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## Abstracts Of Recent Publications Of The Professional Staff Of The Henry Ford Hospital And The Edsel B. Ford Institute For Medical Research

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ABSTRACTS OF RECENT PUBLICATIONS OF THE PROFESSIONAL  
STAFF OF THE HENRY FORD HOSPITAL AND THE EDESEL B. FORD  
INSTITUTE FOR MEDICAL RESEARCH

TISSUE COENZYME A IN NORMAL AND INDUCED STATES OF GROWTH.  
P. D. BARTLETT, P. GRIMMETT, L. BEERS AND S. SHELAT. *J. Biol. Chem.* 218:419,  
1956.

Results of studies from other laboratories on the pantothenic acid requirement of normal adult and rapidly growing immature rats, as well as studies on the effects of growth hormone in pantothenic acid deficient rats, suggest that either pantothenic acid or its metabolically active form, coenzyme A, might be involved in the mechanism by which growth hormone stimulates the growth process. In this connection we have determined coenzyme A concentration in kidney and liver tissue obtained from rats in both normal and induced states of growth, and also in rats in which the growth process has been arrested either by hypophysectomy of the immature animal or by the attainment of the adult state. Concentrations of liver coenzyme A were found to be significantly lower in both hypophysectomized immature and normal adult rats than in rapidly growing immature normal rats. Induction of nitrogen storage and gain in body weight in the normal adult rat as a result of stimulation with growth hormone was accompanied by a significant elevation in the concentration of liver coenzyme A. Stimulation of the growth process in the hypophysectomized rat with growth hormone, however, failed to significantly alter the level of liver coenzyme A. Concentrations of kidney coenzyme A were not significantly altered in any case. There appears to be a direct relationship between liver coenzyme A concentrations and growth in the normal rat.

RESPIRATORY IRREGULARITIES IN NEWBORN INFANTS. A. R. BAUER AND  
P. J. HOWARD. *Postgrad. Med.* 19:161, 1956.

Study of the respiration of the newborn infant has shown irregularities of rate, rhythm and amplitude. A body plethysmograph has been used in this investigation, and a classification of the types of irregularity is offered. The effect of low and high oxygen respiratory mixtures was studied, and led respectively to depression and stimulation. Carbon dioxide respiratory mixtures were shown to be strong stimulants. Irregularity in phase of expansion and contraction was found between chest and abdomen. Administration of 40 per-cent oxygen in the respiratory mixtures gave practically as much stimulation as higher mixtures. This is becoming a matter of great importance, for evidence is accumulating rapidly to indicate that toxic results of oxygen administration, such as retrolental fibroplasia and pulmonary irritation, occur from concentrations higher than 40 to 50 per cent.

EFFECTS OF B-SITOSTEROL AND FERRIC CHLORIDE ON ACCUMULATION  
OF CHOLESTEROL IN MOUSE LIVER. W. T. BEHER AND W. L. ANTHONY. *Proc.  
Soc. Exper. Biol. & Med.* 90:223, 1955.

Experimental studies were made on the influence of B-sitosterol and ferric chloride on liver cholesterol accumulation in mice fed diets rich in cholesterol. The mice were divided into several groups, each group receiving diets containing varying amounts of

cholic acid, B-sitosterol and ferric chloride. Four groups received increasing amounts of cholic acid: 0, 0.25%, 0.5%, and 1%. Cholesterol assay showed that increasing dietary cholic acid significantly increased total liver cholesterol — 10.6 mg., 36.1 mg., 47.1 mg. and 48.0 mg. per liver respectively. Another three groups received diets with the same proportions of cholic acid supplemented with 2.5% of B-sitosterol. B-sitosterol was effective in preventing the accumulation of total liver cholesterol. Total cholesterol per liver was: 10.6 mg., 30.0 mg., 24.9 mg., and 34.2 mg. respectively. In the third part of this experiment, the effect of ferric chloride on accumulation of liver cholesterol was studied. While the concentrations of cholesterol and cholic acid were maintained constant at 1% and 0.5% respectively, increasing amounts of ferric chloride were added to the diets. The percentages of iron added were: 0, 0.05%, 0.5%, 1.0%, and 2.0%. The assay of liver cholesterol showed no change in total cholesterol content of mouse liver.

ACETYLCHOLINESTERASE ACTIVITY IN THE COCHLEA. J. A. CHURCHILL, H. F. SCHUKNECHT AND R. DORAN. *Laryngoscope* 66:1, 1956.

There is an unique nerve bundle arising from cells near the olivary nucleus which passes across the medulla to end somewhere in the contralateral cochlea. The ending of this tract has not yet been determined, and little of its function is understood. If these nerve endings were cholinergic in nature, they might be located by applying Koelle's method for acetylcholinesterase. Furthermore it was worthwhile to determine whether or not acetylcholinesterase was present in the cochlea. The ultimate problem is to determine whether the enzyme is related to the hair cells, afferent endings of the acoustic nerve, or to terminals of the olivar-cochlear bundle. Should it be related to the afferent structures, support is lent to the hypothesis of Derbyshire and Davis that there exists a chemical mediator of excitation in the cochlea. Koelle's histochemical method involves incubating tissue samples in a solution containing acetylthiocholine and cupric ions. The substrate is hydrolyzed by the enzyme, as acetylcholine would be, and the thiocholine released by hydrolysis is precipitated by the cupric ion as copperthiocholine. Later the location of this compound is visualized by developing the tissues in ammonium sulphide which produces copper sulphide, a black insoluble precipitate. All cochleae treated revealed strong indications of acetylcholinesterase activity near the hair cells in the organ of Corti. Some nerve fibers were also stained.

TIME-DOSE RELATIONSHIPS. LUCILLE A. DuSAULT. *Am. J. Roentgenol.* 75:597, 1956.

The time during which radiation is delivered can effect the response to the dose given. There are three aspects of time to be considered: r/min., or the rate at which each treatment is given, the overall time of the series or the time from the beginning of the first treatment until the end of the last, and the degree of fractionation or spacing of the individual treatments. Within the limits commonly used in radiotherapy the first seems to be unimportant. When treatments are given fairly close together, for example daily, the effect is dependent only on the overall time within wide limits. By proper timing of the individual treatments the effect may be either increased or decreased. Plant and animal experiments on the effect of time are cited, and curves based on clinical results in patients are given for iso-effect lines for different tissues and reactions, showing the relationship between dose and time. It is suggested that further

study of the effect of fractionation might yield information which would result in improvement of therapy techniques by increasing the differential effect between tumor and normal tissue.

**EXTRAIESTINAL ROENTGEN MANIFESTATIONS OF INTESTINAL LIPODYSTROPHY.** W. R. EYLER AND H. P. DOUB. *J. A. M. A.* 160:534, 1956.

Intestinal lipodystrophy is manifested in various gastrointestinal symptoms and in characteristic roentgen findings. The barium pattern in the small intestine is one of mucosal coarseness and flocculation or clumping with discontinuity of the column. In addition, certain extraintestinal manifestations aid in making the diagnosis. These are well illustrated in the four cases described. In each instance, the intestinal manifestations were typical. The extraintestinal manifestations included enlargement of mediastinal, retroperitoneal, or peripheral lymph nodes; narrowing of the hip joints; and arthritic changes in the sacroiliac joints. A widening of the duodenal loop observed in one patient was ascribed to pressure from a mass of enlarged retroperitoneal lymph nodes. Patients in whom the symptoms and intestinal roentgen findings suggest lipodystrophy should have further roentgen studies of the duodenal loop, the chest, and the sacroiliac joints.

**MALIGNANT ARGENTAFFINOMA ASSOCIATED WITH CARDIOVASCULAR ABNORMALITIES.** W. R. EYLER, H. TESLUK AND E. H. DRAKE. *New England J. Med.* 254:555, 1956.

A case of malignant argentaffin tumor with an increase in facial telangiectasia and cyanosis, as well as the development of the murmurs of tricuspid insufficiency and pulmonic stenosis during observation, is presented. Progressive enlargement of the right atrium and ventricle was shown by x-ray study and fluoroscopy. Angiocardiography confirmed the diagnosis of pulmonary stenosis of the valvular type. Cardiac catheterization excluded a shunt and indicated the valvular lesion.

**OCULAR MOVEMENT: I. MECHANICS, PATHOGENESIS AND SURGICAL TREATMENT OF ALTERNATING HYPERTROPIA (Dissociated Vertical Divergence, "Double Hyper") AND SOME RELATED PHENOMENA.** JACK S. GUYTON AND NEIL KIRKMAN. *Am. J. Ophthal.* 41:438, 1956.

Alternating hypertropia, wherein the left eye deviates upward while the right eye is fixating and the right eye deviates upward while the left eye is fixating, has always constituted a puzzling and apparently paradoxical phenomenon. Alternating hypertropia is quite common in cases of squint, and it long has been known to impart a poor prognosis for single binocular vision. Nevertheless, its pathogenesis and physiologic mechanics have remained an enigma, and no surgical treatment has been recommended other than correction of any concurrent horizontal deviation. Proof is offered of two theorems which lead to an explanation of alternating hypertropia. These theorems state, in brief: (1) Fixation of an eye on a target, either binocularly or with either eye separately, demands the fixating positions of the two globes relative to any given postural position of the head must be exactly equivalent in all three rotational components for proper (subjectively equivalent) spatial orientation. That is, not only must the horizontal and vertical rotation components of each eye be such as to point the

visual axes in equivalent directions toward the target, but also the torsional components of rotational position must be such as to place corresponding retinal meridians into equivalent positions. (2) A change in conjugately applied motor stimulation which will move the right eye from an initial position  $R_a$  into position  $R_a+b$  should *not* move the left eye from a different initial position  $L_c$  *exactly* into position  $L_c+b$ . Utilizing extensions of the above two theorems, it is shown that the alternate vertical deviations of alternating hypertropia are merely the vertical components which should be expected, on alternate fixation, from deviations which have qualitatively "committant" torsional components. Subjecting the theory to practical test, surgical correction of underlying torsional deviations effectively stops the alternating vertical deviations. Surgical corrections of this nature, the planning of which is given in detail, appear quite important to the attainment of binocular vision in a large class of squints.

THE ROLLER TUBE TISSUE CULTURE TECHNIQUE IN THE EVALUATION OF THE PRIMARY IRRITANCY PRODUCING CAPACITY OF TOPICAL MEDICAMENTS AND CHEMICALS. F. HU, C. S. LIVINGOOD AND J. HILDEBRAND. *J. Invest. Dermat.* 26:23, 1956.

A laboratory method is described for the determination of the potential irritancy-producing capacity of various medicaments (and certain chemicals) used in the topical treatment of skin diseases. The circumcised foreskin from infants was cultivated with the use of the roller tube tissue culture technique. The culture medium consisted of a plasma-embryonic extract clot and a fluid nutrient of balanced salt solution, embryonic extract and malignant ascitic fluid. Pieces of skin were explanted in the clot on a 12 x 50 mm. No. 1 coverslip which was then placed in a test tube with 2 ml. of nutrient fluid. The tube was stoppered and incubated at 37° C. in a roller drum which rotated at a speed of 12 revolutions per hour. Epithelial outgrowth in sheets usually began to appear in five to six days and continued to increase in size up to three to four weeks. Usually, a sheet of epithelial cells about the diameter of the original explant was obtained evenly around the explant after cultivation for ten to fourteen days. The drugs to be tested were incorporated into the cultures at this time; the time of contact with the epithelial cells was 18 or 42 hours. The toxic effects were determined by comparing the controls and test cultures at the end of the period of exposure. The signs of injury were manifested by changes in cellular characteristics — pyknosis of nuclei, karyorrhexis, and loss of cell outline. In some, after the epithelial sheets were in contact with the drug for 18 or 42 hours, the supernatant which contained the test substance was removed and fresh nutrient was reintroduced. These cultures were kept for another week to determine the capacity of the cultures to recover after exposure to the drugs or chemicals was discontinued.

Drugs tested in this study included various antibiotics, topical anesthetic agents, antihistaminics, and other topical therapeutic medicaments; also certain chemicals were studied. The correlation of results obtained with this tissue culture roller tube technique and clinical experience, including patch tests, seems to be of a sufficient degree of accuracy to justify the conclusion that this method has a place in the preclinical evaluation of new topical medicaments. Also, this approach has a possible application in determining the potential toxicity for skin and mucous membranes of new chemicals used in industry.

STUDIES IN RHEUMATIC FEVER. J. A. JOHNSTON. A. M. A. J. Dis. Child. 91:250, 1956.

1. *Nutrition as a factor conditioning its incidence and course.*

From a 25-year experience with rheumatic fever in the Henry Ford Hospital it is concluded that the ultimate outcome as judged by mortality and the occurrence of carditis is conditioned by the nutritional state of the child in his first attack. Valid statistical correlations were established between the ultimate outcome and (1) the child's position on the Wetzel grid; (2) his past history of diet with particular reference to protein. Inferences of previous deficits in the nitrogen pool were obtained by nitrogen balance studies showing large recovery gains of this substance with flat weight curves.

2. *The experience since the advent of corticotropin and cortisone.*

The end results of treatment of 76 cases since 1949 show a highly significant improvement over those recorded in 270 cases seen before 1949. This cannot be adduced as clear-cut evidence in favor of hormone treatment since (1) we have combined cortisone and salicylates, and (2) there is general agreement that there has been a decline in the severity of the disease. If, however, our basic thesis noted in the first section is correct — namely, that anything influencing favorably the nutritional state has a beneficial effect on outcome — then the studies strongly favor the use of cortisone. With salicylates alone we noted no increase in intake or storage of nitrogen; with cortisone, following initial increases in urinary loss, large gains of nitrogen follow the increased intake commonly seen and the net result in the addition to the body of large increments of nitrogen.

3. *Effect of activity and rest on the nutritional state in rheumatic fever.*

The prolonged inactivity commonly imposed in rheumatic fever carries with it, after the temperature and pulse have become normal, the adverse effects of the metabolism of disuse — failure to retain nitrogen and calcium. It is shown that these can be simply offset by moderate activity not sufficient to cause an elevation of pulse or pulse pressure. Amounts causing these changes were accompanied by a fall in nitrogen storage though a continued rise in calcium retention.

BILATERAL ADOLESCENT MAMMOPATHY AS A PRESENTING SYMPTOM OF RHABDOMYOSARCOMA OF THE HEART. G. MANSON AND W. RINDSKOFF. J. Pediat. 48:202, 1956.

Rhabdomyosarcoma of the heart is a rare pathologic condition. When bilateral tumors of the breast are the presenting complaint of such a condition and this is followed shortly by evidence of widespread bony involvement, a bizarre and puzzling picture results. It was felt that the occurrence of a case combining these unusual features merited reporting. This is the nineteenth case of primary rhabdomyosarcoma of the heart together with autopsy findings. The differential diagnosis of bilateral adolescent breast masses includes: virginal hypertrophy of the breast, benign fibroadenoma, non-indigenous breast lesions (fatty, angiomatous, myomatous, cartilaginous and osseous tumors, dermoids, sweat gland tumors both benign and malignant), extra mammary tumors, metastatic to the breast with a final diagnostic consideration. The reasons for considering this tumor primary in the heart a rare site of origin are enumerated, together with a brief review of the literature.

**STUDIES OF THE ADRENAL HYPERFUNCTION IN 2 PATIENTS WITH ATYPICAL CUSHING'S SYNDROME. R. C. MELLINGER AND R. W. SMITH, JR. J. Clin. Endocrinol. & Metab. 16:350, 1956.**

Case studies of two patients with adrenocortical hyperplasia have been reported. Both patients presented a clinical syndrome of marked atrophy of the bones, muscle and skin without other features commonly observed in Cushing's syndrome. It is postulated that the adrenocortical hyperfunction in these cases was characterized by excessive 17-hydroxycorticoid excretion with either a relative or an absolute decrease in protein-anabolic adrenal steroids. Although the urinary 17-hydroxycorticoid level was elevated in both patients, the metabolic derangement was more clearly demonstrated by the 17-hydroxycorticoid-creatinine ratio (steroid index). Both patients responded to small doses of ACTH with marked increases in 17-hydroxycorticoid excretion. This increased sensitivity of the adrenal cortex is interpreted to mean that endogenous ACTH levels are normal or low in these cases, and that the primary derangement is in the adrenal cortex. In another patient with pituitary basophilism, on the other hand, the adrenocortical hyperfunction was considered secondary to increased ACTH elaboration, and the response to administered ACTH was no greater than normal. Both patients of this report underwent bilateral total adrenalectomy successfully. Adrenocortical hyperplasia was the pathologic finding in both cases.

**\*REMOTE TONGS ADAPTED FOR THE SMALL RADIOISOTOPE LABORATORY. L. PREUSS. Nucleonics 14:79, 1956.**

The alteration of two remote control tongs designed for usage in the small radioactive isotope laboratory is described. The basic mechanism is obtained from two commercially available extension cutters. This custom tong construction is rapid, convenient, and well adapted to the needs and budget of the small laboratory.

**\*VACUUM CRUCIBLE VIEWING METHOD. L. E. PREUSS. Rev. Scientific Inst. 27:61, 1956.**

A conventional 3" x 1" glass slide (for a reflector) is positioned with a grey non-reflecting backing, 4 to 8 cm. from the crucible. The backing may be produced by about 5000 angstroms of chromium condensed on a slide or brass plate. A small space between the slide and this background improves the function of the reflector. The mirrored images of the crucible and charge are sighted in the slide by the unprotected eye at a small incidence angle. A shield may be set up to protect the eye from the direct glare. Depending upon the viewing angle, the reflected image will be of varying intensity and the usual painful glare is eliminated. Varying the thickness of the metal film deposited on the wall of the bell jar may also be an adjunct to the procedure. An appropriate combination of absorber film thickness and viewing angle is chosen for a comfortable intensity to the eye. The technique may be used throughout the evaporation procedure until the slide condenses a heavy metal layer. This may be minimized by placing the glass plate in an area with a low evaporant dispersion rate for the particular crucible used.

\*From Edsel B. Ford Institute for Medical Research.

PHENOXYMETHYL PENICILLIN (Penicillin V) THERAPY OF SUBACUTE BACTERIAL ENDOCARDITIS. E. L. QUINN, J. M. COLVILLE, F. COX, JR. AND J. TRUANT. *J. A. M. A.* 160:931, 1956.

Penicillin V was compared with penicillin G as to the concentrations attained in the blood when the two antibiotics were taken by mouth. In eight normal fasting subjects the average serum concentrations showed that penicillin G was absorbed faster and reached a higher concentration during the first half-hour, but thereafter penicillin V reached concentrations 1.7 to 2.8 times as high as those of penicillin G, and this difference was found consistently at the end of the first, second, third, and fourth hours. Penicillin V also gave higher blood concentrations than did penicillin G when given to four patients orally at four-hour intervals over a period of weeks. Case histories of two patients with bacteremia caused by alpha-hemolytic streptococci illustrated the effectiveness of orally administered penicillin V in bringing about a sustained clinical remission. A third patient, whose bacteremia was caused by *Neisseria sicca*, obtained clinical and bacteriological remission for a course consisting of 2 million units of penicillin V orally every four hours with 0.5 gm. each of streptomycin and dihydrostreptomycin intramuscularly twice daily. In a fourth patient, bacteremia caused by a *Micrococcus pyogenes* was halted but temporarily, and at the time of relapse the organism was found exceptionally resistant to antibiotics.

CELLULAR STRUCTURE, FUNCTION AND RELATIONS IN ANTIBODY FORMING LYMPH NODES. J. W. REBUCK, T. N. HARRIS AND S. HARRIS. *Anat. Rec.* 124:351, 1956.

Abstract of a paper presented at the sixty-ninth annual session of the American Association of Anatomists, Milwaukee, Wis., April 4-6, 1956.

SURGICAL SIGNIFICANCE OF MARJOLIN'S ULCER WITH A REPORT OF THREE CASES. R. J. SCHLOSSER, E. A. KANAR, AND H. N. HARKINS. *Surgery* 39:645, 1956.

Marjolin's ulcer is a cancer arising in a burn scar. About 2.0 per cent of burn scars will develop a squamous-cell and 0.3 per cent, a basal-cell carcinoma. Marjolin's ulcer is seen most commonly in the male despite the greater frequency of burns in young women. In contrast to the site of origin of the ordinary skin cancer, it occurs most frequently on an extremity. Moreover, the age of a burn scar has greater significance in the development of a burn scar cancer than the age of the patient. An old extremity scar of an adult burned as an infant or child will more readily terminate in a Marjolin's ulcer than the scar of burns more recently sustained as an adult. The exception arises only in the elderly patient whose senile skin is more susceptible to carcinogenic influences, such as a burn, than the normal skin of a younger person. Virchow's concept of the irritative origin of scar cancer is briefly discussed in relationship to the etiology of Marjolin's ulcer. Reasons for the suggestion that biopsy of suspicious burn ulcers should include tissue from the base as well as from the margins are given. The treatment of Marjolin's ulcer is biphasic: 1. prophylactic-skin grafting of the burn defect is necessary initially and must be adequate; 2. definitive — the lesion must be widely excised surgically with or without lymph node dissection as indicated.



