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CONTENTS

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Staff Meeting Report

A Mechanism For The Effect of A Tranquilizing Drug on Learned Emotional Responses*†

Gordon T. Heistad, Ph.D.‡
Aurelio A. Torres, Ph.D.§

The rapid increase in clinical use of ataractic or "tranquilizing" drugs within recent years has not been paralleled by a proportionate increase in our understanding of the mechanisms by which these compounds influence behavior. The search for mechanisms of action for these drugs has centered primarily upon attempts to locate the brain structures that are excited or inhibited by them, or to identify the enzyme system or other biochemical locus of action. The present study departs from that tradition in attempting to identify the psychological, rather than neurophysiological or biochemical, mechanism by which an ataractic drug influences emotional behavior.

In a recent article[1] one of us (G.H.) has proposed a very simple mechanism by which drugs can influence emotional behavior within the context of well-established principles of behavior theory. Behavioral science rests firmly on the basic assumption that behavior does not occur in a chance or random fashion, but consists of responses to stimulation. A few simple stimulus-response relationships appear to be innately determined (e.g., spinal reflexes), but the vast majority of complex behavior consists of functional relationships between stimuli and responses that have been acquired or modified by the process of learning. In the process of learning, *every* aspect of the environment that is systematically associated with a response may become a part of the total stimulus complex that acquires the capacity to elicit that response on subsequent occasions. Thus, a specific change in the environment, such as the onset of a tone, may be functionally associated, by appropriate training procedures, with a specific response, such as salivation. After such learning has occurred, however,

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‡Assistant Professor, Division of Clinical Psychology
§Postdoctoral Research Fellow, National Institutes of Mental Health

the experimentor quickly finds that many aspects of the environment in addition to the tone have become part of the stimulus for salivation. A change in pitch or intensity of the tone, a change in general noise level or illumination, the presence of different experimenters, or the use of a different laboratory will all interfere to some extent with performance of this learned response. In other words, the response had become associated with all these aspects of the environment, and perhaps many more, and any change in this total stimulus complex will interfere with performance of the learned response.

In the case of emotional learning, specific emotional responses such as fighting, running away, or becoming immobile may all become functionally associated with a wide variety of stimuli in the external environment. For example, if an animal is repeatedly given a painful shock following a clicking noise, that animal will soon learn to run away when the clicker is present, or if escape is impossible, he may develop a characteristic crouching or "freezing" posture. But the onset of a clicker that has been repeatedly paired with a painful event will also elicit complex changes in the *internal* environment of the organism. This change in state of the internal environment is part of the total environmental conditions which are regularly associated with the overt emotional response; thus it has ample opportunity to become an important part of the stimulus necessary to elicit that overt response on subsequent occasions. Since the physiologic changes that accompany emotional states are mediated primarily via the autonomic, endocrine, and extrapyramidal systems, the state of function of these three systems may reasonably be expected to contribute significant stimulus properties for any behavior that is learned under conditions of emotion.

If this is true, any treatment procedure that produces a significant change in autonomic, endocrine, or extrapyramidal function would be expected to interfere with retention of emotional responses associated with the internal environmental conditions that had prevailed during the learning process. Insofar as this view is correct, such treatments would not interfere with an emotional habit (defined as a stimulus-response relationship) but rather they would bring about new (internal) stimulus conditions and thus would reduce the strength of whatever emotional responses had been associated with the old conditions of internal stimulation antedating treatment. By analogy, the effect would be the same as that obtained when an organism which has learned to respond to a specific tone is presented with some different sound to test the strength of the learned response; under these

conditions, the reduction in response strength will be proportional to the amount of change in the stimulus.

Both the clinical literature and the experimental literature on tranquilizing drugs and a variety of other treatments used in psychiatry offer some support to the hypothesis that some of the behavior changes resulting from these treatments may be due to internal stimulus changes. Most, if not all, of the physiologic types of treatment employed in psychiatry have profound effects (usually referred to as "side effects") on autonomic, endocrine, and extrapyramidal function. The *direction* of these effects on the internal environment, however, is by no means the same from treatment to treatment. For example, electroshock, carbon dioxide, and some of the drugs used in psychiatric treatment result in relative sympathetic dominance of the autonomic system, while the rauwolfia alkaloids and phenothiazine derivatives generally produce some degree of parasympathetic dominance. Analysis of the effect of such treatments on endocrine and extrapyramidal function reveal definite changes, but the direction of these changes varies from one form of therapy to another. To the degree that changes in internal stimuli are responsible for the changes in behavior produced by these treatments, the effectiveness of the therapy depends upon the amount of change in these physiological functions; but the direction of change would be relatively unimportant so long as the internal stimulus conditions were made *different* from those which had been associated with the pretreatment behavior patterns.

The effects of substituting new stimulus conditions for the stimuli that prevailed during the emotional learning process might be expected to be similar for both pathologic behavior (psychiatric symptoms) and for normal or adaptive emotional responses. With the increasing use of physiologic treatments in psychiatry, numerous reports in the literature have warned of the danger of precipitating "latent psychoses" when these treatments are applied to patients who are not already psychotic. The frequency of psychotic episodes in tuberculous patients treated with iproniazid and in hypertensive patients treated with reserpine serves to illustrate the possibility of interfering with normal emotional behavior, as well as psychiatric symptoms, by the use of such treatment. Virtually all the somatic treatments employed in psychiatric therapy entail the risk of such adverse effects on normal emotional behavior. Conversely, drugs such as mescaline and lysergic acid diethylamide, which are known primarily for their ability to disrupt normal behavior in nonpsychiatric subjects, have

been reported to produce at least temporary improvement in some psychiatric patients.[2] Similarly, a variety of short-acting drugs that affect the autonomic system—such as atropine, eserine, and the sympathomimetic amines—are said to produce temporary "lucid intervals" in some psychotic paitents but to exert a pathological effect when given to normal subjects.[3]

Perhaps the greatest limitation on the effectiveness of tranquilizing drugs and other somatic treatments employed in psychiatry is the frequency with which symptoms reappear upon discontinuance of the treatment. The temporary character of such relief would be anticipated on the basis of the theory expressed above. For a change in stimulus cannot be expected to weaken the strength of an emotional "habit," defined as a functional relationship between a certain stimulus and a certain response. Rather, the response strength is weakened because the appropriate stimulus conditions are absent during the period when the treatment is effective in changing the internal environment. If and when the original stimulus conditions are reinstated, the original responses can be expected to recur. Thus the temporary nature of symptomatic relief from such treatments, as well as the temporary adverse effects when these treatments are used in nonpsychiatric subjects, is fully consistent with the hypothesis that the behavior changes are mediated by a change in stimulus parameters.

But while the clinical evidence cited above appears to fit with the suggestion that many behavioral effects of tranquilizing drugs and of other somatic treatments may be due to internal stimulus changes, this evidence falls far short of conclusive proof. The hypothesis is more rigorously tested in experimental studies of the effects of such treatments on emotional behavior in laboratory animals. Naturally, great caution must be exercised in attempting to interpret changes in complex human behavior on the basis of evidence derived from studies of restricted samples of animal behavior.

The available evidence from animal experimental studies appears to be fully consistent with the hypothesis discussed above. Thus, electroshock treatment, chlorpromazine, reserpine, and a wide variety of other therapeutic procedures which alter autonomic, endocrine, and/or extrapyramidal function have been observed to be effective in interfering with specific emotional responses that were learned prior to treatment.[4–8] Such treatments differ widely in their physiologic effects, but they all share the common characteristic of changing the internal environment from what it was during the learning of these specific emotional responses.[9–11] Unpublished data from this laboratory indi-

cate, at least in the case of electroconvulsive shock, that when an emotional response is learned under the abnormal conditions of internal environment resulting from the treatment, a change in the internal environment toward normal (i.e., physiologic recovery from the treatments) also results in a loss of the previously learned emotional response. For each of these treatments that has been investigated, the loss of the emotional responses is temporary, and the emotional response returns without additional training as soon as the drug is withdrawn or the physiologic effects of the treatment are reversed through physiologic recovery.[4,8,12,13] A recent study in this laboratory[7] demonstrated that a conditioned emotional response in the rat could be attenuated by either chlorpromazine or electroconvulsive shock treatment, even though these two treatments have roughly opposite physiologic effects, at least on autonomic balance. When, however, an emotional response had already been severely weakened by electroshock, administration of chlorpromazine to counteract the autonomic effects of the electroshock treatment resulted in a significant increase or recovery of the conditioned emotional response.

Further support for this hypothesis can be found in studies of the effects of drugs on extinction of emotional responses. The process of extinction, or "unlearning," requires that the stimuli to which responses have been learned must be presented repeatedly without reinforcement. In the case of emotional behavior, this usually consists of presenting a warning signal without following it by a painful event. But, if the internal environment contributes significant stimulus properties for emotional behavior, presentation of an external warning signal, such as a clicking noise, constitutes only *part* of the total stimulus for the emotional response. Under these conditions, a change in the internal environment would be expected to interfere with the process of extinction, since the necessary conditions for extinction (nonreinforced presentations of the conditioned stimulus) cannot be entirely fulfilled. Firm evidence exists from animal experimentation that chlorpromazine and tetra-ethyl ammonium interfere with the extinction of emotional responses if the training is carried out without the drugs and extinction trials are given under medication.[13,14]

Most of the experiments cited above were not designed to test the specific hypothesis that the behavioral effects of these treatments were due to changes in internal stimulus conditions. But the study to be reported here in detail *is* part of a systematic program designed to test this hypothesis. The general research design to be followed in this program of behavior research is: (1) to train emotional responses

under several conditions of the internal environment, produced by drugs and other treatments, and (2) to test for retention of this emotional learning under conditions of the internal environment which are either (a) the same as, or (b) different from, the conditions that prevailed during the learning process. If the internal environment contributes significant stimuli for emotional learning, maximum retention of the learned emotional responses will be obtained only when retention test trials are conducted under the same conditions of internal environment as those which prevailed during the learning of those responses. In the specific case of drug-induced changes in the internal environment, a shift either from placebo to drug or from drug to placebo should interfere with retention of the emotional response if that drug changes significant aspects of the stimulus for learned emotional behavior as hypothesized above.

Method

Subjects

Sixty-four male albino rats of the Sprague-Dawley strain, approximately 90 days old at the beginning of the experiment, served as subjects.

Training procedures

The learned emotional behavior investigated in this experiment is the conditioned emotional response ("anxiety") which has been described in detail by Brady and Hunt.[5] The training procedure for the entire program consists of preliminarily training the animals to press a lever for an aperiodic water reward in a modified Skinner box. After a stable rate of lever pressing has been established, a clicking noise is presented to the animals during one three-minute period of their daily 9-minute run in the Skinner box. As soon as the clicking noise is terminated, a painful shock (1.5 m.a. for 0.2 seconds) is delivered to the feet of the animals through a grid floor. After several pairings of clicker and shock, a characteristic conditioned emotional response develops in the animals upon the onset of the clicker. This response consists of a crouching or "freezing" posture, defecation, piloerection, and a depression or complete cessation of lever pressing activity. The strength of this emotional response can be assessed by comparing the rate of lever pressing during the clicker with the lever pressing rate during a preceding nonclicker period.

In the present study, at the end of preliminary lever-pressing training, the experimental animals were divided into four groups matched on the basis of lever pressing rate. All animals in groups I

and II received ten emotional conditioning trials (consisting of a three-minute clicker presentation followed by a brief shock) during each of their daily 9-minute trials in the Skinner box. Seven adaptation trials (no clicker or shock during the 9-minute trial) were interspersed among the emotional conditioning trials. All animals in groups III and IV received ten pseudo-emotional conditioning trials during each of which the clicker was presented for three minutes, but no shock was given, and they likewise received seven adaptation trials.

Drug Treatment

The drug selected for study was thioridazine hydrochloride (TP-21 Sandoz), a phenothiazine derivative with a piperadyl radical on the side chain. It was selected for this study on the basis of demonstrated therapeutic value in a variety of psychiatric disorders with a minimum of sedation and motor impairment.[15,16] The relative absence of sedation and motor impairment was particularly important in our research, since these side effects often produced by other phenothiazines result in such serious interference with the lever pressing of animals during non-emotional periods that measurement of the emotional response becomes extremely difficult.

Groups I and III received their emotional training and pseudo-emotional training, respectively, under 5 mg/Kg thioridazine per day. Groups II and IV received their training under isotonic saline placebo medication. Drug and saline medications were first given three days before the first training trial and were continued throughout the training period. Injections were given intraperitoneally approximately one hour before each training trial.

Test Procedure

Following the last training trial, each of the four groups was divided into two subgroups, matched on the basis of lever pressing during the clicker as compared with an equivalent nonclicker period. Three animals in group I (emotional conditioning under thioridazine) were excluded from the study because they were observed to crouch consistently during the nonclicker as well as during the clicker periods. Half of the remaining animals in each group were then given 5 mg/Kg thioridazine per day, and the other half were given saline injections for three days and again approximately one hour before the trial test. Thus, half of the animals in each group were tested under the same internal conditions (drug or saline) as those that prevailed during the learning process, while the other half were tested under conditions that differed from the learning conditions. The retention test for all

animals consisted of one 9-minute period in the Skinner box with a clicker presented during the second three-minute interval. No shock was administered during the test trial for any animal.

Results

To compare lever pressing during the clicker and during an equal period preceding the clicker, an inflection ratio, similar to that introduced by Hunt *et al.*[17] was used ($IR = \frac{B-A}{A}$, where A equals lever presses during the three minutes before the Clicker, and B equals lever presses during the three minute clicker presentation). Complete cessation of lever pressing during the clicker (strongest emotional response) results in a ratio of −1.00, while a ratio of 0.00 or above indicates no suppression of lever pressing during the clicker and an absence of the emotional response.

At the end of ten training trials, all the remaining animals in group I, which had been given emotional training under thioridazine, had reached an inflection ratio of −1.00; and the average inflection ratio among animals in group II, which had received emotional training under saline, was almost as low (−.97). Both groups III and IV had average inflection ratios above 0.00 and showed no evidence of any emotional learning.

On the retention test trials, 13 out of 14 animals which had received both emotional training and testing under identical conditions of medication (drug-drug or saline-saline) showed complete retention of the emotional response. But all of the 15 animals which had been changed from drug to saline or from saline to drug showed some loss in the strength of the emotional response as indicated by an increase in inflection ratio. The Chi square for this observed difference is 22.6, which is significant beyond the 0.001 level.

Groups III and IV (pseudo-emotional training) were included in the study to determine whether or not a shift from drug to saline or from saline to drug might affect the unconditioned response to the clicking noise and, in this way, simulate a change in emotional behavior. Previous research results with chlorpromazine[7] suggested that this was a very real possibility. However, seven out of 15 animals who were given pseudo-emotional training and testing under identical conditions of medication (drug-drug or saline-saline) showed an increase in inflection ratio (comparable to a reduction in the emotional response), while the remaining eight showed no increase (comparable to complete retention of the emotional response). Among animals which received pseudo-emotional training and testing under different

conditions (saline-drug or drug-saline), nine out of 15 showed an increased inflection ratio, and the remaining six showed a decrease or no change. The Chi square for this difference is 0.13, which does not approach significance. Therefore, the increased lever pressing during the clicker period which resulted from a shift from drug to saline or from saline to drug among emotionally trained animals could not have been due to a change in unconditioned behavior, and it can be described with confidence as a loss of a learned emotional response.

Discussion

The present study provides the clearest evidence to date that internal stimulus conditions associated with drug or saline medication may acquire stimulus properties with respect to learned emotional responses. Administration of a tranquilizing drug (thioridazine hydrochloride) to animals which had learned an emotional response under saline resulted in a loss of the emotional response, as has been shown repeatedly for a number of such drugs. But withdrawal of the tranquilizing drug and substitution of saline medication was equally effective in interfering with an emotional response which had been acquired under conditions of thioridazine medication. While comparable data are not available for other tranquilizing drug or for a variety of somatic treatments employed in psychiatry, both clinical evidence and the results of laboratory studies support the hypothesis that a variety of these treatment procedures may interfere with previously learned emotional behavior by changing significant aspects of the internal stimuli for specific emotional responses.

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Staff Meeting Report

Transoral Intestinal Biopsy Studies of Malabsorption Syndromes and Regional Enteritis*

James B. Carey, Jr., M.D.†

Abnormalities of the intestinal mucosa associated with malabsorption syndromes have been known for more than fifty years. These consist of: edema, widening and shortening of the villi, and increased cellular infiltration of the submucosa.

Thin,[1] in 1890, described inflammatory changes in the small bowel and destruction of villi at autopsy in a patient with sprue. Faber[2] (1904) noted inflammation but no change in the villi in a patient with sprue whose abdominal cavity had been injected with formalin immediately after death. Justi[3] (1913) reported loss of intestinal villi in such a patient but attributed this to postmortem changes.

Bahr[4] made an extensive study of sprue in Ceylon from 1912 to 1914 and found changes in five of seven patients. Bahr's report contains an excellent illustration of a section of ileum showing, "distension of goblet cells, atrophy of the villi, infiltration with inflammatory cells, fibrosis of the submucosa, slight perivascular round cell infiltration, great capillary congestion." Mackie and Fairley[5] (1929) also noted a "withering of the villi" at autopsy in eight sprue patients from Bombay, but after examining fresh material, Fairley[6] reported in 1936 that this change had probably occurred after death.

In 1932, Thaysen[7] published a monograph describing autopsy findings in two patients with sprue in whom formalin had been injected immediately after death. He reviewed the literature and concluded that abnormalities in the small bowel were simply postmorten changes. Thaysen's monograph almost sounded the death knell on any further investigation into the question of pathologic changes of the small bowel in malabsorption states.

Meanwhile, chemical laboratory studies began to dominate investigations of malabsorption syndromes. Tests of enzyme activities in the digestive juices and tests of the absorption, tolerance, and

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†Assistant Professor, Department of Medicine, University of Minnesota

excretion of carbohydrates and fats became accepted diagnostic methods. In 1947, Suarez and co-workers[8] described clubbing and shortening of the villi at autopsy in eight of sixteen sprue patients. These pathologic descriptions were actually supplied by a pathologist, Koppisch. But the description of the pathology of the small bowel was simply part of a long article on the treatment of sprue with folic acid, and as such, it went largely unnoticed. In the same year, Schein[9] and Adlersberg and Schein[10] reported similar findings in ten patients with malabsorption syndromes. These however, were again autopsy studies, and the influence of agonal and postmortem changes could not be discounted.

Then, in 1954, Paulley[11] convincingly demonstrated the mucosal abnormalities associated with sprue. After critically reviewing Thaysen's monograph, Paulley had announced in 1949[12] that he believed Thaysen's conclusions were not well supported by the evidence. In the ensuing five years he managed to witness laparotomies on four patients with malabsorption syndromes and to secure fresh biopsy specimens of the small bowel. Photomicrographs in Paulley's report of 1954 clearly show blunting and clubbing of the villi, inflammatory changes in the submucosa, and edema; indeed, these photomicrographs are strikingly similar to Bahr's[4] illustration published forty years earlier. Paulley's observations were confirmed by six additional surgical biopsies of the jejunum reported by Butterworth and Perez-Santiago.[13]

But since patients with malabsorption syndromes rarely come to laparotomy, a method was clearly needed for securing small bowel tissue without abdominal surgery. Wood and co-workers[14] devised a tube for suction biopsy of the stomach in 1950, and in 1956 Shiner[15] lengthened the Wood tube, thus making jejunal biopsy possible. Shiner's tube has a hollow metal tip with a hole in its side. A small piece of mucosa is sucked into the hole and cut off with a knife advanced by a pull wire in the tube.

In 1957, Crosby and Hughes[16] described an ingenious stainless steel capsule attached to a long slender plastic tube. This device permits suction biopsy specimens to be obtained from any desired distance along the small bowel. Mucosa is sucked into the capsule, and increased negative pressure in the capsule causes a rubber diaphragm to bulge, releasing a spring-activated knife which severs a small piece of mucosa. Only one specimen can be obtained with the Crosby capsule, whereas multiple specimens may be secured with

the Shiner tube. Brandborg, Rubin, and Quinton[17] have introduced an improved suction biopsy instrument similar to the Shiner tube.

Materials and Methods

A much simplified stainless steel suction biopsy capsule has been developed at the University of Minnesota Hospitals for our intestinal biopsy studies (Fig. 1). Like an ordinary gelatin capsule, it consists of inner and outer concentric shells which telescope shut with suction. The capsule is attached to a fine plastic catheter, and suction is provided by a syringe. When open, holes in each of the shells are superimposed; mucosa is sucked into the holes and is sheared off as the capsule slides shut. A small mercury bag facilitates passage of the capsule through the pylorus and along the small bowel. The capsule is inexpensive and fairly easily made by a good machinist.

Suction biopsy of the small bowel has been a safe procedure in the hands of those who have reported their experience, which collectively now exceeds fourteen hundred cases. The technique of intubation and biopsy with the simplified capsule is easy, but a few essential maneuvers must be strictly observed to assure successful biopsy. Bleeding tendencies must be excluded. Although the patient preferably should have consumed no food for at least three hours before intubation, clear liquids may be taken at any time before or during the procedure. No premedication is required.

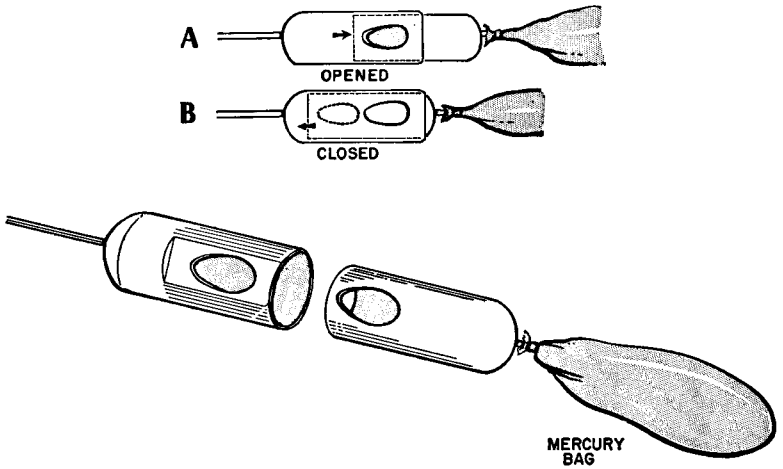

Fig. 1. Simplified suction biopsy capsule

The patient swallows the capsule while sitting upright and bending slightly forward. The capsule with its mercury bag usually descends promptly to the stomach, as indicated by the rapid passage of about 40 cm. of the plastic tube into the mouth. The patient then lies on the left side for about five minutes and then turns to the right side, the hips being elevated slightly with the bed gatch or pillows. The patient remains in this position for 15 to 20 minutes, or at least until passage of 5 to 10 cm. of tube occurs. Then he lies on his back with head and shoulders elevated. This positioning makes maximal use of gravity and of the free-flowing qualities of the mercury bag to pull the capsule through the pylorus and into the jejunum. The patient must be cautioned to avoid obstructing passage of the tube, either by unconscious biting or by letting it catch on bed clothes, under the arm, etc. The position of the capsule in the small bowel can be estimated by measuring the length of tube remaining outside the mouth. The following values for gastrointestinal distances have been established by Blankenhorn and co-workers[18] using fine plastic catheters, metal markers and radiography: nose to pylorus 64 cm., to ligament of Treitz 83 cm., to ileocecal valve 350 cm.

When the capsule has advanced to the desired location, the tube and capsule are flushed with 10 to 20 cc. of saline solution followed by 20 to 30 cc. of air. It is then essential to withdraw the tube 3 to 4 cm. This opens the capsule so that the holes in its sides are superimposed on each other. Suction is then applied with a 50 cc. syringe, and the tube is withdrawn. If multiple biopsy specimens are desired, the suction is released, the tube is pulled back another 3 to 4 cm. to open the capsule, and the process is repeated. In this way, biopsy specimens of the jejunum, stomach, and esophagus have been obtained with a single passage of the tube.

The specimen is removed immediately from the capsule, oriented on a piece of paper, mucosa side up, and put in formalin or other fixative. Inspection with a hand lens will disclose that in the normal specimen the villi have a lush velvety appearance with their conspicuous capillary loops, whereas the villous atrophy accompanying sprue syndrome gives a glistening knobby surface with distorted or absent capillary loops.

Normal Histology

The small bowel mucosa consists of an epithelial membrane supported by a connective tissue framework called the lamina propria.

A thin layer of elastic tissue and smooth muscle fibers forms the muscularis mucosae which separates lamina propria from the submucosa, a layer of loose connective tissue containing blood and lymph vessels and Meissner's plexus of postganglionic sympathetic nerves. It is the looseness of this submucosal layer which permits the mucosa to be lifted free of the outer muscular bowel wall by suction. The mucous membrane of the small bowel is arranged in circular folds called plicae circulares, which, like the villi, are most prominent in the jejunum. The jejunal villi constitute more than half the total thickness of the mucosa. The surface cells of the villi are simple columnar cells having a brush border (microvilli), and goblet cells which secrete a mucus apparently different from that of gastric goblet cells, since the former are stained by mucicarmine but the latter are not.

Beneath the villi are the intestinal glands called crypts of Lieberkuehn, lined with the same type of columnar and goblet cell as cover the villi but containing a special cell which has recently attracted great interest because of its endocrine secretion. Called the Kulchitsky cell, this is a low columnar or triangular cell with a large clear nucleus. Beneath the nucleus are granules containing 5-hydroxytryptamine (serotonin).[19] The granules have the same staining properties as do those in carcinoid tumors. They are strongly eosinophilic and reduce silver salts to metallic silver (argentaffin cells).

A fourth cell type found at the base of the gland is the Paneth cell with its coarse supranuclear eosinophilic granules. The function of the Paneth cell and the nature of the granules remain unknown.

Results

The villous atrophy and other histologic features associated with certain chronic malabsorption syndromes—features which Bahr and Paulley went to such pains to preserve from agonal and postmortem destruction—can now be demonstrated with relative ease in the living patient by means of the suction biopsy technique.

Our biopsy findings in four patients with chronic malabsorption syndromes of the idiopathic type agree with those reported by others.[8,11,13,20] These include shortening and widening of the villi and increased cellular infiltration of the lamina propria and submucosal layers. Alterations in the surface epithelium consist of increased prominence of goblet cells and distortion of the tall columnar cells into cuboidal or triangular shapes with the nucleus no longer at the base of the cell. The hyaline degeneration of the villous tips

described in Schein's[9] postmortem study was not observed in any of our specimens, nor has it been noted in the reports of others. An important aspect of villous atrophy is the reduction in the amount of epithelial surface. Rubin and co-workers[21] have employed a modified Chalkey counting technique, using a micrometer grid to estimate the number of epithelial cells in a given section of mucosa. Butterworth *et al.*[13] have calculated that the absorbing surface of the small bowel in the sprue patient is reduced to one-fourth that of the normal. Other factors, however, besides reduction in the amount of absorbing surface must play an important role in the pathogenesis of sprue.

Rubin[21] and Shiner[22] have shown that the small bowel lesions of celiac disease, adult celiac disease, sprue, and idiopathic steatorrhea are identical histologically, and moreover are not appreciably altered by gluten-free diets, folic acid, B_{12}, cortisol, or antibiotics.

Two patients in our series have exhibited the classic symptoms, signs, and roentgenologic evidence of regional enteritis. Suction biopsy specimens obtained from these patients show very dense cellular infiltration of the lamina propria and submucosa, villous atrophy, an increased number of goblet cells, and the presence of giant cells. These findings agree with the histopathology of regional enteritis described in the detailed review by Van Patter and associates[23] of 600 patients with this disease. Van Patter's more extensive surgical biopsy material, however, reveals that villi may sometimes appear normal except for the increased number of goblet cells. Our specimens also show the presence of Brunner-type glands, which has been reported in about half of the patients with regional enteritis and is apparently associated with a greater likelihood of recurrence following surgery.[24]

Discussion

Chronic malabsorption syndromes constitute a confusing and poorly understood group of clinical disorders. Patients with the sprue syndrome, for example, have unpredictable responses to various therapeutic measures such as folic acid, cortisol, antibiotics, B_{12}, and gluten-free diets. Among the questions that arise are these: Do those who respond favorably have a different disease from those who do not? Are tropical and nontropical sprue simply the same disease occurring in different climates? Perhaps careful studies employing intestinal biopsy will provide insight into these problems. Sufficient material has not yet accumulated to indicate whether or not the intestinal histopathology of chronic malabsorption syndromes is spe-

cific.[25] Additional studies of other chronic intestinal disorders are needed. It is hoped that the advent of suction biopsy of the small bowel will greatly facilitate our understanding of these diseases.

Summary

Historical aspects of the controversy surrounding the intestinal histopathology of malabsorption syndromes have been briefly reviewed.

A newly devised simplified suction biopsy capsule which can pass to any portion of the small bowel and permit removal of multiple biopsy specimens has been described.

The pathology of chronic malabsorption syndromes is described. Patients with such syndromes have abnormal intestinal villi, usually widened and shortened, causing a reduction in the amount of surface epithelium. Cellular infiltration and edema increases in the lamina propria and submucosa. The shape of columnar epithelial cells is distorted, and the uniformly basilar position of the nuclei is lost.

Patients with regional enteritis also have abnormal villous forms. The cellular infiltration of the lamina propria is very dense and there are numerous giant cells. The number of goblet cells in the surface epithelium is greatly increased, and Brunner-type glands can be seen.

Additional studies, especially in other chronic intestinal disorders, are needed before it can be ascertained if intestinal lesions seen in malabsorption syndromes are specific.

The assistance of Mr. Lawrence Espy and Mr. Rudolph Thorness in the construction of the biopsy capsule is gratefully acknowledged.

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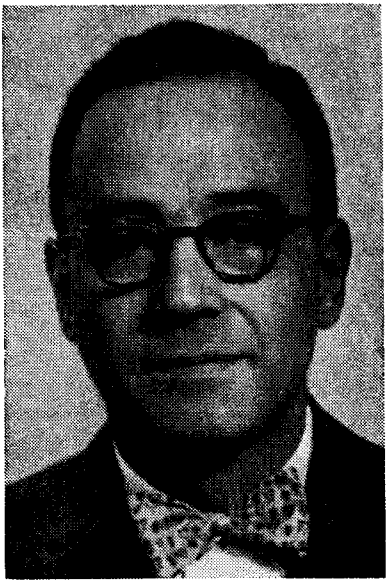
Special Address

The Learned Man*

Irwin H. Kaiser, M.D.†

When it was suggested that I speak to you, it was with the thought that it might be appropriate to say something about the practice of medicine in Sweden, on the basis of personal observation during the sabbatical year the Kaisers lived there. Well, as you know, a year is just about the worst length of time to live in a new country, in a foreign language. Shorter periods of residence abroad allow you to watch what goes on in a strange country much as a spectator watches a prize fight—with a sense of interest but at the same time a sense of detachment. As at a prize fight you don't feel the pain. The short-term tourist can learn a great deal about the places he visits, but he is not involved in their ordinary problems, and he therefore experiences a different spectrum of sensations from those of the resident.



In a year, however, one has enough facility with language to read the daily newspapers with profit and pleasure, to glance at billboards and understand them without translating, to conduct conversations at an elementary level (and at the same time to suffer as he listens to his eight-year-old daughter chatter easily in Swedish with her friends); one knows the bus and trolley net well enough to move about efficiently; one knows how to reserve movie seats by telephone;

*This address was given at the Medical Six-O'Clock Dinner held at the University of Minnesota, Coffman Memorial Union Ballroom on Thursday, May 28, 1959.

†Associate Professor, Department of Obstetrics and Gynecology, University of Minnesota

one knows by the end of the year when to arrive for a dinner party and whether or not the hostess rates a bouquet of flowers. In short, at the end of a year one is about ready to learn; one realizes how little he really understands of the land in which he has been living because of the handicaps his own different cultural background imposes.

The difficulties of an American doctor in Sweden go even further than this. One's associates tend to be medical school people themselves, with therefore a large community of interest which is nonnational, and a facility in English which they are most anxious to polish. If I may digress to illustrate the shattering effect of the Swedes' skill in our native tongue, this incident crushed my ego for weeks. In December, Mrs. Kaiser and I took our small boys to the center of Stockholm to buy them some shoes. We finished the shopping near noon, and by then small stomachs were rumbling audibly. There in Norrmalmstorg was one of the ubiquitous hot-dog merchants who sell their wares either from small kiosks or, as in this instance, from metal hot tables carried over the shoulder on a strap. Confidently I walked up to the vendor and requested: "Få vi har fyra varm korv?" His reply was instantaneous—"Do you want them with ketchup or mustard?"

Despite this language bridge, it is not easy for an American to get to know Swedes of the working or even white-collar class on any basis of real social familiarity. Correspondingly, one does not get to know the ordinary practicing physicians. So I feel ill equipped to say anything more about the practice of medicine in Sweden than what any of you can learn as well as I from the published figures on their almost totally socialized system. My impression is that the quality of medical care is generally very high, that the people in general are satisfied with it, and that most doctors accept the system as being well suited to the needs of their country.

In the course of the year—with my own children in elementary and high school, and with my activities taking me into over-the-teacup conversations with medical students as well as laboratory collaboration with professors, and into student lectures, and the disputation of doctoral theses, and to the Nobelfest and the graduation exercises of Stockholm's högskolan, which includes the medical school—I did have a close look at Swedish medical education, and I wish to describe it briefly to lead to the matter I have really determined to talk about: The Learned Man.

Swedish children begin school at the age of seven, and school is hard work right from the start, with substantial amounts of homework

and drill. At the age of eleven, the children are subjected to a weeding-out process, in which about 40 per cent are sent on to a sort of pre-college high school curriculum, while the others are given four or five more years of a less demanding program. At about age fifteen, this top 40 per cent is again sorted out by examination into an upper group who may go on to the University and a lower group for whom one more year at most is available. It is a matter of much prestige to qualify for this pre-University curriculum, and many hours of study are devoted to preparing for the exams.

There is no college as we know it, and the University includes only what we consider the graduate level of education. By age eighteen or nineteen this program is concluded and the student is ready to tackle the *studentexamen*—a series of oral and written examinations that are standard throughout the country—which qualifies him for admission to the University. If the written exams that are published in the newspapers are any criterion, the standard is higher than that for a baccalaureate in this country. For example, minimal language requirements are a reading and speaking knowledge of English, French, and German as well as Swedish. In addition, the student has had the opportunity in his preparation to specialize in either the classics or science. Successful completion of the examinations is announced at each school as the orals are completed, and every successful student is accorded a public celebration and a parade, ordinarily including a pick-up band of musically inclined friends and relatives. From this point on he is entitled to wear his student cap, a badge of honor which all members of the entourage, regardless of age, who are entitled to do so, wear for the celebrations.

This milestone passed, the student can then apply for admission to the medical school. This course lasts five and one-half to seven years. The first two years are quite similar to ours. The clinical years, however, assimilate the internship into the clerkship, and the students are allowed to spend as much time as they need beyond a certain minimum in any specialties they elect. When they complete all the minimum requirements they can graduate if they wish. At that point they may enter government service as general practitioners, or they can apply at any of the larger hospitals for specialty training. This training is arranged much as it is in this country, with this difference: The man who completes specialty training cannot simply hang out his shingle and go to work. With the exception of a few large cities, there is not enough demand for private practitioners to support specialists. And so the specialists must find a post in the system of government hospi-

tals, each of which has its departmental heads in the several specialties. Appointment to these headships depends on a man's demonstrated qualifications, which generally require the completion of research leading to a doctoral thesis, and the support of the professor under whose aegis the work is done. This generally means that a man stays on at a large hospital, on a small salary, as a sort of senior resident for five to seven years after completing specialty training, before he completes his doctorate. Only then can he hope either for a hospital appointment or for a docentship which then brings him into the even keener competition for the very few professorships.

Now, the Swedes, like most Central Europeans, are very conscious of occupational titles as indices of social status. Indeed, the Stockholm telephone directory is at first a wild confusion for the uninitiated because within alphabetization by last name, subscribers are listed by occupation. This is a big help if you are looking up an Andersson and know that he is an engineer—but if you don't know his occupation you are lost. This classification extends to physicians. The younger men are classified as *läkare*—a word derived from *läka,* to heal, and meaning medical practitioner or physician—or as *medicin licentiat,* the term for those who have fully qualified for the medical degree. They are properly addressed as *Herr*-Mister, although in ordinary social intercourse they are actually called *Doktor.* When a physician has completed the requirements for a doctorate, he then becomes *Medicin doktor,* and the proper form of address is *Doktor* and emphatically not *läkare.* And the docent and professor must always be addressed by these titles, which transcend the doctorate.

In our country and our own society, some of these distinctions of status among doctors exist in actual fact, although the history of the development of medical education in this country, and especially the relationships of medical schools with Universities, are such that the distinctions are blurred, and the words we use to express them are less definite in their meaning than the Swedish words. It is to just these distinctions, however, that I wish to draw your attention.

The doctor is, at one and the same time, three different people. The first of these is of course the *läkare*—the healer, the attendant of the sick and maimed, the physician. In many ways this is the noblest of the three callings. But it must not be disregarded that the physician in this meaning is the descendant of the tribal medicine man, the magician and the barber-surgeon. He is the person who has existed in every gathering of human beings into a society—the person with the practical technical command of what the culture demands by way

of healing arts. If the culture is populated by demons who are the agents of evil, then the healer is the person most skilled in the exorcism of those demons, and he will achieve his cures in a manner understandable to his clientele. The proportion of magic—whose modern counterpart lies in the area of psychiatry, psychosomatics, and that ineffable but essential phenomenon, the doctor-patient relationship—the proportion of magic in the practice of healing depends less on the healer than on the attitudes of the society in which he practices. (It might be mentioned in passing that the not infrequent practice, in the demon-ridden societies, of burying the medicine man with his therapeutic failures has happily been replaced by the malpractice suit. This is certainly no progress in logic, however, and may only reflect a temporary shortage of doctors.)

In more recent times, the practical application of healing was in many instances relegated to the barber-surgeon or his counterpart, the relatively uneducated man with manual skills, in contrast to the thoughtful healer who prescribed drugs only. Indeed, the emergence of the barber-surgeon from his lowly state is in all likelihood related to the growth of our present technical society. Our word "physician" implies the theoretician, the prescriber of remedies, and even today the term is sometimes clarified by the expression "physician and surgeon." The negative aspects, the practical shortcomings of the theoretical healer, have always been clear, and before the physician and the barber-surgeon were united in the modern practitioner, these deficiencies were devastatingly satirized by Molière, just as Sterne, in his portrait of Dr. Slop and his nose-destroying obstetrical forceps, caricatured the technician. The modern physician, product of his times, is envisaged as equipped with the latest antibiotics and hormones, the most recent electric devices, and the best of surgical skills. And by most of his patients he is also credited with all the old magic, the intuitive perceptions with which to use the technical assets to the greatest advantage.

Thus the doctor as healer. The second person a doctor is, in the eye of the general public, is the scientist. Because suitable adjectives to accompany "scientist" are "cold-blooded" or "exact," this role can be perceived only indirectly. The patient does not wish to have himself considered as a statistic, or just another mammal, or to have his problems considered in a wholly impartial manner. The healer assumes that the proper study of mankind is man, while the scientist proclaims that the proper study of man is anything which can be subjected to measurement. There is a real gap here. The wife of one of my col-

leagues on the medical faculty, when asked if her husband was a doctor replied, "No, he's a scientist!" Nevertheless, as Lewis demonstrated by making "Arrowsmith" a household word, and as de Kruif demonstrated with the success of *Microbe Hunters,* the doctor as scientist is a person of great interest and importance, and a career in the laboratory is now solidly established as having a prestige all its own—a type of ascetic renunciation of the pleasures of the flesh which has been admired by weaker mortals since the beginning of time. Motion pictures convey the stereotype—the scientist misses meals, and misses buttons, and misses appointments, but does *not* miss the great discovery from which, however, he gains not one whit of the material things in life. There is even some reality to all this, as a few wives here tonight can testify. But the essential point is that the doctor as scientist has a unique prestige, not only among the laity but also among his fellow doctors. This is a major part of the town-and-gown silliness. The practitioner likes to think of his medical school colleague as someone who has flunked out of practice into the laboratory, where, it may be admitted, he is a success. The scientist likes to think of his practicing colleague as someone without the wit to read a journal, the willing dupe of the detail man and his friendly neighborhood Cadillac dealer. Neither is even slightly correct. By and large in life we end up where we belong, and we do what we enjoy doing, and each of us makes the maximum contribution of which he is capable. The scientist does this also, and it is doubtful that he merits any special encomiums for so doing.

The third person the doctor is, is the teacher. This is after all the original meaning of the word, derived as it is from the Latin verb *docere,* to teach. In a narrow sense, this could be taken to mean that each doctor has the obligation to teach medicine, or the processes involved in healing, both to his patients and to his apprentices. Inevitably, every physician does this, or else he relegates himself to the role of craftsman or mechanic. With the disappearance of the apprenticeship system from medical education, the majority of physicians exert their teaching energies in patient teaching of all kinds—diabetic instruction, natural childbirth classes, the use of a Rutzen bag, and the like. Some few of us have in addition taken on the task of teaching the practice of medicine. But the community insists on more than this from its doctors, possibly because it understands their capacity for teaching better than the doctors themselves do. And so the local doctor is put on the School Board, and on the Boy Scout Troop Committee, and the Church Board. He is depended on for advice and

leadership in *all* the teaching activities of the community. This has led doctors into public office, as far as the Congress in this country. Men who were originally physicians have risen, like Clemenceau to the leadership of France in the First World War, and like Sun Yat Sen to the creation of the first central government of China.

The doctor as teacher is a man of parts. He is accepted as potentially a person of education and learning, of experience and understanding, who is capable of much more than medical practice. True, some doctors, like Arthur Conan Doyle, were never successful practitioners despite great success in other directions. It is perhaps more to the point to mention two American men of letters who succeeded also as doctors. The classic example is, of course, Oliver Wendell Holmes, the magnificent Autocrat, who enshrined himself in the history of obstetrics by a completely accurate description of the cause and prevention of childbed fever at a time when this disease was the major killer of women in the lying-in hospital. A contemporary instance, one of the United States' major living poets, William Carlos Williams, also conducts an active practice in Rutherford, New Jersey.

The physician in this role as teacher has had brushed off on him something of the anti-intellectualism summarized in the absent-minded professor jokes and in the television comedian's version of the professor as a man in a cutaway and pince-nez glasses, who talks, in a rich German accent, a steady stream of complete double-talk. One hears an echo here of the patient's complaint that the doctor never explains anything, and when he does, it's incomprehensible. And yet the doctor to a certain extent must accept the soft impeachment. He is frequently preoccupied, and indeed he does struggle, with what he knows is partial success, to explain in lay terms matters which are simply too technical for such explanation. The busy physician is to a certain extent forgetful, and hence *is* an absent-minded professor. This is what society expects him to be, and with pragmatic good sense, society usually accepts the small liabilities this role endows. It will not accept the physician only as a technician, or only as a scientist, or indeed only as a theoretician. It demands a compound of the three—not in every individual doctor, but certainly in its concept of what doctors should be.

And thus to the conclusion of my sermon. There is at present in medical education in this country and abroad a ferment of changes in medical school curricula. These changes are going on in all directions. One distinguished school has turned its four-year program upside down, to train students simultaneously as family doctors and

laboratory investigators. My own alma mater is about to embark on an accelerated curriculum starting at the third college year, whose outspoken aim is earlier graduation from medical school, an aim based on the dubious premise that all important scientific contributions are made by young men. (The *reductio ad absurdum* of this is clear.) Other schools propose to expand entrance requirements in the liberal arts; still others intend to increase time for independent laboratory investigation by the student.

Perhaps all these projects have some merit. However, I would prefer to hope that the curriculum revisionists will approach their task with at least two basic ideas, both of which might stem from the picture of the doctor I have attempted to draw. This is not to argue that our present curricula cannot produce doctors of the very highest quality. It is however true that present curricula have grown like Topsy and reflect the requirements of medicine of perhaps one or two generations ago. If we are to revise, then let us revise on the basis of fundamental principles.

The first particular idea I would urge therefore is that medical schooling, like the program leading to any doctorate, should last as long as befits the needs of the individual student. It should, as a corollary, include internship within its bounds. The concept of a separate internship, lasting one year and consisting of practical work, is an archaic hangover of the apprenticeship system and is of doubtful merit at present. This loosening of the curriculum will mean a change in clerkship teaching and an expansion of medical school activities into the superior hospitals which presently offer worthwhile internships. Strong trends in this direction already exist.

The other idea I wish to urge is that we accept and teach the medical student as a full-fledged graduate student, from the very start of his medical school career. This will necessitate altering many habits of the faculty and many attitudes of the students. It will thrust on the student more of the responsibility for his education than he now has in many schools—and by the same token it will encourage him to aim at maximal rather than minimal standards of performance. There are again strong trends in this direction. The medical student is after all in the final stages of preparation for his role in society as a doctor—a physician and surgeon, a scientist, and a teacher. He should be dealt with as if this were the case, as if he were what he and we and society expect him to be—a learned man.

Medical School Activities

Student News

The following is a complete list of all of the members of the Senior Class. With each physician's name we have listed the institution in which he will serve his internship.

ALBRECHT, RAYMOND J.
St. Joseph's Hospital
St. Paul, Minnesota

ANDERSON, DALE L.
Bethesda Hospital
St. Paul, Minnesota

ANDERSON, FREEDOLPH D.
San Diego County General Hosp.
San Diego, California

APPELBAUM, BRADLEY E.
Ancker Hospital
St. Paul, Minnesota

ARKO, FRANK R.
St. Luke's Hospital
Duluth, Minnesota

ARLANDER, THOMAS R.
University Hospital
Jackson, Mississippi

AUGHENBAUGH, JOHN W.
Minneapolis General Hospital
Minneapolis, Minnesota

BANOVETZ, JOHN D.
King County Hospital
Seattle, Washington

BENDEL, RICHARD P.
Minneapolis General Hospital
Minneapolis, Minnesota

BERNSTEIN, WILLIAM E.
Cedars of Lebanon Hospital
Los Angeles, California

BERRY, RONALD N.
Bethesda Hospital
St. Paul, Minnesota

BLOOM, PHILLIP
Edward J. Meyer Memorial Hosp.
Buffalo, New York

BLUMENTHALS, AUSMA S.
Charles T. Miller Hospital
St. Paul, Minnesota

BROUSSARD, WILLIAM J.
Letterman Army Hospital
San Francisco, California

CAMPBELL, JOHN B.
Womack Army Hospital
Ft. Bragg, North Carolina

CHRISTENSON, CARL E.
Bethesda Hospital
St. Paul, Minnesota

CORSON, WILFRED A.
King County Hospital
Seattle, Washington

DALE, ROBERT T.
Wayne County General Hospital
Eloise, Michigan

DAVIDSON, ALLAN D.
St. Joseph's Hospital
St. Paul, Minnesota

DAVIS, MICHAEL
U. S. Public Health Serv. Hosp.
San Francisco, California

DEREMEE, RICHARD A.
William Beaumont Army Hosp.
El Paso, Texas

DREDGE, THOMAS E.
Mount Sinai Hospital
Minneapolis, Minnesota

DRILL, DAVID K.
Minneapolis General Hospital
Minneapolis, Minnesota

ECKMAN, PHILIP L.
Denver General Hospital
Denver, Colorado

ELEVITCH, FRANKLIN R.
Mercy Hospital
Toledo, Ohio

EVERS, CARL G.
University Hospital
Jackson, Mississippi

FLORY, SONJA K. M.
Highland-Alameda County Hosp.
Oakland, California

FLORY, WILLIAM D.
Highland-Alameda County Hosp.
Oakland, California

FLUTH, JEROME C.
St. Luke's Hospital
Duluth, Minnesota

FRIEDRICH, BRADFORD E.
Highland-Alameda County Hosp.
Oakland, California

GERDES, ARTHUR J.
King County Hospital
Seattle, Washington

GOLDFARB, BENJIE L.
Univ. of Minnesota Hospitals
Minneapolis, Minnesota

GREENBERG, LAWRENCE M.
Univ. of Minnesota Hospitals
Minneapolis, Minnesota

HAFERMANN, MARK D.
King County Hospital
Seattle, Washington

HALVERSON, KENNETH
Mercy Hospital
Toledo, Ohio

HARNER, RICHARD N.
Ancker Hospital
St. Paul, Minnesota

HENDRICKSON, JOHN M.
Mercy Hospital
Toledo, Ohio

HERBERG, JAMES P.
Gorgas Hospital
Balboa Heights, Canal Zone

HETZLER, JOHN A.
Bethesda Hospital
St. Paul, Minnesota

HIATT, JOHN A.
St. Mary's Hospital
Duluth, Minnesota

HILL, CHARLOTTE W.
Charles T. Miller Hospital
St. Paul, Minnesota

HOIUM, LESLIE H.
Bethesda Hospital
St. Paul, Minnesota

HUBBARD, JACK O.
St. Mary's Hospital
Duluth, Minnesota

JANACEK, JAMES, JR.
Ancker Hospital
St. Paul, Minnesota

JOHNSON, CARL E.
St. Luke's Hospital
San Francisco, California

JOHNSON, FRANKLIN L.
Mercy Hospital
Toledo, Ohio

JOHNSON, THOMAS R.
U. S. Public Health Serv. Hosp.
New Orleans, Louisiana

KANE, MORTON C.
Highland-Alameda County Hosp.
Oakland, California

KELLY, HELEN M.
Ancker Hospital
St. Paul, Minnesota

KIEFFER, STEPHEN A.
Veterans Administration Hosp.
Los Angeles, California

KVAM, LOWELL L.
Bethesda Hospital
St. Paul, Minnesota

LANE, MILES I.
Minneapolis General Hospital
Minneapolis, Minnesota

LARSEN, RUSSELL H.
Denver General Hospital
Denver, Colorado

LEIGHTON, JOHN S.
San Diego County General Hosp.
San Diego, California

LINDELAND, ARTHUR T.
Minneapolis General Hospital
Minneapolis, Minnesota

LITMAN, THOMAS
Health Center Hospital
Pittsburgh, Pennsylvania

LOVRIEN, EVERETT W.
San Diego County General Hosp.
San Diego, California

LOWE, DOUGLASS A.
Univ. of Minnesota Hospitals
Minneapolis, Minnesota

LUNDBORG, RICHARD O.
Tripler Army Hospital
Honolulu, Hawaii

LUNDQUIST, CHARLES B.
St. Joseph's Hospital
St. Paul, Minnesota

MARTELL, CHARLES J.
Southern Pacific General Hosp.
San Francisco, California

MARTINSON, RAYMOND M.
Minneapolis General Hospital
Minneapolis, Minnesota

MARYLAND, DANIEL L.
St. Mary's Hospital
Duluth, Minnesota

MAYER, PAUL D.
St. Mary's Hospital
Minneapolis, Minnesota

McCREARY, CHARLES B.
St. Louis County Hospital
Clayton, Missouri

McGEE, ROBERT C.
Minneapolis General Hospital
Minneapolis, Minnesota

McKINNON, JAMES A.
St. Mary's Hospital
Minneapolis, Minnesota

MELAND, RICHARD A.
Wm. Beaumont Army Hospital
El Paso, Texas

MEYER, MELVIN E.
St. Mary's Hospital
Minneapolis, Minnesota

MUESING, MARK A.
St. Mary's Hospital
Duluth, Minnesota

MULROONEY, THOMAS F.
Minneapolis General Hospital
Minneapolis, Minnesota

NELSON, RODGER K.
U. S. Naval Hospital
St. Albans, New York

NELSON, RONALD J.
King County Hospital
Seattle, Washington

NICHOLS, THOMAS O.
Charles T. Miller Hospital
St. Paul, Minnesota

NIELSEN, DAVID J.
San Joaquin General Hospital
French Camp, California

OLMANSON, VERN C.
Ancker Hospital
St. Paul, Minnesota

ORN, DUANE L.
Mercy Hospital
Toledo, Ohio

OSLUND, RICHARD R.
St. Luke's Hospital
Duluth, Minnesota

PLORDE, JAMES J.
King County Hospital
Seattle, Washington

POWERS, ROBERT L.
St. Joseph's Hospital
St. Paul, Minnesota

PRICKMAN, WILLIAM E.
St. Mary's Hospital
Duluth, Minnesota

PUUMALA, BARBARA J.
St. Luke's Hospital
Duluth, Minnesota

PUUMALA, RICHARD R.
St. Luke's Hospital
Duluth, Minnesota

RATINOV, GERALD
Veterans Administration Hosp.
Los Angeles, California

RILEY, JOHN D.
U. S. Naval Hospital
Oakland, California

RINGHOFER, LAWRENCE R.
U. S. Naval Hospital
Portsmouth, Virginia

ROLLER, FRANKLIN D.
U. S. Public Health Serv. Hosp.
Seattle, Washington

RUSS, HOMER H.
Bethesda Hospital
St. Paul, Minnesota

SADD, MILTON F.
St. Joseph's Hospital
St. Paul, Minnesota

SADOFF, ROBERT L.
Veterans Administration Hosp.
Los Angeles, California

SANTRIZOS, HARRY P.
Detroit Memorial Hospital
Detroit, Michigan

SCHAMBER, DEAN T.
Tripler Army Hospital
Honolulu, Hawaii

SCHMALHORST, WILLIAM R.
Springfield City Hospital
Springfield, Ohio

SELJESKOG, EDWARD L.
Ancker Hospital
St. Paul, Minnesota

SIMSO, LEE A.
Minneapolis General Hospital
Minneapolis, Minnesota

SKAFF, GEORGE
Santa Clara County Hospital
San Jose, California

SMITH, DARLINE, D.
Highland-Alameda County Hosp.
Oakland, California

SPELLACY, WILLIAM N.
Minneapolis General Hospital
Minneapolis, Minnesota

STRAIT, HERBERT S.
Minneapolis General Hospital
Minneapolis, Minnesota

SWALLEN, THOMAS O.
Minneapolis General Hospital
Minneapolis, Minnesota

SWANSON, RICHARD L.
Womack Army Hospital
Ft. Bragg, North Carolina

TELANDER, ROBERT L.
Minneapolis General Hospital
Minneapolis, Minnesota

TESKA, BYRON A.
Minneapolis General Hospital
Minneapolis, Minnesota

THOMPSON, GAIL W.
St. Joseph's Hospital
St. Paul, Minnesota

THOMPSON, JAMES R.
St. Luke's Hospital
Duluth, Minnesota

TOYAMA, ROY
St. Luke's Hospital
Duluth, Minnesota

TUOHY, GERALD F.
U. S. Public Health Serv. Hosp.
New Orleans, Louisiana

WHITE, RICHARD L.
Boston City Hospital
Boston, Massachusetts

WIENS, ALVIN L.
St. Luke's Hospital
Duluth, Minnesota

WILSON, JOHN A., JR.
Minneapolis General Hospital
Minneapolis, Minnesota

WYMORE, ROBERT A.
Mercy Hospital
Toledo, Ohio

YLITALO, ELMER W.
Fitzsimons Army Hospital
Denver, Colorado

ZACHMAN, JOHN F.
St. Joseph's Hospital
St. Paul, Minnesota

Medical School Activities

Faculty News

MR. RAY M. AMBERG, Director of University of Minnesota Hospitals is attending a meeting of the International Hospital Federation in Edinburgh, Scotland. He represents the American Hospital Association of which he is President.

Mrs. Amberg accompanied her husband on the trip, and following the meeting, the Ambergs will travel through Europe, visiting England, Italy, Switzerland, Germany, The Netherlands, and Ireland before returning to Minneapolis in mid-July.

DR. JEROME T. SYVERTON, Professor and Head, Department of Bacteriology and Immunology, was elected the incoming member of the Council of the American Association of Pathologists and Bacteriologists for a seven-year term, 1960-67. Dr. Syverton also presented a lecture entitled "Viruses, Cells and Cancer," at the University of Pittsburgh School of Medicine on May 18, 1959.

DR. HAROLD O. PETERSON, Professor and Head, Department of Radiology, was recently elected to the Board of Trustees of the American Board of Radiology. He represents the American Medical Association's Section of Radiology, and his election to this office was made at the most recent meeting of the A.M.A. in Atlantic City.

IN MEMORIAM

DR. GORDON ERSKINE, '37
Grand Rapids, Minnesota

Faculty Publications

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HINZ, R. W. and SYVERTON, J. T.: Propagation of Influenza Viruses in Monolayer Cultures of Mammalian Cells Dispersed With Collagenase, Bact. Proc. p. 64, May 1959.

HIRSCH, H. M.: Inhibition of Melanogenesis by Tissues and the Control of Intracellular Autoxidations, in *Pigment Cell Biology*, Myron Gordon, Editor, New York, Academic Press, 1959, p. 327.

HOLLAND, J. J. and MCLAREN, L. C.: The Mammalian Cell-Virus Relationship: II. Adsorption, Reception and Eclipse of Poliovirus by HeLa Cells, J. Exp. Med. 109:487, May 1959.

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WEEKLY CONFERENCES OF GENERAL INTEREST

Physicians Welcome

Monday,	9:00 to 10:50 A.M.	OBSTETRICS AND GYNECOLOGY Old Nursery, Station 57 University Hospitals
	12:30 to 1:30 P.M.	PHYSIOLOGY- PHYSIOLOGICAL CHEMISTRY 214 Millard Hall
	4:00 to 6:00 P.M.	ANESTHESIOLOGY Classroom 100 Mayo Memorial
Tuesday,	12:30 to 1:20 P.M.	PATHOLOGY 104 Jackson Hall
Thursday,	11:30 A.M. to 12:30 P.M.	TUMOR Todd Amphitheater University Hospitals
Friday,	7:45 to 9:00 A.M.	PEDIATRICS McQuarrie Pediatric Library, 1450 Mayo Memorial
	8:00 to 10:00 A.M.	NEUROLOGY Station 50, University Hospitals
	9:00 to 10:00 A.M.	MEDICINE Todd Amphitheater University Hospitals
	1:30 to 2.30 P.M.	DERMATOLOGY Eustis Amphitheater University Hospitals
Saturday,	7:45 to 9:00 A.M.	ORTHOPEDICS Powell Hall Amphitheater
	9:15 to 11:30 A.M.	SURGERY Todd Amphitheater University Hospitals

For detailed information concerning all conferences, seminars, and ward rounds at University Hospitals, Ancker Hospital, Minneapolis General Hospitals, and the Minneapolis Veterans Administration Hospital, write to the Editor of the BULLETIN, 1342 Mayo Memorial, University of Minnesota, Minneapolis 14, Minnesota.