such differences could be found between the two dopamine systems, psychochemists might develop a drug that would block the receptors in the striatum without affecting those in the motor system.

Despite intensive efforts, such differences have not yet been found. But the search has recently revealed another difference that may be exploited instead.

The dopamine system associated with schizophrenia, Coyle says, has been found to use a co-transmitter, it speaks, in a sense, with two chemical tongues. The motor system apparently does not use the co-transmitter.

Scientists are now searching for chemical compounds that will suppress the combination without affecting dopamine alone. Such a drug, in theory at least, would knock out the schizophrenic hallucinations and delusions without the devastating side effects on the motor system.

Other scientific teams, in the meantime, are pursuing other ideas. At the State University of New York at Stony Brook, a group led by Dr. Fritz Henn is proceeding on the assumption that the imbalance in the dopamine system is caused by more specific defects in other systems, which, in turn, trigger the abnormal dopamine reactions.

While it is too early to predict which approach will prove most fruitful, scientists involved in the work are generally confident that breakthroughs are coming.

"The pace of discovery bodes well for the future," says Coyle.

"It suggests that we're approaching a point when we'll be able to make some coherence out of this wealth of information. I'm optimistic... we've gone from ignorance to almost a surfeit of knowledge in only 10 years."

As discoveries in the field heighten interest and draw increased funding, Coyle adds, scientists are also beginning to get some clues regarding schizophrenia's puzzling "negative" symptoms of withdrawal and emotional detachment.

Scientists in England and at the National Institute of Mental Health have recently used CAT scanners, for instance, to document widespread shrinkage of the cortex in schizophrenics. The cortex is where the more "human-like" functions of the brain are processed.

"These changes in the cortex," says Coyle, "appear to correlate with the negative symptoms of schizophrenia."

The structural changes are also reminiscent of alterations found in other illnesses long recognized to be physical in nature, such as Alzheimer's disease, or senile dementia.

"Some people feel that the negative symptoms of schizophrenia do have a dementia-like quality to them," says Coyle. "That is, a dilapidation of higher cortical functions and a crudening of the social skills that one sees in other types of dementias, like Alzheimer's."

"There is this growing appreciation of the relatedness of these disorders, and it's become difficult to sort them out in terms of research. The more we understand about the cortex, through research on Alzheimer's, the more we're going to understand about schizophrenia... and vice versa."

According to Snyder, recent discoveries have led to increasing optimism that the negative effects of schizophrenia will, like the positive ones, prove amenable to drug treatment.

He says one drug, being used now in Europe, seems to improve the negative symptoms as well as the positive ones. That drug, in addition to blocking dopamine, interferes with calcium metabolism in the brain cells.

In the meantime, powerful new brain scanners are being developed to augment the chemical techniques that have been used since the '70s to map the distribution and density of receptors in the brain.

Those chemical techniques limited the scientists to working with dead brains that could be sliced and examined.

The new scanners, however, are allowing scientists to monitor the chemical reactions of thought and emotion as they take place in the living, thinking, feeling—and hallucinating—human brain.

Dr. Marcus Raichle, a scanner scientist at Washington University in St. Louis, where one of the most powerful devices was invented, predicts that the scanner technology is certain to dramatically increase the pace of discovery involving schizophrenia.

He says the scanners should allow scientists to discover even more precisely what goes wrong with the

Alzheimer's disease

The mystery with no cure, no prevention, no known cause

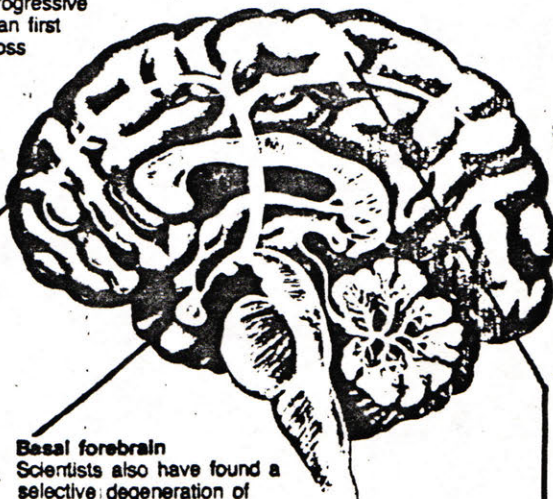
Alzheimer's is characterized by progressive mental deterioration. Symptoms can first appear in persons in their 40s. Loss of memory of events occurring minutes earlier is usually the first symptom. Victims may lose the ability to read, write, calculate or use language appropriately. Other possible symptoms include irritability, paranoia and hallucinations.

Cholinergic pathways
The cholinergic neurotransmitter system—a key part in learning and memory—needs acetylcholine to produce the enzyme choline acetyltransferase, the chemical messenger from the nucleus basalis (basal forebrain) to the cortex.

Basal forebrain
Scientists also have found a selective degeneration of acetylcholine-releasing cells in the basal forebrain.

Cortex
Area of the brain that controls speech, memory and the senses.

Chicago Tribune Graphic: Illustration by Ray Shlomon. Sources: Alzheimer's Disease and Related Disorders Association Inc., Chicago Tribune news reports



brain as the disease takes hold, and to watch the disease as it runs its course.

In a year or so, he predicts, scientists studying schizophrenia with the new scanners will present the world with "studies that are going to mean something."

"It's coming," he says, reflecting the enthusiasm of schizophrenia experts. "I don't doubt that."

But the development of the chemically based brain scanners, in combination with the biochemical tools, has

implications that go far beyond the study of schizophrenia — or even of other diseases.

They are going to lead, scientists agree almost unanimously, to a much broader understanding of the normal brain. They may have the ability to reveal dramatic new truths about who we are, what we're about, and what it means to be human.

The Mind Fixers/Healing the Human Psyche

Brain scanners 'see' ideas

By Jon Franklin

Evening Sun Staff

Brain scientists have developed a new family of high-tech scanners that illuminate the chemistry of thought as it flashes through the living, thinking, feeling human brain.

The devices represent a fundamental breakthrough; they promise to do for human psychology what the telescope did for astronomy and the microscope did for biology.

While the scanners bear a superficial resemblance to the CAT scanners presently used in many of the

■ A skin test may find children likely to develop mental illnessA4

nation's hospitals, the difference in what they can see is dramatic.

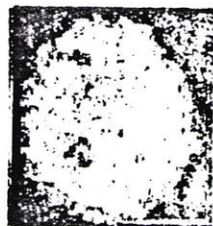
CAT scanners reveal only the structure of the brain. They can detect swelling and pinpoint tumors, but the chemical machinery of thought is beyond their capabilities.

The new brain-mind scanners, however, reveal those chemical reactions. They trace the mental processes of the subject as he moves, sees, hears, listens to music, meditates or experiences emotions.

The instruments are primitive, limited both by their image-resolution capabilities and by the scientists' abilities to interpret the results. But both the



Doughnut-shaped scanner shows changes in psyche. Depression victim's scan shifts from blue to bright colors following therapy.



New high-tech scanners 'see' ideas in the making

machines and the humans who use them are steadily becoming more sophisticated.

Increasingly, the scanner laboratories are producing a cascade of discoveries that illuminate the physical basis of thought and emotion.

At the University of California, Los Angeles, for instance, scientists have photographed epileptic seizures as they explode in the living brain.

At Washington University in St. Louis, doctors have used a scanner to show that patients who suffer a common type of uncontrollable panic attack do so because they have a metabolic abnormality that "unbalances" their emotional brains.

At the University of Texas Health Science Center in Dallas, psychiatrists have established that each individual has a characteristic brain pattern—and that those patterns shift dramatically as patients with multiple personalities switch from persona to persona.

In Baltimore, scientists at Johns Hopkins Medical School have labeled and visualized the dopamine receptor fields believed to lie at the root of schizophrenia. And the Hopkins researchers have discovered that fundamental changes occur as the brain matures.

The list goes on and on and on, each new discovery reconfirming the theory of molecular psychology and offering new insights into what sort of creatures we really are.

Currently, the most popular of the new devices being used to probe the brain is the PET scanner, developed during the late 1970s by Dr. Michel Ter-Pogossian and associates at Washington University.

Like the CAT scanner, PET uses a doughnut-shaped array of sensors into which the subject's head is inserted. In both cases the sensors consist of radiation detectors

that collect the impulses and relay them to a bank of computers. The computers record the collected bits of data and use them to reconstruct three-dimensional images of the brain.

The big difference between CAT and PET has to do with where the radiation comes from.

CAT scanners use X-rays directed at the brain from the outside, and thus produce "shadow" pictures of the shape of the brain.

The PET scanner works quite differently and produces a dramatically more revealing image not only of shape but also of chemical process.

First, before the scan begins, the PET scan team manufactures a radioactive version of some chemical normally used in the thought process.

Then, the subject's head in the doughnut, the chemical is injected or inhaled. The scanner then watches, and records, what happens as the chemical is metabolized during the thought process.

Most scanner experiments are quite complex and difficult to understand without a thorough grounding in the theory of psychochemistry. But the principle can be illustrated with the relatively simple glucose studies.

Glucose is the fuel of the living cell, and the harder the cell works the more it needs. As a result, scientists can use radioactive glucose tracers to reveal which parts of the brain "turn on" during a specific mental task.

A radioactive glucose experiment, for instance, can "light up" the visual centers in the brain as the subject examines a picture or a test pattern. Radioactive glucose tracers can also show which parts of the brain are involved in such tasks as emotional memory, movement coordination, or even meditation.

The trickiest part of a PET scan experiment is not

the scan itself, but the design and creation of the radioactive neurochemical that the scientists hope to trace through the subject's brain.

This preparatory phase of the experiment can take months and involves the effort of a team of brain and chemical specialists.

And, because the radiation must be very short-lived in order to be safe for the human subject, the tracer chemical must be created on the spot. This means that a PET scan facility must include a cyclotron, and the team must include specialists in cyclotron technology.

"It takes a lot of people," explains Dr. Candace Pert, a neurochemist at the National Institute of Mental Health. "It's a team effort... it's 10 people sitting around the table. It's organizational, high-tech, lot of steps, hard to do... like putting a man on the moon."

As a result, a PET scan facility approaches the cost of a small astronomical observatory. Hopkins scientists, for instance, estimate they've got \$2 million invested in their PET scan facility—and that doesn't include the operating budget for the team of specialists required to run it.

The current generation of scanners is also limited by resolution. The chemical workings of the mind take place on a microscopic level and require only milliseconds to occur. The scanners take from one to 20 minutes to record a "picture" and presently have resolutions of about a half-inch.

As a result, the scans they produce are little more than blurs. But those blurs, revealing as they do the chemical dynamics of thought, are of unparalleled value.

So, despite the substantial expense involved in building and operating PET scan facilities, they are rapidly proliferating. To date there are about 15 PET scan facilities in the United States, and at least an equal number are in operation, or soon will be, in Europe and Japan.

As more scientific teams gain access to PET scanners, the techniques are being refined to answer ever more specialized questions.

At Hopkins, for instance, the PET scan facility is dedicated to mapping the all-important neurotransmitter receptor fields.

Receptors are the submicroscopic chemical "antenna" molecules on the surface of brain cells. It's these receptors that make the mind respond to natural transmitters, such as dopamine, and unnatural ones, such as heroin and nicotine.

Discovering exactly where the different types of receptors are located, and how they proliferate or die off in illnesses such as drug addiction or schizophrenia, is a central issue in neurochemistry.

Dr. Michael Kuhar, a Hopkins pioneer in that effort, explains that his early receptor-mapping work required that the brains be sliced, exposed to radioactive chemicals that locked onto the receptors, and then laid on photographic film for several weeks. During that time the radioactive chemicals burned their image into the film and revealed the location of the receptors.

The technique, though considered revolutionary when Kuhar started using it in the 1970s, had severe limitations. The most obvious was that he could use only

dead brains, and thus couldn't observe how the receptors changed over days and weeks and how, in the process, the patient's personality was altered.

The Hopkins PET scanner, the first to successfully map a receptor field in the living brain, changed all that. "Man, that thing's incredible," Kuhar says. "It used to take us weeks to produce a study. Now a guy lies down on the table, you inject him [with radioactive tracers], you turn on the scanner... and there's his receptor map."

And he gets up off the table and walks away.

"And you can do him again if he gets well, or gets sick, or whatever, and you can compare the two studies."

The specific ambition, at Hopkins and elsewhere, is to record the dynamic process of mental disease and thereby discover the nature of that disease. At Hopkins, for instance, PET scan scientists have a particular interest in the changes that occur in schizophrenia and drug addiction.

But first the scientists must scan normal brains under a variety of circumstances. Until the meaning of "normal" is understood, scientists can't probe the biochemical definitions of words such as "insane."

Those normal studies, as preliminary as they may be, are anything but dull. The chemical dynamics of the human personality are the darkest of all scientific mysteries. The exploration is yielding an endless supply of eyebrow-raising results—and generating new questions about who we are and how we work.

At the University of Texas Health Science Center, for instance, scientists using a scanner similar to PET have discovered that each normal person has a characteristic way of using his brain. This is reflected in very individualistic scanner patterns.

"We call it a fingerprint," says Dr. A. John Rush, a research psychiatrist at the Dallas facility.

"What we've found is that there's a great range of normal people. They have no brain disease, no psychiatric disease, but they all have a distinctive [scanner] pattern."

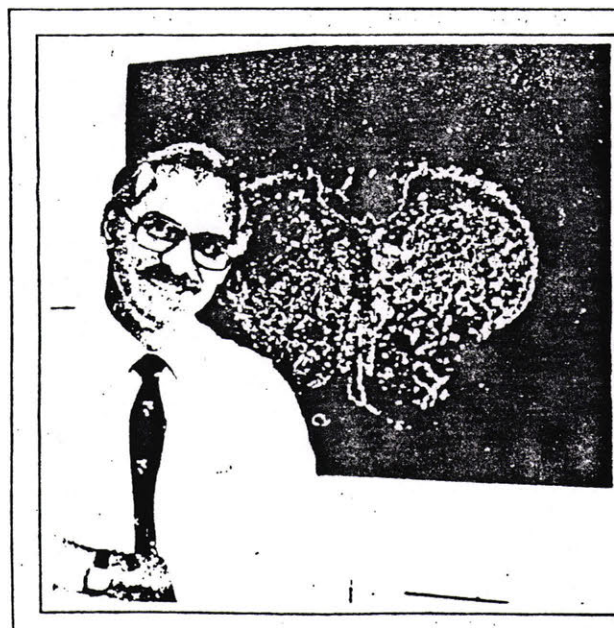
"If you ask the same different, normal person to come back three times... say separated by a week... they have basically the same [scanner] pattern. But that pattern could be quite different from that of other very normal people."

Though there is yet no proof, presumably the patterns found by the Dallas scientists reflect individual personalities. Presumably they change over time as the person experiences new situations, learns new things and matures.

In Baltimore, Hopkins scientists led by Dr. Henry Wagner, chief of nuclear medicine, have discovered a more puzzling peculiarity of the normal brain, this one involving the all-important dopamine receptor fields.

Dopamine receptors in primitive structures at the base of the brain serve in part to modulate alertness, changes in the density of those fields are suspected of playing a key role in the development of schizophrenia.

But in the examinations of dopamine receptor densities in normal brains, a surprising observation emerged. In females, dopamine receptor fields remain stable for life, but in males the fields become less dense with age.



Michael Kuhar

At the Johns Hopkins Medical Institutions, high-tech brain scanning helps scientists map the receptor molecules that play a key role in the chemistry of thought. Dr. Kuhar describes the new technology: "It used to take us weeks to produce a study. Now a guy lays down on the table, you inject him [with radioactive tracers], you turn on the scanner...and there's his receptor map."

Photo by Ellis M. Lashak - Evening Sun Staff

Do these changes correlate with the increasing calmness observed in the maturing male? Might the changes have to do with the observed tendency in male drug addicts to "mature out" of their addiction in their 30s? Might they reveal something about differences in male and female behavior?

No one knows. And, at PET scan facilities all over the world, such surprising findings abound.

"This whole field is incredibly exciting," one PET scan scientist said. "It's like pointing a telescope at the heavens for the first time. Everywhere we look, we see something new and unexpected."

"And every time we see something, even if that something is normal, we've discovered two more diseases. In principle, for every normal reaction you can bet there's someone, somewhere, who has an under-reaction... and someone else who has an over-reaction. The trick is going to be linking what we're seeing to known mental diseases."

That such linkages could be made was, until recently, a matter of faith among neurochemists. But this year, scientists at Washington University, where the PET scanner was developed, used the instrument to forge just such a cause-and-effect connection.

Dr. Marcus Raichle, a neurologist and a senior PET scan scientist at Washington University, said the disease in question is Decosta's syndrome.

It affects between 1 and 2 percent of the population. The chief symptom is periodic panic attacks that strike without warning or provocation.

Because such patients also have an exercise intolerance, and because panic is characterized by changes in heart function, Decosta's syndrome victims were for many years thought to be suffering from heart disease. Frequently they end up in emergency rooms with what appear to be heart attacks.

But in recent years the panic attacks were found to be triggered by elevations in blood lactate levels, which are normally produced by exercise.

This deepened the mystery: Normal people have elevated blood lactate levels when they exercise, too, but the lactate doesn't trigger panic attacks. Presumably the high lactate levels triggered some otherwise benign defect in the brain.

The primary defect was discovered when Raichle and his group examined Decosta's syndrome patients in a

PET scanner. It quickly became apparent that emotional centers in the left mesial temporal lobe, a part of the emotional brain, were not "kicking in" when they should. The companion centers on the opposite side of the brain were functioning normally.

"These people are different," Raichle explained. "The brain, if you will, is kind of unbalanced."

One of the most striking results of the experiment is that there were no exceptions, every Decosta's syndrome patient had precisely the same abnormality.

"This is the cleanest piece of data we've generated in a long time. To our knowledge this is the first study to identify a discrete brain abnormality in patients with a primary psychiatric disorder," he said.

A similar linkage between scanner images and specific diseases appears to be developing at the University of Texas facility in Dallas, where personality "fingerprint" scans are being studied.

According to the Dallas team's Hush, the group recently put a patient with multiple personalities on the scanner—and were able to observe a personality switch.

The results were spectacular. As the patient's personality changed, so did his scanner "fingerprint."

Similar preliminary work at other centers has scientists hopeful that scanners will soon produce characteristic patterns for schizophrenia and depression. There are indications that receptor field changes may also play a role in addiction.

As mental illnesses become identifiable by means of chemical scanner patterns, those patterns should tell neuropharmacologists what sort of drug they need to design to treat each illness.

The scanners should also play a major role in the development and testing of those new drugs. With the scanners, the effects of experimental compounds can be observed directly. This should eliminate the decades of experimental fumbling that now characterizes the development of psychoactive drugs.

Though scanner scientists share a confidence that the new machines will lead to breakthroughs in the understanding of mental disease and in the development of drug treatments, there is debate over whether the devices will ever play a direct role in clinical psychiatry.

At Hopkins, for instance, Dr. Joseph Coyle suspects that the high cost of PET scanners, coupled with the need for teams of experts to tend the machinery, will



Washington University photo

Marcus Raichle

At Washington University in St. Louis, Dr. Raichle and other scientists have used a scanner to show that victims of one kind of panic all have the same metabolic quirk in their brains. Says Raichle: "These people are *different*. The brain, if you will, is kind of unbalanced. This is the cleanest piece of data we've generated in a long time."

forever bar the routine scanning of mental patients. A majority of scientists interviewed by *The Evening Sun* expressed similar views.

But at least some experts take an opposite tack. They predict that the cost of routine scans may be offset by dramatically improved therapy.

Misdiagnosis and ineffective treatment, they point out, can also be very costly—both in terms of money and human suffering.

Dallas' Rush is one of the hopeful ones.

The most obvious application, he says, would be in diagnosis. For one thing, diagnostic scans might tell doctors not only what disease they are dealing with, but also what type of treatment might be most useful.

Scanners could also be used to monitor a patient in treatment to determine whether or not the drugs are improving his condition, and to determine when he's cured.

Documentation of cure could be especially valuable when a patient's illness is characterized by violence, or when the treatment is court-ordered.

The type of information produced by scans might also prove to be of great value to classical psychiatrists, who use interpersonal therapy instead of, or in addition to, drugs. Such psychiatrists have historically been forced to infer brain function from what the patient says and does—a notoriously tricky and imprecise process.

"We have this tendency to think that the only way to change a patient's mind is with drugs," says one brain scientist. "But in the normal course of events, experience changes the mind, too. And that includes the therapeutic experience of visiting a psychiatrist."

"A person who has gone through psychotherapy is in many important respects different than he was before the treatment began. We can't quantify this difference yet, but it must exist. If it didn't, people wouldn't go to therapists."

But to Rush the most exciting possibility—if perhaps the most speculative—is that the scanners might be used for the early diagnosis of mental illness.

Today, mental illness is rarely diagnosed until it has progressed to full-scale insanity.

"But we know that depression, schizophrenia and a variety of other disorders run in families. They appear to be genetic, at least in part. And it's intriguing to think that [scanners] could tell us who might develop one of these diseases," Rush says.

"That would allow us to intervene with some sort of preventive strategy before the patient actually develops the illness."

If that could be done, he says, presently incurable mental illnesses might be prevented, the same way the treatment of high blood pressure is now used to prevent strokes.

The Mind Fixers/Healing the Human Psyche

Culture at doorway of enormous change

By Jon Franklin
Evening Sun Staff

The brave new science of molecular psychology is caught up in gold rush fever, an excitement heightened each month as still more breakthroughs are announced in the journals.

There are great principles to be discovered, Nobel Prizes to be won, fortunes to be made with new drugs.

And, day by day, the precise chemical nature of human thought and emotion grows ever more clear.

In the beginning the fever engulfed only scientists; the rest of the

world continued as it always had, oblivious to the events taking place in brain laboratories.

But with each new realization, each new finding, each new paper, each new heightening of the fever, the implications grew ever broader.

The science, after all, is psychology—and psychology encompasses all of human existence. Its metamorphosis into an exact science, and even into an engineering discipline, brings human culture to the threshold of great and unpredictable change.

"It's going to be incredible," says

Dr. Candace Pert, a key scientist at the National Institute of Mental Health. "It's going to revolutionize how we think of ourselves as minds, and bodies, and free will . . . and all that."

As a researcher at Johns Hopkins Medical School in 1973, Pert was a partner in the original discovery of chemical receptors in the brain.

The first and most obvious impact, of course, will be an indisputably humanitarian one: the diagnosis, treatment and finally the cure for the classical mental diseases.

The hope that such advances are imminent burns bright in many scientific minds.

"Just thinking three or five years ahead," says Pert, "I can see us understanding all kinds of brain diseases . . . understanding them at a molecular level and understanding them in rigorous fashion."

Brain technology foretells great change in culture

Dr. Fred Goodwin, chief scientist at NIMH, admits it's an effort to contain his excitement as he reads the research reports that come across his desk.

"We're being flooded with data. We may need to stop and develop new mathematical and conceptual models to figure out how all this stuff fits together. We have to keep stopping and saying, 'How are things ordered?'"

He says the pace of discovery, in and of itself, lends credence to the predictions of the most enthusiastic scientists.

"If you look at the revolution in pharmacology with respect to the major psychiatric illnesses, for instance, it's amazing how short a time we're talking about."

"I mean, 25 years ago we were primitive in our ability to treat depression and schizophrenia . . . and I mean primitive."

"Schizophrenics were warehoused in the back wards of state mental hospitals and were given wet sheet packs. They were occasionally given electroconvulsive therapy when they got out of control. Depressives killed themselves 15 to 20 percent of the time, or toughed it out, or got electroconvulsive therapy. And that was it."

"We now can treat, pharmacologically, about 70 percent of all patients with major depressive illness. We can prevent the occurrence of major depressive illness in about 80 to 85 percent of the patients who have the disease recurrently."

"That's an enormous advance . . . in less than a quarter of a century. Some of those things weren't around just 10 years ago. Certainly the use of lithium to prevent manic-depressive illness wasn't."

"If you project the rates of growth [of knowledge], you'd have to say it's still accelerating . . . expanding exponentially."

"And there's so much pressure to treat mental illness! With each new turn of the research data, we're looking to see if there's something practical that might be derived from it."

"And that research data is turning very fast. Each time a new neurotransmitter is discovered, someone is going to try to apply it to some major clinical problem. Just the odds of some hits in that are very, very high."

"We could run into a brick wall, of course. There's always that. But I'm optimistic that we'll see developments on several fronts."

In those mental diseases for which there are already specific drugs, the drugs are sure to get better, with fewer side effects, Goodwin says. New drugs will be developed for the small percentage of patients who don't respond to current ones.

Perhaps equally important, the new knowledge developed by laboratory scientists will enable psychiatrists to use the drugs, as well as other therapies, more effectively.

"For instance," he says, "we'll see a lot of progress with patients with depression who don't respond to standard treatment. There will be a lot of progress in manic-depressive illness, for the 15 percent of those who don't respond to lithium."

"In the case of Huntington's disease, I think there's going to be a breakthrough in the development of a diagnostic test for predicting who is vulnerable to it. That's really an engineering job now that we've got the gene for it. It may take five years, but I don't think it's very speculative."

"I also think we'll make progress in solving the problem of severe anxiety. We now know from work here and elsewhere that there is [a neurotransmitter] for [Valium], and so we now know biologically what anxiety is. We can turn it on and turn it off."

The government's chief mental health scientist is more cautious in predicting new treatments for schizophrenia. That field, he says, is in a ferment as never before, but the research hasn't shaken down yet.

Likewise, he hedges his bets on Alzheimer's disease. "Although," he adds, "there are exciting discoveries. For instance, the recent discovery that there are specific areas in the brain involved."

"For these diseases, as far as prediction is concerned, we have to fall back on the general experience that the more one knows, the more likely it is that we'll find a treatment."

As applied scientists work to link the new knowledge with clinical psychiatry, Goodwin believes, the bench scientists and theoreticians will continue to leap ahead.

They are already finding, he says, specific chemical links by which the brain-mind "talks" to the immune system.

This leap in understanding how the brain communicates with the rest of the body could have a

profound effect on the treatment for—or prevention of—heart diseases and even cancer.

His colleague Pert points out that such work might also reveal the mechanisms behind the "placebo effect," in which a patient's condition improves after he is given a sugar pill—or even, according to some reports, following the "laying on of hands."

Once explained biochemically, such phenomena might be harnessed to help the patient treat himself with his own thought-generated neurochemicals.

As research into the molecular basis of thought continues, Pert believes, we will inevitably begin to see a long-overdue change in the social perception of insanity.

As it becomes increasingly clear that behavior in general has a physical basis, she says, we should become more tolerant of one another's differences. In the process, we are likely to develop a kinder attitude toward those whose minds are clouded by some defect.

Dr. A. John Rush, a research psychiatrist at the University of Texas Health Science Center in Dallas, says the ability to make specific diagnoses of brain disorders is inevitably going to spill over into attitudes toward criminals.

"We all assume, though it's probably not accurate, that by willpower we can control virtually everything we do."

"I think a lot of psychiatric technology and information is revealing the fact that the brain, which is the basis for all we do, is an organ like any other organ in the body... and it will not always obey our commands. That's a scary concept. It puts sort of a limit around free will."

Ultimately, he says, molecular psychology will force us to rethink our attitudes about guilt and innocence.

The trigger for this change may be the new brain scanners, with their ability to reveal organic brain

malfunctions and to correlate those changes with such things as aggressive behavior. Eventually this tool may prove useful in the courtroom.

"I think it will require some very substantial revisions in the insanity defense," Rush says. "What they will be, I wouldn't care to speculate. But I think they will evolve over the next 20 or 30 years."

Beyond the insanity defense, some believe that psychiatrists will one day be able to tell a judge how likely an individual is to commit a future crime.

"With the advent of biological technology," says Rush, "it could occur that we could have a reasonable degree of prediction... in theory at least, and say

"... Of course, neuroscience is a two-edged sword. Whatever you use, you can use it to do good or bad things. You can use water for torture. I think you have to be careful..."

—Dr. Paul Mandel

perhaps 80 percent of the time."

Such a prediction, he quickly adds, would forecast the likelihood of violent behavior, not a specific act.

"What I don't foresee, within the next 30 years or so at least, is a capacity to make a cold, scientific case for a single individual... that he will do 'X' at this particular time. I just don't think we'll see that in the moderately near future."

Pert and Goodwin



Dr. Candace Pert and Dr. Fred Goodwin of the National Institute of Mental Health believe the new science of molecular psychology has arrived at an exciting threshold. "It's going to be incredible," says Pert. "It's going to revolutionize how we think of ourselves as minds, and bodies, and free will." Says Goodwin: "We're being flooded with data... With each new turn of the research data, we're looking to see if there's something practical that might be derived from it. And that research data is turning very fast."

"But should that occur 50 years from now, or 75 years from now, that raises tremendous ethical issues. Even if you make a 90 percent prediction, that's not a basis to incarcerate somebody before they can conduct that particular behavior... even if it's illegal, or dangerous to other people. So, if our predictive capacity grows, one runs immediately into ethical issues."

In the meantime, as the biochemical workings of the brain-mind become better understood, many scientists foresee that the new technology will be used to improve "normal" functioning as well as to combat disease.

"One area that represents considerable interest," says Goodwin, "is the development of agents that would alter what we now consider normal behavior... like memory enhancers, or drugs which could enhance creativity."

"That's not just pie in the sky. We're doing work on that right now. We know we can enhance memory in normal individuals... Right now there's the question of whether we can do it under practical conditions... but that's an engineering problem."

"So we know that there are drugs that do correct memory deficits of certain sorts, and that will enhance memory even in normal people."

"Unfortunately they don't seem to do much for the clinical problem in Alzheimer's, because there you're missing the cells. They degenerate. But in patients who have memory deficits, even associated with normal aging, these drugs can in fact enhance their recall mechanisms—their memory. And [enhancing memory in normal people] might be a socially desirable thing to do."

"Then again, of course, it might not be. It's as possible to have too much memory as too little. If you take a person who's obsessive, and who can't forget... that's a problem, too."

"Obsessives aren't able to clear out their memory banks, and they keep harping on pain... In fact, an obsessive can remember a past painful experience as if it's right now. I mean, they have no capacity to forget. Forgetting a certain amount is healthy."

"So enhancing memory is not an unambiguously good thing. But it might be good for some people under some circumstances."

"Another thing is creativity enhancers. Candace Pert is working on the phencyclidine [PCP] receptors—PCP is a hallucinogen. She's found a place in the brain that binds quite specifically to PCP, and others have replicated it now, and she and a couple of other groups are madly racing to find the [natural analog for PCP]. What the hell is normally in the brain that binds to that place?"

"Whatever it is, the question is... what does it do? One speculation is that it has a part of the brain's normal mechanism for the capacity to experience imagination, reverie, creative experiences... milder forms of hallucination."

"It's sort of a neuroscientist's way of conceptualizing the relationship between creativity and craziness... which of course has been noticed in many artists and highly creative people, who seem to be just on the edge of being crazy."

"So such a peptide might turn out, when administered in small amounts to certain people, to make it easier for them to imagine, or to fantasize, or to connect disparate thoughts together. In other words, we could conceivably make some people more creative."

Taken together, many scientists feel, these hoped-for or predicted advances point the way toward an increasingly drug-modulated society. Scientists may develop very specific drugs to reduce appetite, enhance learning—even, one top scientist speculates, to reduce shyness.

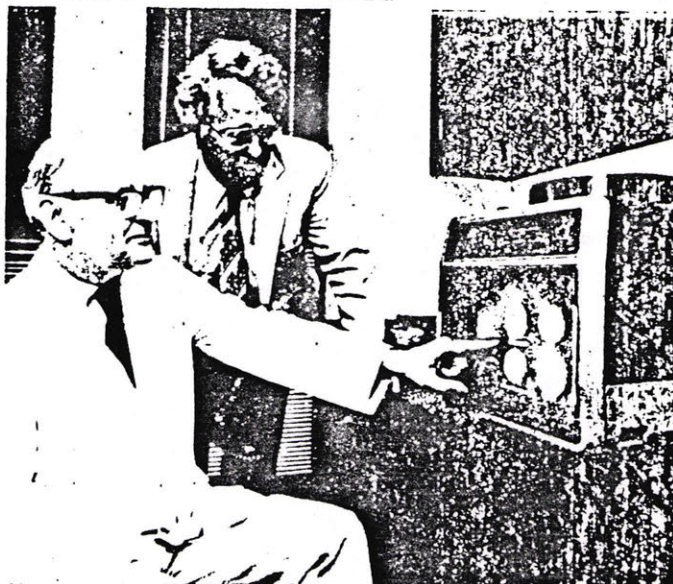
"A drug for shyness?" responds Pert. "Yeah, I can see that."

"Drugs to alleviate shyness, drugs to make us get along better. Those are all theoretically possible—I can conceive of them, easily."

"I can conceive of a drug, or a battery of drugs, that make some cortical connections... zzzt! zzzt!... and you will fall passionately in love for life with the face that you're presented with during the next 60 seconds."

"I can see that. But I can also see somebody who's shy getting transformed by self-awareness training and to make up for missed cuddling. We may just learn to understand ourselves well enough that we won't need drugs."

A. John Rush



Dr. Rush (standing), a research psychiatrist at the University of Texas, confers with colleague Frederic Bronte. Rush says advances in brain science are proving that we can't always control our psyches, and in the future this may affect concepts of criminal justice. "The brain, which is the basis for all we do, is an organ like any other organ in the body," Rush says, "and it will not always obey our commands. That's a scary concept. It puts sort of a limit around free will."

"There are true diseases that will actually be helped by drugs, but . . . scientists who consult for drug companies think [drugs are] the first thing that's going to come out of all this. I don't know about that.

"I think it's more the consciousness, the concept of knowing who and what you are and taking responsibility for yourself and your body. Your body and your mind. Your mind is your body!

"That's the big news, not that some big company is going to make more money on some new drug. It's much more profound than that. It's a mental revolution.

"It changes the way we think about ourselves. Knowledge changes how we act, and that in turn changes how we feel about ourselves."

Other scientists echo Pert's suspicion that the upshot of the revolution in molecular psychology may ultimately lie not in drugs but in more subtle forms of mind control.

This could take many shapes, from belated self-modification brought about by self-knowledge, to the therapeutic use of new principles by psychiatrists, to the development of new brainwashing techniques by dictatorial governments.

The Soviet Union, for instance, has traditionally viewed political nonconformity as a mental illness and has "treated" malcontents in psychiatric institutions. The revolution in molecular psychiatry should make such treatment all the more effective. This could usher in an Orwellian age.

"In principle," says Dr. Fritz Henn, chief of psychiatry at the State University of New York at Stony Brook, "it looks as though we're going to develop controls for a lot of things. And they may include things like aggression . . .

"And it's certainly clear that those things can be used in various ways. And I . . . you know, one of the things is that we're not there yet. The fact is that we're still a very long ways away.

"But yes, I can see it as potentially very dangerous. If we ever got good enough to make everybody totally cheerful, unconcerned and productive all at once, it would be a very bland society, I'm afraid. And I'm not sure that's a useful goal to aim at. We've got to give some thought to it.

"The things that we can control are still pretty subtle . . . although, when you look at the anti-anxiety drugs, and at their uses throughout the world, you realize that the potential for the utilization of these things is enormous . . . and maybe we ought to stop and think about controls. Or think about what the appropriate use of perception-changing drugs ought to be."

Dr. Paul Mandel, a biochemist with the Center for Neurochemistry in Strasbourg, France, and a chief developer of anti-aggression drugs and drug theories, readily concedes that there's a danger involved in his work.

"Of course," he says, "neuroscience is a two-edged sword. Whatever you use, you can use it to do good or bad things. You can use water for torture. I think you have to be careful.

"But when you can do something positive, why not do it?"

Marcus Raichle, a PET scanner scientist at Washington University in St. Louis, agrees. He cautions that it would be a mistake to consider the new power bad simply because it could be abused.

"I think we already know enough about the nervous system that one could manipulate it to the disadvantage of a patient. Being a physician requires a certain level of responsibility.

"But you can't help patients without understanding these things. Ignorance doesn't necessarily protect the patient; it also deprives him of the beneficial use of that knowledge.

"It's obviously a complex issue. And obviously, you're getting very close to home here in terms of being able to understand changes in emotional behavior, changes in the ways that make us human. And the more you understand it the better able you are to manipulate it. And I think one has to be very aware of that, and trust that it won't be misused.

"And don't forget—we're not talking about rare or trivial diseases. Take anxiety, for instance. Anxiety may affect 1 to 2 percent of the population. That's a lot of people. Or depression. Or schizophrenia."

Henn, too, agrees that work should go on and even, perhaps, be speeded up.

"But I don't think the long-term risks are minuscule," he says. "I think they can be dealt with, but I think we ought to deal with them up front. It's probably up to those of us in the profession to start thinking about that—to start doing some education.

"It seems to me like, in a democracy, this is something that the society as a whole ought to address. If we can get people thinking about it, thinking about what is a reasonable way to handle [molecular psychology], then I think we can make informed decisions.

"But I think it's not a bad time to start worrying about it."

The Mind Fixers/Healing the Human Psyche

Criminality is linked to brain chemistry imbalances

By Jon Franklin
Evening Sun Staff

Is much or even most violent criminal behavior caused by imbalances in brain chemistry? Could such imbalances be treated with drugs, reducing the general level of violence in society while at the same time substantially alleviating overcrowding in our prisons?

Increasing numbers of molecular psychologists think the answer to both questions may be yes.

If they are correct, isolating those imbalances and developing drug treatments could prevent crimes, restore criminals to productive lives, and save billions of dollars a year that are now spent to warehouse convicts.

But even within the ranks of molecular psychiatrists there are doubts about whether such an achievement would be legally, ethically and emotionally acceptable to the American people.

One of the most visible proponents of psychiatric treatment for violent criminals is Dr. Fred Goodwin, chief scientist at the National Institute of Mental Health.

"As we become sophisticated about understanding the biology of behavior," he says, "the more potential we get for altering behavior biologically."

"The question is, how much of the enormous cost of violent crime in this country is based on aberrant

brain behavior? What percentage of people who episodically kill or assault or rape have a brain disorder?"

Lion believes that at least some violent behavior can be traced to epileptic-like "storms" in the emotional brain. Like many of his colleagues, he successfully treats many such patients with anti-convulsants.

But, he says, scientific knowledge of the biochemistry of violence lags far behind research on the more classical mental illnesses, such as depression or schizophrenia.

The reason, he says, is that American society is profoundly ambivalent about violence and isn't at all sure it wants science to tamper with it.

For example, Lion says a section of the emotional brain called the amygdala is known to be involved both in the expression and control of violence—but attempts to do human studies on the criminal population in the '60s and '70s were quickly squelched.

"To make a long story short," says Lion, "the ACLU and patients' rights groups vehemently objected to the study of aggression in man."

"What I'm trying to point out is that the idea of tampering with man's aggressive drive is very hazardous and controversial in this society."

"It's OK to tamper with depression... that's bad. We all know it's bad to be depressed. Anything that fixes up depression is good. And we know that schizophrenia is tragic. Do what you want... however you can help a schizophrenic is good."

"I can treat a depressed patient and make that patient lethargic, even induce cardiovascular toxicity, or a parkinsonianism... such side effects are acceptable in a psychotic patient or in a depressed patient as a price to be paid for liberating him from the psychosis or depression."

"But if I have a drug that will control aggression, but makes people lethargic or has some other side effect... that may not be so acceptable to society."

Goodwin believes that rising concerns about the costs of violence and of prisons, coupled with an increasing ability to diagnose criminals with organic brain malfunctions, will eventually lead to a more sympathetic public attitude. But Lion isn't so sure.

"Sometimes I wonder," he says. "I think violence is a very highly valued trait in Western societies. I think we give lip service to a lot of these concerns."

"You know... it's like we can send a man to the moon but we can't seem to stop drunken drivers. The largest, most easily identifiable subgroup of violent people in the United States is recidivist drunken drivers, but nothing is done about it. There's an astonishing tolerance for that."

"The whole issue of violence is politically laden, it has many social-policy implications, particularly in America. You can't do research on prisoners in America, right?"

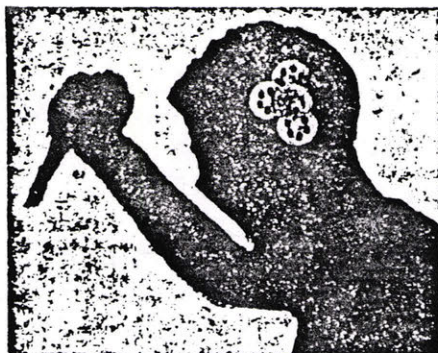
"Isn't that strange? How can we study those who commit violence if the government does not allow it? See? You can't get informed consent, so you can't study them. The only studies you can do on a prison population are demographic studies."

"I think it's political. I think it's like gun control."

But if research into the biochemistry of violence is being retarded in this country the same is less true in Europe, where psychological treatment and even procedures such as surgical castration for rapists have long been a traditional part of penology.

There, one of the leading researchers is Dr. Paul Mandel, a biochemist with the Center for Neurochemistry in Strasbourg, France. Working with rats, mice and other animals, he and his group have focused on two major neurochemical systems.

The systems, he says, involve brain cells that communicate with serotonin and GABA. Both are chemical inhibitors that serve to dampen the function of



brain behavior? What percentage of people who episodically kill or assault or rape have a brain disorder?

"Pilot studies indicate quite a high percentage. A majority."

In one study, he said, prisoners who were repeatedly sent to solitary confinement as a result of violent episodes were treated with lithium, a mood stabilizer generally used for manic-depressive patients.

"There was a very substantial reduction in episodic violence, a very substantial reduction."

"We might have a very revolutionary impact. And I use the word 'revolution' advisedly."

But is the world ready for such a revolution? Would society allow it? On these questions, many molecular psychiatrists have their doubts.

"I can't share [Goodwin's] optimism at all," says Dr. John Lion, formerly a staff specialist in violence at the University of Maryland School of Medicine in Baltimore and now in private practice.

"My skepticism has to do with the politics. Treating prisoners... we're talking about treating criminals! That's something that's not possible in current American penology."

the emotional brain.

Using different strains of rats, some of which are inherently violent and some of which are not, he has been able to show that the violent tendencies are characterized by uncommonly low levels of the inhibitor transmitters in the brain.

Further, he has been able to manipulate those behaviors. Aggressive rats become markedly less so when they are given substances that raise serotonin and GABA levels; passive rats can be made aggressive by administering chemicals that lower those levels.

In his original series of experiments, the aggressive and passive rats were produced by breeding—evidence that genetic predisposition can play a role in serotonin and GABA levels and, thereby, in aggression.

But Mandel says levels of GABA and serotonin can also be changed, and behavior altered, by environmental manipulation.

One classic experiment involves isolation, which is known to produce aggressive behavior in both animals and humans. Studying several groups of rats, the Mandel group found that isolation lowered GABA and serotonin levels for all the animals.

But those that had a genetic disposition to violence, as measured with low GABA and serotonin levels, became much more violent than the others—and tended to do so with less isolation stress.

When the rats were subjected to overcrowding, the opposite effect occurred. GABA and serotonin levels went up, and the animals became passive and lethargic. But the violence-prone animals, apparently protected by their already low levels of GABA and serotonin, suffered the least.

In another, highly suggestive set of experiments, Mandel demonstrated that rats became more violent, and that their brain inhibitor levels dropped, by merely seeing other animals being aggressive.

Mandel, less cautious than many of his colleagues about extrapolating to the human condition, says those experiments indicated that human children do become more violent when they watch violence on television. Likewise, publicizing crimes—and capital punishment—presumably begets still more violence.

Extrapolating further, Mandel believes that emotional self-stimulation can also change serotonin levels and trigger changes in the tendency to solve problems by violent means. Religious fanaticism, he predicts, will one day prove to be linked to lowered serotonin levels.

"The Ayatollah Khomeini, for instance," says Mandel. "He's suppressed his GABA and serotonin levels through religious excitement... and now there's no inhibition."

Mandel believes that violence is a result of a psychochemical disease process and should be viewed, and treated, in that fashion.

"Aggression is like any other disease," he says. "It's the lack of inhibitory mechanisms that can be produced

by genetics and/or the environment, and there's no reason not to treat it if we can."

The French group's purpose is the development of drugs that can produce changes in human patterns of aggression. He has already produced one such drug, Valproic acid, which has been at least partially effective in reducing violence in some patients with emotional-system disease.

But Mandel does not claim that drug treatment alone can convert violent criminals into model citizens.

Rather, he sees drugs as an adjunct to other treatment—including psychotherapy and environmental changes, such as improved living conditions and better education, that would work together to raise serotonin and GABA levels.

At NIMH, Goodwin believes that such combination treatment schemes will eventually prove so effective, both medically and economically, that they will achieve acceptance even in the United States.

"I grant you," he says, "that there are dangers in that. Everyone gets concerned, perhaps overly concerned, about the specter of mind control—particularly when you're talking about criminal justice."

"Criminal justice is extremely sensitive to any efforts to intervene medically with any individuals whose misbehavior may be a function of a brain disorder. And the system is geared, maximally, to protect people from such intervention... on what I think is a rather old-fashioned notion that there are greater risks than there are benefits."

"I acknowledge that there are risks, but I think society is sufficiently alert to those risks that it's rather farfetched to think that properly monitored treatment programs, with properly selected individuals, wouldn't in fact be much more beneficial to the individuals—not to mention society."

Dr. A. John Rush, a research psychiatrist at the University of Texas Health Science Center in Dallas, agrees that molecular psychiatry, coupled with the new scanners and other technology for diagnosing mental disease, is on a collision course with the legal system.

"I think we all assume that we can by willpower control virtually everything we do. But a lot of psychiatric technology and information is revealing the fact that the brain, which is the basis for all we do, is an organ like any other organ in the body and it will not always obey our commands. That's a scary concept. It puts sort of a limit around free will."

"To the layman, it sounds very scary—your brain can go bad, and you do not know that it's going bad, and you can't control it. It's a mixed blessing."

Rush, who has used scanners to watch shifts in the brain processes of patients with multiple personalities, believes that the new technology will inevitably alter how we think about right, wrong, and criminality.

"I think if you look at [John] Hinckley, [ruled insane in the shooting of President Reagan], for example, at one

John Lion

Dr. Lion, an expert on causes of violent behavior, agrees that brain chemistry plays a role in criminality. But he points out the political and practical pitfalls of tampering with man's aggressive drives and trying to change views on criminal justice—even if psychic engineering could reduce the country's swollen prison population.



level he knows he's absolutely crazy. And at another level he knows he can't control it. And he has, as far as I can tell—and I'm relying on the public media—it would appear that he has some variant of schizophrenia.

"And while he knows that it's crazy, he also realizes over time that he really cannot control it. If you asked him if he really wanted to do what he did, at one level he'd say yes... and on another level he'd say, 'Absolutely not. It's crazy!'"

"All of us are vulnerable to that kind of thing, where we find ourselves doing things that we don't want to do, that we cannot control.

"At one level the biological approach to psychiatry is reassuring. It indicates that yes, there are diseases of the brain, the effects of which you cannot control.

"On the other hand they're very frightening to average people, like most of us, who think they can control most of the things that they do. But there are great limits to willpower, motivation, decision or a sense of reality. I think this is frightening."

As the science of molecular psychology evolves, Rush says, the legal system must evolve with it.

"I think, for instance, that it will require some very substantial revisions in the insanity defense. What they are... I wouldn't care to speculate. But I think they will evolve over the next 20 or 30 years as our ability to diagnose gets better and better."

But skeptics such as Lion believe that evolution, if indeed it occurs at all, will be slow and painful.

"At the moment," he says, "there's not even any official rehabilitation program in the American penal system.

"I think that in order for a biochemist to exert an effect on a criminalologic system there would have to be massive dialogue and profound policy changes. And I don't see any evidence of that."

It's true, he concedes, that there is an increasing willingness to use drugs such as depo-Provera to chemically castrate rapists, as an alternative to prison. But he points out that those programs, and the drugs

used in them, are still experimental and very controversial.

And while drug companies are working on drugs to control aggression, he says, such projects have a very low priority.

"The politics are very formidable. These companies know very well that if they're going to come out with a drug to tamper with aggression, they've got big problems ahead.

"I mean, what's it going to be called... a 'pacifier'? What's it going to do? It's a dicey endeavor.

"So yes, there is some background ferment. But it's a low hum, not a big roar."

Besides, he says, he has strong personal doubts that drugs and related treatments aimed at changing the chemistry of aggression can ever change the hard-core criminal.

"There just are evil people in the world. Always have been and always will be, and we're not going to be able to do anything about them."

"I've seen real bad, evil people. I see a lot of patients, and there are some you want to treat, some you don't want to treat. Just real bad."

"That's not a diagnosis, it's a value judgment. But the levels of their [violent] behavior transcend mental illness. The heinousness of their behaviors, actions and crimes are just not referable to the mental health system, diagnostic code or whatever."

"I've seen these people. They're just... they've... they're recidivist criminals. They have no remorse. And so forth."

"I guess we could argue that they have a latent depression or something, and I guess they could, but

"You know, when you've worked with behavior disorders enough, you come to the conclusion that there are certain behaviors that simply reflect... evil."

Does "evil," as he defines it, have a biochemical basis?

Lion sighs, then laughs.

"Sure," he says. "I'm sure Satan's got bad hormones. What can I say?"



Khomeini's brain chemistry

Dr. Paul Mandel, a biochemist with the Center for Neurochemistry in Strasbourg, France, who is outspoken about molecular causes of behavior, suggests that lowered levels of a certain brain chemical can lead to both violence and religious fanaticism. For example, the Ayatollah Khomeini may suffer from the problem, Mandel says, and would benefit from drug treatment.

January 13, 1987

MEMORANDUM

TO: Donald I. Abrams, M.D. Gayling Gee, Ward 86 Adm Nurse
John Mills, M.D. Lawrence Kaplan, M.D.
Palmer Beasley, M.D. Barbara Woodruff, Adm Analyst
Merle Sande, M.D. Constance Wofsy, M.D.
Phil Sowa, SFGH CEO Paul A. Volberding, M.D. ✓
Media Relations Dept. SFGH Lt. Greg Corrales, SFGH Police

FROM: Roberta R. Wilson
AIDS Programs Coordinator - SFGH

RE: Visit from British Government Officials
Tuesday, January 20, 1987
2:30 - 4:00 pm

The British government is sending a group of government officials on an AIDS fact-finding tour of the United States. Washington DC, New York City and San Francisco have been selected as resources of information. The group includes the following members:

Norman Fowler, Secretary of State Social Services
Sir Donald Acheson, Chief Medical Officer
Strachan Heppell, Deputy Undersecretary
Romola Christopherson, Director of Information
Graham Burton, Consul General
Sandy Burke, Vice Consul of Information

They will have extensive press coverage on their visit. The SFGH Media Relations Dept. will supervise all members of the press and provide press packets. Dr. Kaplan will meet with and brief the members of the press on SFGH's AIDS programs and answer questions.

The schedule for the 2:30 - 4:00 pm visit is as follows:

2:30	Arrival	Ward 84 Conference Room
2:35 - 2:50	Donald I Abrams,	Overview of SFGH Clinical Care Program
2:50 - 3:00	John Mills,	Overview of AIDS Research
3:00 - 3:10	Palmer Beasley,	AIDS Epidemiology in SF
3:10 - 3:20	Discussion	
3:20 - 3:35	Tour	AIDS Outpatient Facilities
3:35 - 4:00	Merle Sande, Chair	Dept Med Services SFGH 5F40
	Tour	AIDS Inpatient Facility
4:00	Departure	SFGH Entrance

MEDICAL SERVICE
SAN FRANCISCO GENERAL HOSPITAL

January 21, 1986⁷

Paul Volberding, M.D.
Associate Professor of Medicine
Chief, AIDS/Oncology Division, SFGH

Dear Dr. Volberding:

Thank you for agreeing to speak at San Francisco General Hospital Medical Grand Rounds on February 3, 1987. We understand that you will speak on antiviral therapy in AIDS: current data and implications. Grand Rounds begin at 11:30 on Tuesday morning and are held in Carr Auditorium.

We would appreciate it if you would prepare a handout summarizing the key points of your talk. Many people who attend Grand Rounds have commented that this helps them in understanding and recalling the information presented. We would be happy to arrange for the distribution of these handouts if you would send a copy to Nancy Cox, Room 5H-22, SFGH approximately 1 week prior to Grand Rounds.

We appreciate your willingness to speak.

Sincerely,



Chuck Daley, M.D.
Chief Medical Resident



Chris Forsmark, M.D.
Chief Medical Resident

TO: CRI FACULTY
FROM: Ravee Vorachard

Attached is an updated schedule for 1987 Combined Hematology/Oncology Rounds.

HEMATOLOGY/ONCOLOGY GRAND ROUNDS
THURSDAY 1:30-2:30 P.M.
MOFFITT-1296

SCHEDULE FOR JANUARY-DECEMBER, 1987

JANUARY	<u>SPEAKER</u>	<u>TITLE OF PRESENTATION</u>
8	PAUL VOLBERDING, M.D.	"Directions In Experimental Therapy of HIV & Coordination of Clinical Research in S.I
15	BART KAMEN, M.D.	
22	FRANK VALONE, M.D.	"Role of Platelets and Platelet-Activating Factor In Inflammatory Reactions"
29		
FEBRUARY		
5	GEORGE RODGERS, MD, PhD	"Vessel Wall Procoagulant Activity In Atherosclerosis"
12	JAY LEVY, M.D.	"HIV And The Pathogenesis Of AIDS"
19		
26		
MARCH		
5	CHRIS BENZ, M.D.	"Development of A New Class of Chemotherapeutic Agents with Antimitochondrial Specificity"
12	RAY STRICKER, M.D.	"AIDS-Related Immune Thrombocytopenia"
19	MOHAN NARLA, D, Sc.	"Red Cell Membrane Biology"
26	DON ABRAMS, M.D.	"ARC: Clinical Investigations and Natural History Studies"
APRIL		
2	DENIS GOSPODAROWICZ, Ph.D.	"FGF Molecular & Biological Characterization"
9	JOHN ZIEGLER, M.D.	"Cancer & AIDS"
16	ALEX TSENG, M.D.	"Strategies in the Chemoprevention of Cancer"
23	DOUG ARMSTRONG, PH.D	"Therapeutic Interaction of 6-thioguanine with Interferon"
30		
MAY		
7	JOHN MORROW, PH.D.	
14		
21	AL LOPEZ, MD	
28		
JUNE		
4	ED LIU, M.D.	"Molecular Studies In Breast Carcinoma Tumorigenesis"
11	JOEL CHASIS, M.D.	"Red Cell Membrane Proteins & Their Functional Roles"
18	BRIAN LEWIS, M.D.	"Update on Pain In Cancer"
25		

JULY	<u>SPEAKER</u>	<u>TITLE OF PRESENTATION</u>
2		
9	MARGARET CLARK, Ph.D.	"Disorders of Red Cell"
16	MARC SHUMAN, M.D.	"Activation & Inhibition of Fibrinolysis: Physiologic & Pathologic Consequences"
23	MICHAL MCGRATH, M.D.	"AIDS-Associated Lymphomagenesis"
30		
AUGUST		
6		
13		
20		
27		
SEPTEMBER		
3	AL DEISSEROTH, MD, PhD	"Molecular Defects in Leukemia"
10	PAUL BRAY, M.D.	"Biosynthesis of the Fibrinogen Receptor"
17	BRUCE MACHER, Ph.D.	"Glycosphingolipids Recognized by Myeloid Specific Mouse Monoclonal Antibodies"
24	JUDITH LUCE, MD	"Hepatocellular Carcinoma"
OCTOBER		
1		
8	LAWRENCE KAPLAN, M.D.	"Treatment of AIDS-Associated Malignancies"
15	LOIS EPSTEIN, M.D.	"New Interactions between the Interferons, Interleukins and Tumor Necrosis Factor"
22		
29		
NOVEMBER		
5	LAURIE WEISBERG, M.D.	"Factor XIII - The Fibrin-Stabilizing Factor"
12	MAREK BOZDECH, M.D.	"BMT Experience at UCSF"
19		
26	THANKSGIVING	

DECEMBER	<u>SPEAKER</u>	<u>TITLE OF PRESENTATION</u>
3	CRAIG LINDQUIST, M.D,Ph.D.	"Kaposi Sarcoma: In Vitro Modeling of New Therapies"
10	ROBERT DEBS, M.D.	
17		
24	NO ROUNDS	
31		

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SCHOOL OF MEDICINE, Rm. 569-U
EXTENDED PROGRAMS IN MEDICAL EDUCATION

SAN FRANCISCO, CALIFORNIA 94143

~~(415) 860-1231~~

NEW NUMBER: (415) 476-4251

January 21, 1987

Paul Volberding, M.D.
SFGH Ward 86
Campus Mail

RE: COMPREHENSIVE CARE OF THE AIDS PATIENT: A WORKSHOP
May 1 - 2, 1987 - EPME #M64125

Dear Doctor Volberding:

Extended Programs in Medical Education is pleased to sponsor the above program with the Department of Medicine.

I have reviewed the program on behalf of the CME Governing Board. It meets the requirements for EPME sponsorship, and it has been designated for 13.5 hours of Category 1 Credit.

This program will be conducted according to the terms of financial Plan "A", whereby the net gain or loss will be transferred to your department after fiscal closing.

It is good to know that the program has reached this stage of planning. It looks to us as though it should be very well received and worth all of your effort.

Sincerely yours,

Abraham M. Rudolph, M.D.
Reviewer
CME Governing Board

AMR:11m

cc: Richard K. Root, M.D.

January 20, 1987

TO: ✓ Paul Volberding
Don Abrams
Merle Sande
Dave Werdegarr

FROM: Phil Lee

I talked with Sam Matheny of the Public Health Service on January 15 regarding the Institute's cost of care study and also regarding the problem of professional education and the limited number of private physicians willing to care for persons with AIDS. He is the key person in the Health Resources and Services Administration, which will be funding centers for the training of health professionals, and is currently in the process of developing policies for the program. I will be meeting with him to discuss the program, and I would very much appreciate any advice or suggestions you might have.

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SCHOOL OF MEDICINE

Please address reply to the undersigned at:

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SAN FRANCISCO, CALIFORNIA 94110
(415) 476-4638

January 30, 1987

To: Ed Biglieri
Paul Volberding

From: Mike Humphreys

Re: AIDS proposal

Attached is the current version of the fellowship application I want to submit to the AIDS Task Force to study water metabolism in AIDS patients. It is still unfinished, but I have to leave town and would like you to review and comment so that I can complete it on my return February 9. The application has to be at Systemwide on February 17.

Please evaluate the proposal from the practical as well as the scientific viewpoint. It is possible to recruit patients for 3 nights on the GCRC? Do we need to pay them? Should we also study normal controls? I would also propose to restudy those patients who are found to be adrenally insufficient after they have been put on glucocorticoid replacement therapy (that part is not yet written)

I shall eagerly await your responses.

MHH:mln

DRAFT

WATER METABOLISM IN PATIENTS WITH THE
ACQUIRED IMMUNE DEFICIENCY SYNDROME

BACKGROUND

A variety of renal abnormalities has been described in patients with the acquired immune deficiency syndrome (AIDS)(1). Structural abnormalities have largely related to the presence of glomerular pathology, with focal and segmental glomerulosclerosis being the most commonly described lesion and accompanied clinically by renal insufficiency and the nephrotic syndrome (2,3). A variety of functional abnormalities also occur, including hyponatremia, hypokalemia, and hyperkalemia (1). In many circumstances, these abnormalities can be related to concurrent illnesses such as diarrhea, or to medication administration. However, many patients with hyponatremia, the abnormality in water metabolism causing in the hyponatremic state cannot be explained by other illnesses or by treatments being received by the patient. Hyponatremia in this setting can be severe, and could contribute to central nervous system abnormalities often experienced by the AIDS patient (4). This proposal has as its goal the characterization of water metabolism in patients with AIDS.

In order for normal water balance to occur, renal water excretion must be adjusted to match variations in water intake: in times of relative excessive water intake, urine dilution results in enhanced water excretion, whereas during relative restriction in water intake, a concentrated urine must be elaborated to maintain balance. The renal diluting mechanism depends on an adequate amount of solute (sodium chloride) delivered to and reabsorbed by the thick ascending limb of Henle's loop. Solute delivered to this nephron

segment is critically related to extracellular fluid (ECF) volume: when ECF volume is depleted, a reduced filtration rate and enhanced reabsorption of fluid in the proximal tubule reduces the delivery of fluid to the loop of Henle; as a consequence, diluting ability is impaired. Diluting ability also depends on suppression of vasopressin (ADH) secretion from the pituitary. ADH secretion is regulated by plasma osmolality; a reduction in plasma osmolality of as little as 1% will reduce ADH secretion. It is also regulated by nonosmotic means related to input from arterial baroreceptors. Consequently, states of hypovolemia, with reduced arterial pressure and/or impaired cardiac function, are usually associated with enhanced ADH released even in the presence of a dilute plasma osmolality. Thus, maintenance of normal water balance is critically dependent on volume factors allowing an optimal amount of sodium chloride to be delivered to the diluting segment as well as a normal suppression of ADH secretion in the presence of a dilute plasma osmolality.

The incidence of hyponatremia in patients with AIDS is not known. However, a recent preliminary report indicated that 50-60% of patients may be hyponatremic(5). A recent survey of 22 patients hospitalized on the AIDS ward at SFGH indicated that 15 (68%) had a serum sodium concentration during the hospitalization of less than 133 meq/L (range 123-133 meq/L). While hyponatremia is a common occurrence in hospitalized patients in general (6), these figures nevertheless suggest that AIDS patients may be particularly susceptible to clinically significant degrees of hyponatremia. Possible causes of hyponatremia in a patient with AIDS are many. Certainly, volume depletion, cause by poor intake perhaps coupled with excessive losses from vomiting or diarrhea, is a major possibility. Hyponatremia in this setting is accompanied by characteristic changes in the composition of the urine as well

as clinical signs and symptoms, and so is easily detected and readily corrected by administration of intravenous saline solutions. Hyponatremia can also result from the syndrome of inappropriate secretion of ADH (SIADH). This in turn could result from pulmonary or central nervous system infections which often beset the AIDS patient, or, less commonly, from medications given to the patient.

A third mechanism by which hyponatremia could occur in the AIDS patient relates to altered adrenal function. Adrenal functional abnormalities, ranging from isolated defects in one or another of the steroid biosynthetic pathways to frank adrenal insufficiency, have been reported (7-11). Altered adrenal function impairs water metabolism through at least two separate pathways, a mineralocorticoid effect, and a glucocorticoid effect. The mineralocorticoid effect appears mediated chiefly through associated volume depletion: salt lost into the urine because of the absence of aldosterone results in ECF volume depletion, impaired water excretion, and hyponatremia (12). This form of hyponatremia is corrected by a high salt diet and by mineralocorticoid replacement therapy. The glucocorticoid effect on water metabolism is more complex. It was initially hypothesized that glucocorticoids were necessary in order for the renal tubular epithelium to be relatively impermeable to water in the absence of ADH. This view has subsequently been proven incorrect, and at least two other possibilities have been offered to account for the glucocorticoid effect on water metabolism (13). One is related to stimulation of ADH secretion through a baroreceptor mechanism: impaired cardiac function in glucocorticoid deficiency states activates baroreceptor-mediated release of ADH, with attendant impaired water excretion. Glucocorticoid replacement improves cardiac performance, and

suppresses this baroreceptor effect on ADH release. Alternatively, it has been argued that glucocorticoids are necessary for the normal osmotic regulation of vasopressin secretion in the central nervous system, and that, in the absence of glucocorticoid, hypoosmolality is inadequate to suppress ADH release. Regardless of the mechanism, the data suggest that the impaired water excretion associated with glucocorticoid deficiency states is related to enhanced levels of ADH (13).

Studies by the Division of Endocrinology at SFGH, funded by a grant from the AIDS Task Force, have clarified the spectrum of adrenal steroid biosynthetic abnormalities in patients with AIDS (14). Plasma concentrations of a number of steroids emanating from the zona glomerulosa and the zona fasciculata have been measured in AIDS patients in the baseline state and following cortrosyn^R stimulation. The conclusions from these studies are that function of the zona glomerulosa, responsible for aldosterone (mineralocorticoid) production, is largely intact in the AIDS patient unless frank adrenal insufficiency has developed. The major abnormalities are confined to the zona fasciculata responsible for glucocorticoid production. Two major biosynthetic pathways exist in this zone of the adrenal. One leads to the production of the 17-deoxy steroids deoxycorticosterone, 18 hydroxy DOC, and corticosterone. The other leads to the production of cortisol. The earliest abnormalities are detected in production of 17-deoxy steroids; later, biosynthetic abnormalities are also detected in the cortisol synthetic pathway. In either circumstance, glucocorticoid deficiency, whether mild and subclinical or frank and full-blown, results. The impact of this spectrum of glucocorticoid deficiency on the clinical course of these AIDS patients is not yet known, but could be considerable. With respect to the question of

hyponatremia in AIDS, it seems plausible to consider that this degree of glucocorticoid deficiency could contribute to the hyponatremia frequently observed in these patients.

We propose to look in detail at water metabolism in patients with AIDS, relating impaired water excretion to simultaneously measured adrenal function and plasma ADH concentration.

METHODS OF PROCEDURE

We shall invite patients with AIDS who are followed in the AIDS Clinic or hospitalized on the AIDS ward at SFGH to participate in the study. Criteria for inclusion in the study include normal renal function as assessed by normal BUN and creatinine; no previously identified endocrine dysfunction; ability to comply with the experimental protocol as described below; and ability to give informed consent. We shall study the ability of AIDS patients to concentrate the urine after overnight dehydration and to excrete an orally ingested water load under standardized conditions. We shall attempt to recruit patients with a spectrum of baseline serum sodium concentrations from normal down to frankly hyponatremic levels, in the range of 130 meq/L. These responses will be correlated with measurements of plasma vasopressin and of adrenal gland responsiveness to cortrosyn^R stimulation in the following protocol.

Patients will be admitted to the General Clinical Research Center (GCRC) at San Francisco General Hospital. They will be placed on a diet of known electrolyte composition for two days. After breakfast on the second day, all fluids will be withheld; food intake will continue in the normal manner, and fluid will only be administered in small amounts as necessary for any medication that the patients may be taking. Patients will void at 7:30 AM on the third day; this specimen will be saved for later measurement of

osmolality, and a ten ml blood sample will be drawn for determination of plasma ADH concentration. An indwelling venous catheter will then be placed through which an infusion of meglumine iothalamate (Conray 60^R) in 5% dextrose/water will be infused at 1 ml/min for subsequent determination of iothalamate renal clearance. Patients will also receive a loading dose of iothalamate as calculated from the formula

$$\frac{\text{Body Wt in kg} \times 0.2}{2.82} = \text{cc Conray } ^R$$

The patient, in the fasted state, will ingest a standard oral water load of 20 ml/kg given over a 30 min interval; the volume ingested and the time will be recorded. Patients will be asked to void every 60 min for five hours; the volume of each voiding will be recorded and an aliquot saved for later measurement of osmolality and iothalamate concentration. Blood samples will be obtained at the midpoint of the 2-5 hours (10 ml each) for plasma iothalamate concentration, and at the 3rd and 5th hours for determination of plasma ADH.

Interpretation of Results

1. Urinary concentrating ability: an overnight dehydration test will result in normals in a urine osmolality in excess of 650 mOsm/kg H₂O. Concentrating ability is dependent on renal function, volume status, and integrity of the hypothalamic-posterior pituitary axis. Impaired concentrating ability would suggest deficient ADH secretion or interference with its action on the renal tubule (nephrogenic diabetes insipidus). At present there is no reason to anticipate any impairment in renal concentrating ability in patients with AIDS. These studies will, however, characterize the relationship between urine

osmolality and plasma ADH concentration in these patients.

2. Urinary dilution: in normal individuals, 80% of the standard water load is excreted within five hours, with the osmolality of at least one urine voiding being less than 100 mOsm/kg H₂O, indicating virtually complete suppression of ADH secretion. In patients with AIDS we expect a spectrum of results ranging from normal to blunted diluting capacity. In patients with impaired water excretion

January 13, 1987

TO: Participants, Oral AIDS Research Project
FROM: John S. Greenspan, Director 
RE: Enclosed Directory

We have put together the enclosed directory (names, addresses and phone numbers) to assist you in getting in contact with each other. A couple of notes for those of you who are off-campus and do not have access to the UCSF campus mail system:

1) UCSF addresses (e.g., Box 0512, HSW 604)

Add the following 2 lines to the address given (be sure not to omit the box #) and use the U.S. Mail.

University of California San Francisco
San Francisco, CA 94143

2) SFGH addresses

Add the following 2 lines to the address given and use the U.S. Mail:

1001 Potrero Avenue
San Francisco, CA 94110

We hope this will prove helpful. If you have any questions, changes or additions to this directory, please contact Diane at (415) 476-9169.

JSG/pkr

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Department of Public Health

San Francisco General Hospital
Medical Center

February 5, 1987

To: Protocol Managers, Principal Investigators, Barbara Woodruff,
Interested Others

From: Debbie Hahn *DH*

Re: IRB issues

The UCSF Institutional Review Board (IRB), known locally as the Committee on Human Research (CHR), has several guidelines and standards for submission and review of protocols needing approval. I have become quite familiar with the rules over the years and would like to share some of my knowledge with you if it will help make the transition of my departure a little easier. At the regularly scheduled protocol managers' meeting next Wednesday, Feb. 11, 1:30 pm., in the Ward 84 conference room, I plan to give a little background and informal training and question-answering session. Everyone interested is invited to attend.

Attached are some documents which you might find helpful to read ahead of time, or just keep on file for future reference. The first page is taken from the "Clinical Trials Policies and Procedures" I wrote in October, 1985. The first "Consent Forum" newsletter and sample forms which follow pertain to submission procedures. The second "Consent Forum" newsletter contains consent form guidelines and is followed by a sample Ward 84/6 consent form that was recently approved.

For everybody's information, the current CHR chairperson's name is Carol Viele, R.N., M.S. The CHR office phone number is 476-1814, and the mailing address is Box 0616, UCSF. Donald Abrams is currently a member of the committee and can answer many questions that come up.

DIVISION OF AIDS ACTIVITIES

WARD 84/86

SUMMARY OF UCSF COMMITTEE ON HUMAN RESEARCH REQUIREMENTS

Generally speaking, when innovative diagnostic/therapeutic procedures are considered part of a study/experiment and data will be collected, they must be reviewed by the CHR in accord with DHEW regulation for the purpose of evaluating individual patient risk/benefit ratio.

I. What Constitutes a Research Project Requiring Approval

- A. Full Committee approval (15 copies of protocol)
 1. Any randomized drug trial
 2. Any investigational drug trial
 3. Any trial of standard drug being investigated for new indication
 4. Any study of blood samples by venipuncture exceeding 450 ml in an eight week period and/or more often than two per week.
- B. Expedited review by sub-committee (4 copies of short form)
 1. Study of blood samples by venipuncture not exceeding 450 ml in a eight week period and no more often than two times per week.
 2. The study of existing data, documents, records, pathological specimens, or diagnostic specimens.
 3. Recording of data from subjects using non-invasive procedures routinely employed in clinical practice.

II. Modifications and amendments of active/approved protocols must be approved when such changes might potentially alter the patient risk/benefit ratio. Examples are:

- A. Change in drug dosage/schedule/route of administration
- B. Change in procedure - e.g. instituting pharmacokinetics
- C. Redefining eligible patient group

CONSENT FORUM

A Newsletter from the: COMMITTEE ON HUMAN RESEARCH

Issue No. 9 June, 1984



EDITORS: Erica Heath / Louise Tipton

CHAIRMAN: Walter Way, M.D.

NOTES ON MAKING APPLICATION TO THE COMMITTEE ON HUMAN RESEARCH

There are five main types of application one might make to the Committee on Human Research. These are:

- 1) an initial, regular, full review application
- 2) an initial, short form application
- 3) a continuing review, annual renewal application (full or short form)
- 4) a modification application
- 5) a general approval application

The weekly deadline for all applications is WEDNESDAY EVENING AT 5:00 P.M. (Both regular and short-form applications have the same review schedule). Items to go to Committee will be circulated the following day for review at the meeting the next Thursday. Written responses from the Committee usually go out from the office by the Wednesday following the meeting.

It is recommended that applicants allow one month from submission for the review process to be completed, though it may take less or more time in some instances. Please be aware that it is the investigator's responsibility to make submissions early enough to meet deadlines such as those of granting agencies, sponsoring companies, or CHR expirations. Investigators who do not renew their protocols before the expiration date and continue to work with subjects place themselves at risk, since the University will not indemnify a principal investigator in any legal actions arising from human research activities unless the activities had current CHR approval.

CHR Guidelines, newsletters on expedited review categories, and application forms are available in ~~416 Clinics~~. ~~The Computer Survey Form is no longer being used~~ new Laurel Heights office. - or write to CHR, box 0616, UCSF

1. INITIAL, REGULAR, FULL REVIEW APPLICATION:

Fifteen copies of the initial full application are required.

Each copy should include a cover letter (optional), a completed CHR Cover Page form, protocol, and consent form(s). The protocol and consent form should be written according to the CHR Guidelines.

NO APPLICATION MAY CONSIST OF MORE THAN TEN PAGES OF TEXT. The CHR has instructed the staff to return any application longer than ten pages. Appendices may be used for items such as questionnaires or forms.

Sponsored or multicenter studies may comply with the 10-page rule by providing a good synopsis for everyone, plus two copies of the Investigator's group protocol.

For protocols involving investigational new drugs or devices, two copies of the Investigator's Brochure must be submitted. One copy will be retained.

2. INITIAL, SHORT FORM APPLICATION:

Four copies of the short-form application are required.

DHHS regulations made final in 1981 allow for certain categories of research to be given "expedited review" (See Consent Forum 5). At UCSF, the Committee on Human Research implemented these regulations with an "expedited" or "short" form and a sub-committee review process.

The short form may be used only when the research being done fits into one or more of the DHHS categories listed in the Consent Forum 5 newsletter.

Short forms are seen by three selected members who present their findings at a regular meeting. They must (a) find that the procedures fit into one or more of the listed categories, (b) find that the study presents less than minimal risk, and (c) feel comfortable recommending approval without having all the other members read it. Their options are to recommend approval, to recommend minor changes, or to refer to full committee. If the last option is selected, there will be delay due to further circulation.

3. CONTINUING OR ANNUAL REVIEW APPLICATION:

Four copies are now required for both regular and short-form renewal applications.

The CHR must review every application on an annual basis. It is recognized that some studies are well under way in that year and that others are not even funded or started. Nevertheless, to keep a protocol active, it must be submitted for renewal.

Annual review is required in order to have periodic re-evaluation of the evolving risks and benefits. Information developed within the study and in the rest of the community have an impact on the re-evaluation. The Committee is finding tremendous variation in the quality of progress reports. The minimum needed is a few sentences; generally, no more than two pages is necessary. If multiple study centers are involved, please include information from this center plus whatever information is available from the main study center. The progress report should address the following points:

- If nothing has happened, that should be clearly stated.
- If the study has started, what progress has been made? What has been learned?
- What risks have been noted? Have there been any unanticipated side effects or an unexpected frequency or severity of anticipated effects? If so, has the consent form been updated appropriately?
- Is there any reason to change the view of the expectation of benefits?
- How has the consent process worked? How many people have been asked? How many, if any, have refused? Is the process working or is some modification needed?
- How many subjects have been enrolled? How many more are needed to complete the study? How long is the study expected to go on?

4. MODIFICATION APPLICATION:

If the modification requested is major, it is considered through the full review process, and fifteen copies are required. If it is a minor modification, it is considered through the expedited review process, and four copies are required.

The initial evaluation of whether a modification is major or minor rests with the principal investigator, who should consider the change in procedures and risks.

Applicants should submit a letter which provides information on the nature of the modification, why it is being requested, and the effect of the modification on the study and on the consent process. If the changes will affect the information given in the consent form, an appropriately revised form should be included. It is helpful to highlight the changes on the new consent form.

The members reviewing modifications have before them only what is sent in; they do not have the previous file. They may or may not recall what the study is all about and may never have seen the study before if they are new on the committee. Thus, the modification request should include copies of the previously approved protocol or a good, complete summary of the study, to put the proposed changes into perspective.

5. GENERAL APPROVAL APPLICATION:

Four copies of the general approval application form are required.

This type of application is not circulated to Committee members; it is administratively reviewed by the Committee chairman.

A general or blanket approval is given for purposes of grant application. It indicates that there has been administrative review of a description of a grant only; IT INVOLVES NO REVIEW AND NO APPROVAL OF ANY SPECIFIC INVOLVEMENT OF HUMAN SUBJECTS IN RESEARCH.

The general approval is given only for certain limited circumstances, usually program project or training grants, involving multiple projects or research plans which cannot yet be specified. For these, one date of specific review and approval cannot be given on the human subjects certification form (DHHS Form 596), which is required as part of the grant application. General approvals are not given for a grant involving one specific project which the investigator has failed to submit for CHR review before the grant deadline.

This approval allows the grant applicant with a program project or training grant to complete the form by checking off the section which states:

"This activity contains multiple projects, some of which have not been reviewed. The IRB has granted approval on condition that all projects covered by 45 CFR 46 will be reviewed and approved before they are initiated and that appropriate further certification (Form HHS 596) will be submitted."

COMMITTEE ON HUMAN RESEARCH
COVER PAGE

PRINCIPAL INVESTIGATOR _____ UNIVERSITY _____
(UCSF FACULTY) _____ TITLE _____ DEPT. _____
MAILING ADDRESS _____ PHONE _____ Is P.I. sponsor/
(CAMPUS IF POSSIBLE) _____ NUMBER _____ advisor only? _____

CO-INVESTIGATOR _____ TITLE _____ DEPT. _____
MAILING ADDRESS _____ PHONE _____ SUBMISSION
PROJECT _____ NUMBER _____ DATE _____
TITLE _____

NAMES/TITLES OF ALL OTHER INVESTIGATORS:

PROCEDURES (List all procedures to be
done for purposes of the study):

HISTORY OF THIS PROJECT:

Previous CHR
approval # _____

____ New
____ Modification
____ Renewal Expiration Date ____/____/____
Does this submission differ from the
previous submission(s)? ____ Yes ____ No

Explain any differences within protocol.

SUBJECTS (Explain in detail in protocol):

Subjects: _____ Number _____
Source(s) _____
Compensation _____

Controls/Normals: _____ Number _____
Source(s) _____
Compensation _____
Source(s) _____
Compensation _____

Will any minors (under 18) be
involved? _____

SITE: _____ Yes _____ No _____
Will SF VAH be a study site? _____
Will SFGH be a study site? _____

COSTS:

Will there be any charges to the subjects
or their third party carriers incurred
through participation in the study?

Yes _____ No _____

Which costs? _____

Maximum amount (approximate): _____

RADIOISOTOPES:

Will any radioactive materials be
used? _____ In vivo? _____ In vitro? _____
What materials? _____

Approval of the Radiation Safety Committee
is required prior to CHR approval.

Number of RSC approval _____
Date of RSC approval _____

DRUGS & DEVICES:

List all approved drugs and/or devices to
be used with subjects.

List all new drugs and/or devices. All
new drugs and devices, and all approved
ones being investigated for a new use,
must have an exemption number from the FDA
(unless a non-significant IDE is being
sought from the IRB). If applicable, list
exemption number.

IND/IDE #

FUNDING:

Will this study be funded? _____ Pending
Federally? _____ Yes _____ No
Other? _____
Agency/Sponsor _____ # _____

INSTRUCTIONS FOR CHR FULL COMMITTEE APPLICATION:

FIFTEEN complete packets of material are required. Each packet must be identical and must contain:

- a) A cover page - 3/86 version
- b) A cover letter (optional)
- c) The working protocol, which should not be the grant application and should be no more than 10 pages, not including attachments. Appendix A in the CHR guidelines includes a checklist of the topics which should be discussed in the protocol.
- d) All consent forms/documents necessary
- e) Two copies of the Investigator's Brochure when the study involves an investigational new drug (IND) or investigational device (IDE) (The brochures are usually available from sponsoring drug/device companies).

Consent forms should be written according to the current, standard format as discussed in the CHR Guidelines (Amended September, 1985), Appendix E, pages xiii-xix. Sample forms are included in this section of the Guidelines.

If consultation is desired when writing the consent form, an appointment should be made with an administrative assistant to the CHR (ext. ⁴⁷⁶~~6-1814~~). Pre-review of the form can help familiarize the investigator with the requirements of the Committee on Human Research for consent forms and may help avoid delay in the review process.

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
COMMITTEE ON HUMAN RESEARCH

INITIAL SHORT-FORM APPLICATION
Submission Date _____

Principal Investigator _____ University _____
(UCSF Faculty) _____ Title _____ Dept. _____
P.I. Mailing Address _____ P.I. _____
(campus if possible) _____ Phone No. _____
Co-Investigator _____ Is the principal investigator _____
and Title _____ the sponsor/advisor only? Yes ___ No ___
Co-P.I. Mailing _____ Co-P.I. _____
Address _____ Phone No. _____
Project _____
Title _____

INSTRUCTIONS: PLEASE TYPE; SUBMIT
-4 COPIES OF THIS TWO-PAGE FORM
-4 COPIES OF ANY ATTACHMENTS (CONSENT FORMS, QUESTIONNAIRES, ETC.)
To be safe, allow at least 4 weeks for processing.

- A) The point of this project is (Explain background, rationale, hypothesis, basic design, etc.):
- B) The subject population(s) will be selected (or excluded) on the following criteria (Discuss how access will be gained as well as any problems relevant to special subject populations):
- C) The following procedures involving humans will be done for purposes of the study (If applicable, include interview themes and questionnaires if not commonly known):

CHR SHORT-FORM APPLICATION

Page 2

Investigator: _____

- D) The risks involved in these procedures and the methods of minimizing the risks, inconveniences, or discomforts are (Include any potential for loss of privacy):
- E) Describe the anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result:
- F) Describe the consent process and attach all consent documents. If waiver from use of written consent is requested, give the justification.
- G) The number of subjects to be enrolled per year: _____ Total for study: _____.
- H) The expedited review category number from Consent Forum, Issue 5, is _____.

CONSENT FORUM

A Newsletter from the:

COMMITTEE ON HUMAN RESEARCH

MAY, 1980 No. 3

UCSF
University of California San Francisco

EDITOR: Erica Heath

CHAIRMAN: James Lindauer, M.D.

CONSENT FORMS FOR RESEARCH AND EXPERIMENTATION

Past issues of CONSENT FORUM have introduced some new elements of consent. This issue will address some of the more common difficulties encountered in writing consent forms, and may help applicants avoid such problems.

Most investigators obtain consent through personal discussion. This is highly recommended, since it allows specific questions to be answered. Consent documents added to oral consent may appear to be an unnecessary and quasi-legal burden. However, there are two quite practical uses for a consent form. (1) It can aid the investigator by providing a checklist of discussion items. (2) It can aid the subject as a memory tool. Should a subject have difficulty recalling any aspect of the discussion, a clear and understandable form, left with the subject, may help clear up the confusion and refresh the memory, and help gain compliance. The latter aspect suggests that a consent form should even engage the subject's interest. How can this be done?

A basic rule is that the text should inform a reasonable person from the proposed population with appropriate language for that population. A form for medical students could be technical, whereas a simpler form would be more appropriate for subjects who may have less formal education, or may be pressed for time. An intelligent prospective subject should not be insulted by a simple consent form which can communicate with a wide segment of the proposed population.

The suggested formats that follow are meant to replace the often stilted samples in our guidelines. The organization is adaptable and should be useful to all disciplines, with appropriate style changes. The elements can be put in narrative, letter or outline form, as desired. Exceptions to this organization are acceptable, provided they meet the goal of clear communication of all elements.

There are special elements required when consent of children and/or their parents or the mentally disabled are involved. These will be covered in future issues. Advice is available in the CHR office for those who need it immediately.

The staff in the CHR office is willing to provide assistance in writing consent forms as time permits. Investigators are encouraged to consult with them when a typed rough draft has been prepared.

GENERAL RULES

- 1) The title should be "Consent to Be a Research Subject."
- 2) The Committee suggests use of the first person, but is willing to accept forms in second person if they are consistent and grammatically correct.
- 3) The date typed should appear in the lower left of each page.
- 4) Legal language is discouraged. There is no reason to use "hereby" (or "hearby!"). "I understand that" is also discouraged.

ELEMENTS OF CONSENT

The following sections are examples of ways to state the required elements of consent.

PURPOSE/INTRODUCTION: What is being studied? Why? Why me? Who are these people? What is going on that is different than normal? This section should set the stage and provide a quick overview.

- A study is being done by D. Jones, M.D. and R. Smith, Ph.D. to learn more about the causes of (condition), the disease I have. They have invited me to be in the study.
- A drug called XX is currently the standard treatment for (disease). It is known that a percentage of people do not respond to XX. An experimental drug called YY is being tested in people who have not responded to XX. Since I have not responded to XX I have been invited to be in the study.

Note: The word "new" now brings to mind "better." "Experimental" is a more descriptive and a fairer word to use for IND drugs.

PROCEDURES: What will happen to me if I participate? This should not include procedures that are part of standard or excellent care. Standard procedures or new procedures that are different from or in addition to standard care must be included. They should be described in terms of subject experience (blood drawing) rather than laboratory tests (CBC, etc.). Procedures affecting selection of care (randomization) or that a subject might wish to know about (contacting of a relative) must be included. It should be complete enough to allow a subject to make plans (babysitting, transportation). Conveying information at this point should decrease lack of compliance.

- If I agree, I will return to the clinic for 10 additional monthly visits of one hour each. At each visit I will have the following tests that are not for my treatment or diagnosis:
- If I agree to participate I will be interviewed for one hour. The questions will concern my background and how I feel about the treatment my family has received in the clinic. This will take place in my home or another agreed-upon place. If I agree, the interview will be tape recorded.
- If I agree to be in the study I will be randomly assigned to one of two groups. This means I will have a 50/50 chance of being in either group. Neither my doctor nor I will make the decision. The two groups are:
 - A. Group A will have the standard treatment total dose but for 6 weeks instead of the usual 3 weeks.
 - B. Group B will have the usual treatment time but at twice the usual dose.

RISKS/DISCOMFORTS: Subjects should be able to gain a fair idea of the risks that they are taking and of the discomforts they might experience as a result of consenting. These include not only physical risks but also potential legal, economic, or psychological risks that are relevant.

A general rule of thumb is that any side effect that is "relatively" frequent or that is "relatively" serious or permanent should be included. Any side effect that a reasonable person would wish to know about (sterility, scarring) should be mentioned.

- This drug may cause an allergic reaction such as skin rashes or hives. It can cause a rare, penicillin-like, allergic reaction that could be life-threatening.
- I may be assigned to a group that is later shown to have more side effects or have less effective treatment. This information will not be known until the study data is analyzed.
- Taking blood from a vein may cause a bruise or, rarely, an infection.
- As a result of answering these questionnaires there is a possible loss of my privacy. The investigators will separate names from responses and will keep names coded and the code locked. My confidentiality will be protected as much as is possible within the law.
- The amount of radiation I will be exposed to is relatively small. Small doses may be potentially harmful but the risk is difficult to determine with any precision. If I have had lots of x-ray exams or if I am or might be pregnant I should not participate in this study.

Do not forget to include the statement on treatment and compensation for harm (CONSENT FORUM, issue 2) if there is any real or foreseeable risk of physical harm. If the study is being done at another center (including VAMC), contact that research office. It might be necessary to include both statements.

- ut in
compensation
section
- If I am physically injured as a result of being in this study, treatment will be available. The costs of such treatment may be covered by the University of Calif. depending on a number of factors. ✓ For information I may call (415) 836-1814.

The university does not normally provide any other form of compensation for injury.

BENEFITS: An unbiased statement should be included. This should discuss personal benefits (ranging from none to some) and may include societal benefits. It should not be overstated or read like an advertisement. This section could become important in considering eligibility for compensation for injury under the University policy described in the second issue.

- There will be no direct benefit to me from participating. The investigators hope to learn more about x and y which may help treat patients like me more effectively in the future.
- The additional tests I will have done are not needed for my treatment or my diagnosis. The information will be put in my medical record and could be of interest to my personal physician.

Note: Money paid to subjects is not to be considered a benefit.

ALTERNATIVES: This section should describe the options open in lieu of participation. If the only alternative is simple refusal (to throw away a questionnaire) this section may be omitted.

-- Instead of having my treatment chosen by the study, I may ask my own doctor to make the decision. The treatments available to him/her are drugs A or B but not C.

QUESTIONS: Few subjects are able to comprehend the details immediately and may have questions later. It is important to offer a way to find an investigator for discussion. If there is a possibility of late effects, offer a 24 hour number.

-- I have talked with --- about this study and have had my questions answered. If I have other questions I may call him/her at ----.

COMPENSATION

An earlier issue described a paragraph about contacting the CHR. It is redundant if the Experimental Subject's Bill of Rights is to be used as it must in medical experiments.

FINANCIAL CONSIDERATIONS - (eg. what is or is not paid for)

PAYMENT: Money is offered to pay for expenses, time, trouble and inconvenience. It is not for inducing people to assume any risk.

-- I will be paid \$10.00 for each visit plus an added \$5.00 whenever blood is drawn. Since there are five visits and three blood drawings the total is \$65.00. I will also receive another \$15.00 for completing all the visits.

RIGHTS:

-- I have received a copy of this consent form and a copy of the Experimental Subject's Bill of Rights to keep.

-- Participation in research is voluntary. I have the right to refuse to participate and the right to withdraw later without any jeopardy to my treatment at the medical center (my grades, my employment, etc). I just have to say so.

NOTE: There are many ways to express each of the above elements. Remember that simplicity, brevity, completeness, accuracy and fairness are the goals.

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
San Francisco General Hospital
CONSENT TO BE A RESEARCH SUBJECT

A Study of Diethyldithiocarbamate (DTC) in Patients with AIDS and AIDS Related Conditions (ARC)

- I. PURPOSE AND BACKGROUND: I have AIDS or an AIDS Related Condition (ARC), which means that my immune system is impaired and I am more susceptible to serious and/or life threatening infections than I would be if I had a normal immune system. Dr. Abrams, Dr. Gorter and other associates at Ward 86 are conducting a study of a drug called DTC, which has been shown to improve immune function in laboratory animals, cancer patients, and some ARC and AIDS patients. I have been invited to participate in this experimental research program which will more conclusively study the immune restoration effects on patients with ARC and AIDS.
- II. PROCEDURES: If I agree to participate in this study, I will have some standard lab tests. A positive result on the AIDS antibody test and impaired immune function based on other tests must be demonstrated before I can be officially entered into the study. If I am eligible for this study, I will be randomized (assigned by chance) to one of two oral treatment groups: DTC or placebo. A placebo pill is a substance that contains no active drug. I will take one or more DTC or placebo pills once a week for up to six months. I must come to clinic every two weeks to get my pills. I will take one dose in clinic and take the following weeks dose home to take a week later. This is a "double-blind" study; neither I nor my physician will know whether I am on DTC or placebo. However, in the unlikely event that I experience a severe reaction, my doctor(s) will be able to find out which treatment group I am in so they can provide the best possible medical care. I may still participate in this study if I have AIDS and am on AZT once it has been licensed. However, I will not be able to start AZT (licensed) once I begin this study, but may go on AZT, if it is appropriate, after I complete this study.

I should not drink any alcohol around the time I take DTC/placebo because of a possible severe reaction from combining alcohol with DTC. (See Risks section).

During the course of this study, I must come to clinic every four weeks for a physical exam and standard lab tests. I will have immune function tests every eight weeks. Altogether 5-15 tablespoons of blood will be taken each time - less than would be taken if I were to donate my blood once. Physical exam and immune function tests will be repeated at one and three months after therapy has finished. Treatment may be discontinued or modified depending on my response and/or any severe reactions to DTC/placebo. If I am an ARC patient and progress to AIDS while

on study, participation in the protocol will be discontinued, but other treatment, if available, will be offered to me. If I have AIDS now and develop an opportunistic infection or progressive Kaposi's sarcoma while on study, participation will be discontinued and other treatment may be offered.

- III. RISKS AND SIDE EFFECTS: DTC usually does not produce any side effects. However, burning chest pain may occur, but this will decrease with a lower dose of DTC. Nausea, vomiting, and behavior changes have been observed in laboratory animals receiving very high doses - higher than will be given in this study. DTC is related to a drug given to alcoholics, Antabuse, and can cause nausea and vomiting when alcohol is taken. Therefore I should not drink alcohol from 12 hours before to 48 hours after my weekly DTC/placebo dose. There may be some other unanticipated adverse reactions associated with DTC because it is still an investigational drug and less is known about it than if it were a standard drug.

There is a risk that I may be assigned to the placebo group and DTC is later proven to be effective in treating AIDS and/or ARC. On the other hand, if I receive DTC and it is later shown to be ineffective, I will have been subjected to potential side effects without benefit.

The risks of drawing blood include mild pain, bruising, or rarely, infection at the needle site.

- IV. BENEFITS: I may obtain some benefit from treatment if I participate in this study, though the primary goal of the study is to learn more about the efficacy and safety of DTC in treating AIDS and ARC patients. Future patients may benefit from the knowledge gained from this study.
- V. COMPENSATION: If I am injured as a result of participation in this study, treatment will be available. The cost of such treatment may be covered by the University of California depending on a number of factors. The University does not normally provide any other form of compensation for injury. For more information, I may call (415) 476-1814.
- VI. FINANCIAL CONSIDERATION: There is no monetary reimbursement for my participation in this study, but DTC/placebo and all clinic visits and lab tests will be free of charge to me.
- VII. CONFIDENTIALITY: My records will be kept as confidential as is possible within the law. Representatives from the Merieux Institute (the study sponsor), the Food and Drug Administration, and authorized study managers and researchers from San Francisco General Hospital (Drs. Abrams and Gorter, coordinator Deborah Hahn, protocol manager Lilian Kaufman, and lab manager Dale Hirschhorn) may have access to my records for data collection and to monitor the study. The data from the study, including my

case data, will be shared with other researchers or institutions, but no names will be given out.

VIII. ALTERNATIVES: If I choose not to participate in this study, it will have no effect on my continued care at San Francisco General Hospital. I may participate in other treatment protocols or be followed as I have been until this time.

IX. QUESTIONS: I have talked with Dr. Abrams, Dr. Gorter or _____ about this study and my questions have been answered. If I have any other questions, I can call (415) 821-5531 or 821-8830.

X. CONSENT: In consenting to participate in this study, I am also consenting to having my blood tested for the AIDS virus antibody.

Participation in this study is entirely voluntary. Refusal to participate will involve no penalty or loss of benefits to which I would otherwise be entitled. I will be kept aware of significant developments arising from this study which may affect my participation. I may withdraw from the study at any time. This will in no way prejudice my future care. This study may be terminated by the investigator at any time s/he determines it is in my best interests. I have read and had explained to me all details of my participation in this study. I have been offered a copy of this consent form and the experimental subject's Bill of Rights. If I wish to participate, I should sign this form.

Signature of Subject

Date

Print Subject's Name

Date

Signature of Investigator (optional)

Date

Signature of Witness (optional)

Date

1/13/87

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

The rights below are the rights of every person who is asked to be in a research study. As an experimental subject I have the following rights:

- 1) To be told what the study is trying to find out,
- 2) To be told what will happen to me and whether any of the procedures, drugs, or devices is different from what would be used in standard practice,
- 3) To be told about the frequent and/or important risks, side effects or discomforts of the things that will happen to me for research purposes,
- 4) To be told if I can expect any benefit from participating, and, if so, what the benefit might be,
- 5) To be told the other choices I have and how they may be better or worse than being in the study,
- 6) To be allowed to ask any questions concerning the study both before agreeing to be involved and during the course of the study,
- 7) To be told what sort of medical treatment is available if any complications arise,
- 8) To refuse to participate at all or to change my mind about participation after the study is started. This decision will not affect my right to receive the care I would receive if I were not in the study.
- 9) To receive a copy of the signed and dated consent form,
- 10) To be free of pressure when considering whether I wish to agree to be in the study.



If I have other questions I should ask the researcher or the research assistant. In addition, I may contact the Committee on Human Research, which is concerned with protection of volunteers in research projects. I may reach the committee office by calling: (415) 476-1814 from 8:00 AM to 5:00 PM, Monday to Friday, or by writing to the Committee on Human Research, University of California, San Francisco, CA 94143.

Call X1814 for information on translations.

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SCHOOL OF MEDICINE

Please address reply to the undersigned at:

THE MEDICAL SERVICE

Room 5 H 22

San Francisco General Hospital

1001 Potrero Avenue

San Francisco, California 94110

TO: Members, Mayor Dianne Feinstein's Task Force on AIDS

FROM: Merle A. Sande, M.D.

RE: Next meeting

DATE: 5 March 1987

During our meeting with Mayor Feinstein this week, a number of issues that need to be addressed by the task force as a whole were raised and discussed. I am therefore scheduling a meeting of the task force Monday, 16 March at 5:10pm (Room 5K8, San Francisco General Hospital) and requesting that each of you make every possible effort to attend. The meeting will probably last about two hours. Please call Rebecca (821-8317) if you will not be able to attend.

Thanks very much.

MAS/rab-f

March 4, 1987

Dr. Paul A. Volberding
SFGH Ward 84

Dear Dr. Volberding:

I want to let you know how much we all at UCSF appreciate your willingness to be called on to help with campus referrals. Your assistance in facilitating special cases is very important to furthering the goals of the campus.

Pat and I would like to extend our thanks to you and the others on whom we similarly rely by having you join us for luncheon on March 31 at the Chancellor's Residence at 12 noon. Please call Robin McCartney in my office at 6-2401 to let us know whether or not you can join us.

Best regards.

Sincerely yours,


Julius R. Krevans, M.D.
Chancellor

JRK:mm-s

P.S. We suggest you take the shuttle bus which departs from the entrance of LPPI at 11:55 and 12:05.

April 21, 1987

TO: ✓ Paul Volberding
David Werdegart
George Rutherford
Jeff Amory
Ted Benjamin
Tom Hall
Merv Silverman
Pat Franks
Cliff Morrison

FROM: Phil Lee

I talked with Sam Matheny, Health Resources and Services Administration, regarding HRSA's early thinking about needs for FY 1989. David Sundwall will be attending a critical executive committee meeting for the AIDS task force in approximately two weeks. I would appreciate any information that we can provide that would be helpful with respect to: (1) the impact of AZT on costs and what the Public Health Service should do to fund the cost of AZT treatment, particularly the cost of the drug; (2) the need for post-hospital care, including subacute, skilled nursing, hospice, home health and other in-home services, as well as psychosocial support services; (3) what would be the value of a Medicaid waiver; (4) what kind of incentives the Public Health Service could provide to create a sufficient number of skilled nursing beds and subacute beds to meet the needs by the year 1991; and (5) what the cost of an adequate post-hospital care delivery system will be and what its configuration should be.

Sam visited Seattle-King County recently and was very impressed with what they've done in analyzing current patterns of use for long-term care and in developing mathematical projections based on patterns of use. Based on a study done by Jane Crigler, M.S.W. (consultant to the Seattle-King County Department of Public Health), they estimate one long-term care bed will be needed for every 70 AIDS patients. They've thus estimated 22 beds for 500 persons with AIDS. I told them that San Francisco was estimating a need of 200 to 300 skilled nursing or subacute beds in 1991, and that we were considering use of the Public Health Service Hospital to meet those needs.

Our very rough estimates are similar to the more sophisticated mathematical projections made in Seattle. We do need, however, to provide more factual information to Sam if we possibly can do so. It would be very helpful if we could also contact the people in Seattle regarding their methodology; Sam suggested we talk to the director of the Seattle-King County project funded by the Robert Wood Johnson Foundation AIDS Health Services Program.

April 20, 1987

TO: Fellowship Committee Members

FR: Philip C. Hopewell, M.D. *PC*

RE: Michael Clement, M.D.

Enclosed are the application and letters of reference for Michael Clement. I've talked to several of you about him. He is currently a staff physician at San Francisco General Hospital and has an appointment as an instructor. He is responsible mainly for the AIDS inpatient service and for liaison with the AIDS clinic. Michael would like to be trained in pulmonary diseases rather than being strictly an AIDS-ologist and professes a commitment to an academic career. He would like to do 12 months of clinical training over a 24 month period. For the other 6 months each year he would continue in his present clinical job. Both Merle Sande and Paul Volberding have indicated their willingness to continue to pay Michael his current salary, thus our taking him would entail no financial commitment. We could fit him into the schedule as we see fit, although he would like not to be included for the first 4 months.

We can discuss this at the meeting on April 29, and if we agree, we can ask the whole group for their concurrence.

PCH:d1

cc: Merle Sande, MD

Paul Volberding, MD