SENSORY DEPRIVATION. A NEW DEVELOPMENT IN PSYCHIATRY. By Philip Solomon, Physician-in-chief for Psychiatry, Boston City Hospital, Boston, Massachusetts.

Nine poliomyelitis patients treated in tank-type respirators developed psychotic-like symptoms after having been in the tanks for a few hours to a few days. Clinical evidence ruled out febrile, anoxic, toxic, and metabolic changes as the cause of these symptoms which consisted of well-organized visual, auditory, and somesthetic hallucinations and delusions.

To test the hypothesis that this temporary psychotic state was produced by the conditions of life in a tank respirator where the absolute intensity and meaningful pattern of stimuli were reduced, 17 normal male volunteers were confined in respirators for periods of time up to 36 hours with restrictions on vision, hearing, and touch. All the subjects experienced anxiety, oppression, inability to concentrate, and disorders in time judgment. Six subjects had pseudosomatic delusions, illusions, and hallucinations. The implications of these findings in clinical medicine, “brainwashing,” and experimental production of psychosis by psychological techniques were discussed.

JOHN M. DAVIS
Asian influenza have revealed that, as in the case of most influenza epidemics, the spread is apparently facilitated by cold and damp weather. This may be related either to the degree of aggregation and crowding in the community, thus giving a better opportunity for the virus to spread, or it may be due to lowering of the hosts' resistance by local climatic conditions. In any event, the environmental and climatic factor in the spread of influenza seems to deserve more study.

With regard to the common cold, Dr. Andrews intimated that, from the standpoint of etiology, the term "common cold" is now outmoded, for evidence suggests that there are a variety of "colds" due to a variety of agents. These viruses continue to elude experimental study because of their apparent inability to propagate in any host except man and the chimpanzee. Practically, this confines experiments to human volunteers. In spite of this obvious limitation, much information has been obtained. The most reliable method of transmitting colds is by intranasal instillation of filtered nasal washings from subjects with colds. Interestingly enough, however, experimental transmission by close contact among volunteers is most unreliable.

J. R. PAUL

ZOOLEGY JOURNAL CLUB
April 9, 1958

FREEZING IN INTERTIDAL ANIMALS. By John Kanwisher, Woods Hole Oceanographic Institution.

Intertidal invertebrates and algae are able to live through the winter, even though they may be exposed to temperatures as low as -25° C. Within a few minutes after the tide recedes, the exposed organisms fall to the ambient temperature. Calorimetry on frozen animals indicates that as much as 80 per cent of the water present is frozen at -15° C. The remainder is bound water.

Histological examination revealed that all of the ice is formed extracellularly, causing the cells to become clumped, disoriented, and shrunken from dehydration. But immediately after thawing, the tissues appear normal again, and the animals are alive and active.

Respiratory Q10's were determined by gas analysis: Above 0° C. the Q10 was a normal 2 to 3, whereas below freezing the Q10 ranged from 25 to 50. High internal osmotic pressures, produced by hypertonic medium or desiccation and corresponding in magnitude to those resulting from freezing, depress respiration sufficiently to account for the discrepancy between the Q10's of frozen and unfrozen organisms.

Closely related organisms in different geographical ranges differ widely in their resistance to freezing, according to the temperatures to which they are normally subjected.

F. M. W.
April 16, 1958

Coral Reefs of the West Indian Province. By Norman D. Newell, Curator of Historical Geology and Fossil Invertebrates, American Museum of Natural History, New York, New York.

Reef corals in the West Indian province are represented by far fewer genera and species than the luxuriant Pacific group. Fossil evidence indicates that the two faunae have been discontinuous since the Miocene when the Mediterranean became separated from the Indian Ocean. Coral extended further to the north during the Cretaceous than in later periods. Oligocene forms in the Atlantic were far more diverse than today's, perhaps due to cooling and extinction but more probably caused by the Miocene separation.

Wide platforms ("reef flats") surround many Pacific atolls and islands probably as a result of planation since sea level reached its present height. Deep drilling has revealed that Tertiary reef limestone lies over volcanic rock, supporting Darwin's theory of continual growth during submergence. West Indian corals, however, form as encrustment on narrow submarine terraces which represent drowned shorelines. These drop off precipitously to thousands of feet. There are no broad reef flats as in the Pacific so that the islands are not protected; undercutting is common. Channels are found in noncoraline rock in the West Indies suggesting that similar formations in Pacific living coral are due to physical factors rather than coral growth patterns. Elevated reefs are found 10-15 feet above sea level. Coral types show conspicuous zonation. Branching corals extend down to 30 feet. A massive annularis zone follows. Below this edge, isolated corals stand on pedestals. At 65 feet, all coral growth stops.

The Bahamas lie on a 100-mile-wide sea level shelf extending north to Savannah, Georgia. Seismic studies indicate that this limestone shelf is 2½ miles deep. The shelf sequence, which began forming at the close of the Jurassic, is identical with that in the Florida Keys. Reef formation is restricted to the windward (eastern) sides of islands probably due to sedimentation, but isolated corals can grow on the leeward side without forming reefs. Hydrographic conditions determine the specific makeup of the community.

This evidence suggests the following geological history of West Indian reef formation: In the Mesozoic and Tertiary, a continuous barrier reef formed the continental shelf. This subsided slowly. The northern portion died during the Miocene, however, due to temperature and sedimentation. Corals survived south of Florida into the Pleistocene; no species were extinguished in this refugium. Profound changes in sea level due to glaciation and melting in this period allowed growth only on the highest parts of the shelf. Modern growth resumed only 3-4000 years ago.

G. E. W. 3rd
April 23, 1958

The Chemistry and Physiology of Insect Hormones. By Howard A. Schneiderman, Department of Zoology, Cornell University, Ithaca, New York.

A high level of juvenile hormone secreted by the corpora allata normally blocks metamorphosis in larvae of the Ceropia silkworm until the pupal stage from which the imago emerges. If a pupa is grafted to an adult male abdomen, however, the pupa metamorphoses into a second pupal stage showing some adult characters. As Carroll Williams first showed, a golden oil extracted from the male abdomen with a lipid solvent will produce the same inhibitory results when injected into a pupa. This juvenile hormone has now been partially purified. Various doses give quantitatively different intermediate results ranging from adult to almost pupal cuticle. The activity of the hormone can be bio-assayed on various pupal organs. Antennae show the most sensitive assay. Regenerating tissue is also especially sensitive to hormone administration. A Polyphemus unit is defined as that amount producing a detectable change in 7 of 10 pupae. The hormone must be administered when the pupa is on the brink of developmental change (i.e., metamorphosis) or it will be broken down. A five-gamma dose of concentrated extract of juvenile hormone causes a noticeable change.

The purified hormone is remarkably stable; it is not inactivated by heating for four hours at 140° C, nor by hydrogenation nor mild saponification. The purified extract inhibits complete adult metamorphosis of almost all insects if administered at the right stage.

Juvenile hormone has been extracted from adults of 30 species of Lepidoptera in far greater concentration than from the larval instars; also from unfertilized eggs and diapausing pupae; from beetles; and from beef adrenal cortex. This beef extract mimics in detail the action of the insect hormone. It is rich in steroid material which may be the active principle. This finding suggests that the juvenile hormone itself may be a steroid and that steroid hormones, rather than being a recent innovation of the vertebrates, have a far more ancient lineage.

G. E. W. 3rd

April 30, 1958

Transplantation of Antibody-Producing Cells. By N. Avrion Mitchison, University of Edinburgh, Scotland.

Inbred mouse strains may be used as immunological "test tubes" since tissue culture cells do not retain their normal antibody function after division in vitro. Transplantation experiments have provided information on antibody-producing cell autonomy, localization, multiplication, and reactivity.

Adoptive immunity may be induced in a host mouse by implanting lymph nodes from a mouse of the same strain previously immunized to implanted tumors from a mouse of a different strain. Tumor implants are reacted against far more vigorously than in controls. Such adoptive immunity
may be demonstrated in host mice rendered tolerant to the challenger strain. This evidence indicates that antibodies are produced autonomously by the donor lymphoid implant. Mechanically disaggregated spleen cells from a mouse immunized against Salmonella typhi actively produce antibodies when injected intraperitoneally. Controls receiving only antiserum or killed spleen cells show passive immunity which is progressively lost. Antibody titers in the experimental animals are maximal at five to seven days after injection. They remain high in isologous hosts, but in homologous hosts, decline with about the same half-life as in controls. Thus, in the homologous hosts, implanted cells are killed by host antibodies after one week. In a homologous host which has been previously immunized, the implanted tissue will be killed even sooner. This experiment further confirms the existence of autonomous antibody production by the host implant cells.

Lymph node cells from an immune mouse transferred subcutaneously to a host also produce antibodies autonomously. If the cell nodule is removed after four days, antibody production is impaired, but after ten to twelve days no impairment takes place following removal. Therefore, functionally active donor cells have emigrated from the subcutaneous site.

After host antibody-producing cells are x-irradiated with 500r, antibody titer increases ten-fold when donor spleen is introduced. This suggests that donor cells capable of producing antibodies multiply with genetic continuity. This view is further supported by "cellular memory" experiments. An organism which has stopped previously induced production of antibodies will show higher antibody levels when challenged a second time than controls not previously immunized.

Intravenously injected adult turkey erythrocytes are tolerated by chick embryos but agglutinate in embryonic blood vessels. If leucocytes are thus introduced, however, donor immunological reactions set in as side effects similar to "runt disease" in mice. An enlarged spleen is one symptom of this reaction in pseudochimaeræ. This enlargement is probably due to antibodies from the donor lymphoid tissue coating the chick cells; it may also be due in part to colonization by donor cells which apparently become localized in the homologous tissue of the host.

Experiments of this sort have clinical applications in transplantation of human tissues.

G. E. W. 3RD

YALE MEDICAL SOCIETY

March 10, 1958

Dual Infection of Cells with Measles and Polio Virus. By Magdalena Reissig, Research Associate in Epidemiology and Preventive Medicine, Francis L. Black, Research Associate in Epidemiology and Preventive Medicine and Lecturer in Microbiology, and Joseph L. Melnick, formerly Professor of Epidemiology at Yale University School of Medicine.

As shown by Anderson (1942), and others, two viruses which cause the production in the host of the same intranuclear or cytoplasmic inclusions
are mutually exclusive, but if there is a differential localization of inclusions, double infection is possible. In the present experiments, dual infection of monkey kidney cells in culture was effected and analyzed morphologically.

In the normal kidney cell, the nuclear membrane is indistinct, but a chromatin network is visible. Cells infected by poliomyelitis virus show a more distinct nuclear membrane which gradually becomes considerably wrinkled, and a chromatin network which slowly disappears as eosinophilic inclusions appear in the nucleus. Somewhat later an eosinophilic paranuclear mass is prominent in the cytoplasm of these normal-sized rounded cells. Contrasted with this, measles virus characteristically produces giant cells with a homogeneous eosinophilic cytoplasm, intranuclear inclusions of a larger size than in polio, and causes no wrinkling of the nuclear membrane. Each of the inclusions is surrounded by a “halo” of light-staining chromatin and is itself less eosinophilic than a polio inclusion.

Since the polio virus has a shorter cycle than that of measles, cells were first infected with measles and 4-5 days later with polio. These doubly infected cells, when examined histologically after fixation with Zenker-formol, at once resembled measles—and polio-infected cells, some having an eosinophilic cytoplasmic mass and small inclusions while also containing halo-surrounded inclusions. Polynucleate cells had normal and abnormal nuclei within one plasma membrane. In one instance, five shrunken nuclei, an eosinophilic mass and large intranuclear inclusions were encountered in a single cell. Virus assays carried out at 20, 48, and 72 hours after secondary infection by Type 1 polio virus indicate that polio virus yield in the doubly infected cells is as high as in mono-infected cells. Objections that the 10 per cent of the cells uninfected by measles in the 20-hour group contributed disproportionately to the total yield were overcome by examination of single cells. These were isolated under oil after having been inoculated with polio virus five days after measles infection, incubated for 1½ hours, washed, and suspended in versene. After seven hours at 37° C. to allow for virus particle formation, assays were run and compared with controls and mono-infected material. Giant round cells had as many particles as singly infected cells, some having more than 1,000 particles. Giant flat cells (dead) of equal surface area had 0-20 particles, ruling out adsorption effects. The site of production and precise nature of polio inclusions are unknown, although it is certain they are neither DNA nor RNA. That they are neither the virus nor precursors is proved by their appearance after the completion of virus production in the host.

Morphological evidence thus suggests that double infection is possible, producing intranuclear and cytoplasmic inclusions, at least for measles and poliomyelitis virus, and that the doubly infected cells produce polio virus comparable to that of polio-infected cells alone. Clinical observation of this phenomenon has not been made, since the epidemic seasons for measles and polio differ.

MALCOLM S. MITCHELL
April 14, 1958

A New Look at Pulmonary Pathology. By Jethro Gough, Professor of Pathology, Welsh National School of Medicine, Cardiff, Wales.

The preparation of sections of whole lungs is a technique which facilitates correlation between roentgenological studies and pathological anatomy. Sections are generally cut sagittally, rather than coronally, in order to emphasize the summative aspect of the x-ray shadow. One aspect of lung pathology thus emphasized is that of the lobule. Lobular septa penetrate into the lung and are recognized roentgenographically as Kerley's "B" lines, as for instance when edematous in mitral stenosis. In "honey-comb" lung, new formed fibrous tissue, which is radio-opaque, outlines the lobule, and many pathological varieties of this pattern may be distinguished from each other.

More than half of the cases of large lung emphysema examined show a centrilobular lesion due to destruction of tissue and dilatation of respiratory bronchioles. In uncomplicated asthma, even of long standing, this lesion is never seen.

It is emphasized that this technique furnishes a superb pedagogical tool, applicable not only to lung, but also to bony and porous tissues. Sections are mounted on paper, and it is possible to build up rather extensive tissue libraries with truly minimal demands on space.

N. R. M.

NU Sigma Nu Lecture

April 17, 1958

Historical Considerations in the Treatment of Burns. By Carl A. Moyer, Professor of Surgery, Washington University, St. Louis, Missouri.

There has been a variety of methods of treating body burns over the years including the use of grease, Syme's dry cotton wool binding, carbolized oil, picric acid, aluminum acetate, and tannic acid application, and a host of others. Interestingly enough, the over-all mortality from burns rose from about 17 per cent in 1833 to a peak of 38 per cent in 1903, after which the figures began to decline. The mortality from 25 to 100 per cent body burns in 1903 was 100 per cent, but in 1905 Sneve in St. Paul introduced the "open dressing" method and early grafting along with the administration of saline orally, per rectum, and subcutaneously. In that year the mortality in this 25 to 100 per cent burn group declined to 50 per cent, and even today the figure has only been reduced to 30 per cent.

At this point we have more information available to us. Underhill showed that there is a body loss of water and sodium when burns occur. In addition, it has been found that a decrease in body sodium leads to decreased oxygen utilization and shock, hence the rationale for saline administration. Lesser demonstrated that the red blood cell mass is decreased immediately after a burn. Later evidence showed that heat leads to stasis of flow in capillaries as well as hemolysis of red blood cells. One stumbling block in the past was that people believed that a high hematocrit, due to
hemoconcentration in the case of burns, was incompatible with life, but Moyer and others showed that burn patients could be given whole blood with safety. Thus it seems that in moderate shock saline, in preference to plasma expanders, should be used; and in severe states whole blood should be added to this.

Newer experimental evidence gives us further information. Basal metabolic rates are increased when burns are left open, and this is due to an increased rate of water vaporization and of heat loss. Dressings and early grafting prevent water from going off, lower the BMR to nearly normal, and now we also know that they help to prevent infection. Diet used to be a worry, too, but the author and his coworkers have shown that rats losing 40 per cent of their body weight on a protein-free diet for 80 days healed 20 per cent burns just as quickly as did control rats.

Finally, if we consider the results of treatment, most of the progress has been made in the 25 to 65 per cent burn groups with a mortality of 26 per cent or less. Almost no therapy in the less than 20 per cent burn is as good as anything. The results of treatment of greater than 65 per cent burns have not been appreciably improved. One method of approach would be to prevent the occurrence of burns by improving home engineering and making clothing from nonflammable fabrics such as wool, silk, or pure synthetics. The equivalent of six one-thousand-bed hospital units is required yearly to care for burns, so it would behoove us to think more along these lines.

J. A. O’N.

THIRD ANNUAL LEON E. SAMPLE LECTURE

May 7, 1958

Pancreatitis. By Charles G. Child, III, Professor of Surgery, Tufts University School of Medicine, Boston, Massachusetts.

Pancreatitis is commonly associated with disease of the biliary tract, particularly cholelithiasis. However, as opposed to the usual high incidence of gall bladder disease in obese women, pancreatitis is usually found in thin men over 40 years of age. Other dissimilarities between these entities may be seen in the role of surgery and the use of morphine during the acute attacks, both employed in gall bladder disease but contra-indicated in pancreatitis. Another important correlation is the high incidence of pancreatitis among alcoholics, many of whom are under 40 years of age. Two rare types of pancreatitis have been described, one being a Mendelian inherited trait starting in childhood, the other being found in certain forms of hyperlipemia; neither of these entities has contributed much to our basic knowledge of pancreatitis.

The etiology of pancreatitis is not well understood. Gross and microscopic studies as well as animal and biochemical experimentation have contributed but incompletely to this understanding. The common channel theory proposed that with obstruction at the ampulla of Vater (e.g., by a gallstone) a common channel exists whereby bile flows from the common duct into the pancreatic duct to produce acute pancreatitis. Since its intro-
duction in 1901 by Opie, there have been conflicting reports in support of this theory. More recently, the experimental creation of a common channel without the production of pancreatitis in the goat, the failure to demonstrate a common channel with IV cholangiograms, and physiological studies which indicate that the pressure in the pancreatic duct is equal to or greater than that in the common duct all have tended to discount the validity of the common channel theory. On the other hand, present evidence supports the view that partial obstruction of the pancreatic duct in association with maximal stimulation of pancreatic exocrine secretion is operative in the production of both acute and chronic pancreatitis. The factors which may be responsible for producing partial obstruction of the pancreatic duct include edema, cicatrization, and duodenal wall compression. The latter may explain the failure of sphincterotomy in certain cases.

S. I. H.

PRESENTATION OF THESES OF CLASS OF 1958

May 22, 1958

THE INACTIVATION OF SECRETIN. By J. W. Love.

Greengard, Stein, and Ivy reported in 1941 that secretin is inactivated by serum when the two are incubated together \textit{in vitro}. The inactivation was observed to proceed optimally at 37° C. and at neutral pH with a fall-off in the speed of inactivation as these parameters were varied above or below the optimal values. The degree of inactivation varied directly with the concentration of serum, and serum previously heated at 60° C. for 30 minutes was ineffective for the inactivation. From these observations it was concluded that serum contains an enzyme which inactivates the hormone; Greengard, Stein and Ivy proposed the name secretinase for this substance.

The project began as an attempt to repeat the work of Greengard, Stein, and Ivy using hog secretin obtained from Oxford University, rat serum, and the rat assay for secretin described by Love. Early experiments established that rat serum does inactivate hog secretin when the two are incubated \textit{in vitro}, that serum previously heated at 37° C. for 30 minutes is ineffective for the inactivation, and that the inactivation proceeds optimally at 37° C. This much stood in confirmation of Greengard, Stein, and Ivy. While investigating the effect of varying serum concentration in the system, it was observed that the sera were only weakly effective for inactivating the hormone; the undiluted serum from one rat was totally inactive against secretin. The experimental protocols were reviewed in an attempt to discover some alteration in the experimental conditions which might have accounted for the apparent loss of secretin-inactivating capacity that was being observed.

Only the technique for obtaining serum for incubation purposes had changed. The technique consisted in anesthetizing a rat with ether, and, when the animal was sufficiently deep, opening the anterior chest to obtain blood by direct cardiac puncture. In the earlier experiments the anesthet-
ization of the rats to be exsanguinated was prolonged and awkward due to the inexperience of the author; with practice the anesthetization was accomplished quickly and smoothly with a minimal phase of excitement. To test the possibility that the technique of anesthesia might be related to the secretin-inactivating capacity of the serum, two subsequent rats for exsanguination were anesthetized with deliberate slowness to encourage a long phase of excitement. Significant inactivation of the secretin solution was produced with both sera. The thought occurred that adrenal-cortical activity might be playing a role; the cortices of an exsanguinated rat were extracted with saline and the clear filtrate added to secretin. The astonishing result was an 86 per cent inactivation after three minutes of incubation, total inactivation of the hormone after two hours of incubation. This effect of adrenal cortical extract was verified in subsequent experiments. Extracts of adrenal medulla and skeletal muscle did not appear to inactivate the hormone. No apparent inactivation of the hormone was produced by incubations with cortisone, hydrocortisone, or prednisolone.

Conclusions drawn from these preliminary observations are that secretin derived from hogs can be inactivated by rat serum in vitro at neutral pH and 37° C., but the secretin-inactivating capacity of rat serum is labile and some sera are totally inactive against the hormone; that a saline extract of rat adrenal cortex can regularly, rapidly, and completely inactivate secretin at 37° C.; that the adrenal cortex may produce one or more factors which are responsible for inactivating, or initiating the inactivation of secretin.

**The Mechanism of Hypochloremia in Respiratory Acidosis. By William C. Branscome.**

It has been repeatedly observed that, in animals and man, a decrease in the concentration of plasma chloride and a reciprocal increase in the concentration of plasma bicarbonate characteristically develops following exposure to an increased concentration of inspired carbon dioxide. Acute studies of CO₂ inhalation have heretofore failed to demonstrate losses of chloride in the urine in excess of sodium. It has therefore been suggested by some that the hypochloremia of respiratory acidosis might arise from the transfer of chloride to an intracellular position, particularly a shift into red cells, or from the dilution of the extracellular fluid with sodium bicarbonate. This study was undertaken in an effort to determine whether increased urinary excretion of chloride might continue to the hypochloremia of respiratory acidosis.

Twenty-four male albino rats with average weights of 375 grams were placed in individual metabolism cages and were given Purina lab chow and water *ad lib*. Urine was collected under mineral oil, feces being excluded but not analyzed. The experimental groups were placed in an airtight plastic chamber through which was circulated a mixture of 7½ per cent CO₂ in air or 12 per cent in air for periods of one to four days. All animals were anesthetized with Nembutal immediately following removal from the chamber, the entire exsanguination procedure requiring from four to six minutes.
On exposure to $7\frac{1}{2}$ per cent CO$_2$ serum changes typical of respiratory acidosis were produced, with an elevation of the serum bicarbonate of about 10 mEq./L and a reciprocal and equal depression of serum chloride. The concentration of chloride in red blood cells increased 9 mEq./L, but this shift accounted for only 15 per cent of the chloride lost from the extracellular space. No significant change in extracellular fluid volume was produced. Potassium was lost from the intracellular fluid space but no significant change in the quantity of sodium in the intracellular fluid was observed. During the first 24 hours of exposure, a significant negative balance of chloride was observed, accompanied by an increased renal excretion of potassium and ammonia and a decreased urinary pH. These balances returned to normal by the second day.

A decreased intake of food was noticed in those rats exposed to 12 per cent CO$_2$. The serum changes were similar to those seen in the previous group, with an elevation of the serum bicarbonate of about 15 mEq./L and a depression of the serum chloride of about 15 mEq./L. The chloride shift into red cells accounted for less than 2 per cent of the chloride lost from the extracellular fluid. Extracellular fluid volume decreased 14 per cent, and potassium was lost from the intracellular space. The first day of exposure was marked by a net output of chloride in excess of sodium, a negative balance of potassium, and an almost threefold increase over the normal in the excretion of ammonia. The balances returned to normal by the third day, though ammonia excretion remained high.

Exposure to room air following two days of a 12 per cent CO$_2$ atmosphere produced a return of the electrolyte pattern to normal. There was a significant positive balance of chloride, potassium, and sodium on the first day of exposure to room air, accompanied by a decreased ammonia formation and an increased urinary pH.

These data suggest that renal compensation, characterized by excretion of chloride in association with potassium and ammonium, plays an important role in adjustment to respiratory acidosis in the rat. It may be that there is a tubular mechanism for anion absorption and anion exchange that operates independently of the mechanisms already described for the exchange of cations. If this were the case, inhibition of active chloride reabsorption by CO$_2$ would explain the findings encountered in the present study.