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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 EISEL B. FORD
INSTITUTE FOR MEDICAL RESEARCH

TREATMENT OF ADVANCED BREAST CANCER WITH FLUOXYMESTERONE (HALOTESTIN). V. L. BECKETT, and M. J. BRENNAN. *Surg., Gynec. & Obst.* 109:235, 1959.

This report concerns our experience with 23 cases of carcinoma of the breast with metastasis, treated with the oral androgen 9 alpha-fluoro-11 beta-hydroxy-17 alphamethyltestosterone or fluoxymesterone (halotestin). This new oral androgen has been found to be effective in suppressing advanced mammary cancer in postmenopausal patients. Remission occurred in 7 (30 per cent) of our 23 patients—in 2, after hypophysectomy. Fluoxymesterone appears to be less masculinizing than injectable androgens in therapeutic doses. It can cause liver dysfunction such as seen with methyltestosterone.

*BUILD-UP AND REGRESSION OF INHIBITORY EFFECTS OF CHOLIC ACID ON IN VIVO LIVER CHOLESTEROL SYNTHESIS. W. T. BEHER and G. D. BAKER. *Proc. Soc. Exper. Biol. & Med.* 101:214, 1959.

A study of sequence of events during initiation and regression of inhibition of cholesterol synthesis by dietary cholic acid was made in rats. In the initiation study, increases of liver cholesterol and serum bile acid levels paralleled decreases of liver cholesterol-x-C¹⁴ activity. There was a decrease in liver phospholipid during the same time interval. In the regression study, serum bile acid and liver cholesterol returned to control levels more rapidly than the rate of liver cholesterol synthesis. The results suggest that dietary cholic acid initially elevates liver cholesterol, which in turn leads to the inhibition of acetate-1-C¹⁴ incorporation into liver cholesterol.

PLACE OF RADICAL NECK SURGERY IN THYROID CARCINOMA. M. A. BLOCK, J. M. MILLER, and B. E. BRUSH. *A. M. A. Arch. Surg.* 78:706, 1959.

A radical neck dissection should be carried out for patients with operable carcinoma of the thyroid and evidence of metastases to cervical nodes. Approximately 30% of patients with thyroid carcinoma without palpable cervical lymphadenopathy were found to have metastatic carcinoma to the cervical nodes removed by neck dissections at the time of thyroid surgery or at a later date. Evidence of metastases to cervical nodes will appear later in at least 10% of patients with thyroid carcinoma without palpable cervical lymphadenopathy. A modified neck dissection appears to be justified for many patients with carcinoma of the thyroid in the absence of palpable cervical lymphadenopathy. Although the data do not dictate the absolute necessity for this procedure, better results are suggested if it is done. Complete local eradication of thyroid carcinoma is the most important component of the surgical treatment of this disease. This consists of total lobectomy as the minimal procedure, and frequently total thyroidectomy. Long-term experience with thyroid carcinoma indicates the advisability of a more radical surgical approach in the early stages of the disease. This is in accordance with basic concepts of the surgical therapy of malignancy.

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MANAGEMENT OF THE SWOLLEN ARM FOLLOWING MASTECTOMY. B. E. BRUSH, J. H. WYLIE, J. BENINSON, M. A. BLOCK, and T. J. HELDT. *J. Michigan M. Soc.* 58:216, 1959.

Edema of the arm may be successfully treated by means of an appliance to reduce the swelling plus the use of a custom-fitted sleeve when the pump is not in use or no longer needed. The pain, discomfort, and swelling are relieved. The incidence of chills, fever, and localized infection is greatly diminished. Strict adherence to instructions is important and medical supervision of the device is imperative. Swollen arm, a troublesome sequela of radical breast surgery, need not be tolerated.

SUBCORNEAL PUSTULAR DERMATOSIS. R. E. BURNS and G. FINE. *A. M. A. Arch. Dermat.* 80:72, 1959.

Two cases, presenting pustular lesions clinically and histologically similar to the recently described subcorneal pustular dermatosis, are presented. Although there may be a superficial clinical or histologic similarity between it and other bullous and pustular eruptions, we feel histologic examination justifies its separation from the previously described pustular and bullous eruptions.

TREATMENT OF MACRODACTYLISM: A CASE REPORT. R. H. CLIFFORD. *Plast. & Reconstruct. Surg.* 23:245, 1959.

This is a case report of a child with single macrodactyly and treatment which appears to be successful. The plan of operation was to staple the epiphyses of this finger. Very small staples were made by an instrument maker out of stainless steel Kirschner wire. Incisions were made down the lateral side of the finger and all the epiphyseal lines were exposed. Attempts to place these tiny staples across the epiphyseal lines met with failure. The staples were made deliberately small to fit across this area without splitting the articular surface and because they were so small and fragile, it was impossible to drive them into the bone. Since we were unable to staple the epiphysis, it was decided to destroy the epiphysis itself. To do this we used a motorized drill. The drill was inserted directly into the epiphyseal lines and drilled through to the opposite side of the bone. Then, with lateral pressure being applied both on the volar and the dorsal surfaces, the drill cut with its side as does a milling machine, and a slot was cut out of the bone destroying the epiphysis except for a small bony bridge at the dorsal and volar extremities of the slot. The wound was closed in the usual manner and the operative site healed without complications. In the following 3 years it was found that the deformed and treated finger had gained nothing in length, remaining at the 88 mm. originally measured.

COMPARATIVE STUDIES OF OLEANDOMYCIN, TRIACETYLOLEANDOMYCIN, AND ERYTHROMYCIN, WITH A BRIEF REVIEW OF THE LITERATURE CONCERNING OLEANDOMYCIN. J. M. COLVILLE, F. COX, JR., E. L. QUINN. *Antibiotics Annual* 1958-59, p. 401.

The purpose of this report is to review briefly the literature concerning oleandomycin and triacetyloleandomycin; to present certain laboratory data comparing erythromycin with oleandomycin and triacetyloleandomycin, with particular reference to the *in vitro* antibacterial activity of these agents; and, finally, in view of these data, to attempt to evaluate the place of triacetyloleandomycin in the treatment of staphylococ-

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occal infections. The first part of the present study indicated that within our own geographical area, the large majority of staphylococci isolated from patients with active staphylococcal infections were sensitive to both erythromycin and oleandomycin. The majority of these sensitive strains were eightfold more sensitive to erythromycin than to oleandomycin. The second part of the present study consisted of a comparison of triacetyloleandomycin and erythromycin, with reference to serum concentrations, serum antimicrobial activity, 24 hour urinary excretion, and urinary antimicrobial activity by means of crossover studies in healthy adult volunteers. Comparison of serum concentrations following triacetyloleandomycin with published figures of concentrations after a similar dose of oleandomycin base, indicated that the triacetyl salt produced considerably greater concentrations. The comparative study of erythromycin and triacetyloleandomycin indicated that triacetyloleandomycin produced higher serum antibiotic concentrations throughout the experimental period than did erythromycin. However, serum antibacterial activity studies indicated that despite the previously observed superior serum concentration of triacetyloleandomycin, the antibacterial activity of serum after ingestion of this agent was slightly less than that observed after a similar dose of erythromycin. Third, despite its ability to produce higher serum concentrations, triacetyloleandomycin induces serum antibacterial activity which is somewhat less than that produced by an equal dose of erythromycin. On this basis, it would appear that in staphylococcal infections due to organisms sensitive to both antibiotics, erythromycin is the agent of choice.

NEGLECTED HEARING IN CHILDREN. J. L. DILL. JOURNAL-LANCET, 79:357, 1959.

Impaired hearing may be noted at any age. There are two types of hearing loss—the nerve, or perceptive type, and the conductive type. The former may be congenital or acquired. The nerve type of hearing loss cannot be improved. Special education and amplification as indicated should begin at an early age. The conductive type of hearing loss is preventable and should respond to therapy. In the small child, we must differentiate among impaired hearing, mental retardation, language disturbance as a result of a mild brain injury, and psychologic factors. Audiometric tests may be given successfully at 3 years of age; others may be given earlier. The majority of children with a moderate hearing loss can be fitted with hearing aids. In children with a nerve type of deafness, hearing aids should be advised by a competent otologist or audiologist. Practically all children handicapped by a hearing loss can be helped either by medication, surgery, or educational means or by any combination of these measures. The results should be as good as the otologist. His careful examination and tests, his accurate diagnosis, and his therapy should produce satisfactory results.

TUMORS OF THE GLOMUS JUGULARIS; REPORT OF NINE CASES, J. L. DILL. Laryngoscope 69:248, 1959.

A report is made of nine cases of benign tumor arising from the glomus jugulare. The majority (eight) of these tumors were slow growing; however, one patient with cerebellar symptoms had an apparent rapid onset, and a rapid downhill course. The symptoms produced by these tumors depend on the site of origin and their extension. In six patients, the tumor appeared to have its origin in the middle ear;

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two had neurological and aural symptoms develop at approximately the same time, and one patient developed aural symptoms, followed a few years later with neurological symptoms. The age of onset (judged from the history) varied from 18 years of age to 51 years of age. Six patients were female, three were males, a ratio of two females to one male. Five of our patients were white, four were colored. Five patients with symptoms and tumors limited to the middle ear, who received either surgery, X-ray, or a combination of both, are alive with no evidence of recurrence of their tumor. X-ray therapy appeared to be beneficial in our patients but has not eradicated the tumor. Bleeding has not been a serious complication except in two cases. At surgery, removal of a rather extensive growth was attempted and produced excessive bleeding with inability to remove the growth entirely in these two patients. Of nine patients with a tumor of the glomus jugulare, six are alive and well with no evidence of recurrence of their tumor. One patient is alive (has had four pregnancies since onset of her tumor) with no local evidence of recurrence, but there is a suspicion of intracranial extension. One patient died of cerebellar extension. One patient is presumed dead.

BRACHIAL PLEXUS BLOCK FOR HAND SURGERY; EXPERIENCE AT HENRY FORD HOSPITAL—600 CASES. J. W. DITZLER, AND R. H. CLIFFORD, J. Occup. Med. 1:363, 1959.

Careful evaluation of 526 brachial plexus blocks for hand surgery indicated 85% to have been completely satisfactory: less than 1% had pneumothorax. Patient acceptability and anesthetic induction time were not problems. Actual complications were significantly few, but those which did occur were either perplexing as to etiology or distressingly difficult to manage. Subsequent to this study, 130 additional brachial blocks were performed, the criteria for selection being essentially the traumatic industrial admission. This has resulted in far less "alleged" complications. It can be said, therefore, that we have somewhat changed our opinion as to the appropriateness of brachial plexus block for hand surgery; we now consider it the best anesthetic for the emergency admissions, who have usually been unprepared for anesthesia and in whom general anesthesia creates a distinct but often overlooked hazard. This is also true of geriatric patients as well as patients suffering from various disease states, particularly those who are on drug therapy which might produce complications, i.e., cortisone, insulin, rauwolfia, and others. From this survey, we now feel that brachial plexus block anesthesia is reasonably safe and usually efficient, but for the young healthy adult in whom elective surgery of the hand is to be performed the institution of an anesthetic method which in our hands is only 75% to 85% successful on the first administration is not ideal. Ideally, this procedure should be reserved for patients in whom general anesthesia is definitely contraindicated, i.e., patients who have recently eaten, geriatric and debilitated patients, or persons on drug therapy which might be interrupted by or in which general anesthesia is a hazard.

SHOULD SPINAL ANESTHESIA BE USED IN SURGERY FOR HERNIATED INTERVERTEBRAL DISK? J. W. DITZLER, P. R. DUMKE, J. J. HARRINGTON, and J. D. Fox. *Anesth. & Analg.* 38:118, 1959.

Follow-up studies were made on 1062 patients who underwent a total of 766 operations under spinal anesthesia and 333 operations under general anesthesia for

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herniated intervertebral disk. Thirty operations with spinal anesthesia and seven with general anesthesia were repeated operations. Follow-up study has not been less than 2 months in any case, and in most the study covered several years. Seven of the patients who had general anesthesia had adhesive arachnitis at the first operation; the condition progressed to paraplegia in two of them. Three patients who had no pathologic condition at the time of the first operation, had adhesive arachnitis at the time of the second operation. Two others had cauda equina syndrome at the time of the second operation. We wish to emphasize that in each of these patients general anesthesia was used. Cauda equina syndrome, which resulted from Nupercaine and cold sterilized ampules in 1937, developed in one patient who had had spinal anesthesia. Spinal anesthesia given to 10 patients with adhesive arachnoiditis had no adverse effects and, in fact, six of the 10 showed remarkable improvement. Spinal anesthesia is an acceptable method when strict adherence to techniques is exercised. It may be used for surgical treatment of herniated intervertebral disk whenever the anesthetic and surgical requirements indicate that the use of a regional technique is desirable. In our experience, no residual neurologic deficits attributable to spinal anesthesia with Spinocaine or Pontocaine occurred.

LEIOMYOSARCOMA OF THE UTERUS WITH UNUSUAL METASTASES. E. T. DRAKE and G. D. DOBLEN, J. A. M. A. 170:1294, 1959.

It appears possible that recurrence of leiomyosarcoma may develop many years after presumably complete excision of the primary tumor. In this patient, metastases became symptomatic 18 years after total hysterectomy. It is the fifth case reported in the literature of metastases in a long bone and the second with retro-orbital metastases. One kidney was also extensively involved.

SIMPLIFIED METHOD OF TREATMENT PLANNING. L. A. DUSAULT. Radiology 73:85, 1959.

Composite isodose curves for a combination of fields give the most complete information about dose distribution. The length of time consumed in constructing such curves for each plan to be considered in treatment of a patient is, however, prohibitive. Precalculated plans can be made up which can be tested in a minimum of time for applicability to a given patient by laying them over his contour tracing. These are simple to construct, and their accuracy is satisfactory. Residents using them soon acquire an understanding of the effect of field arrangement on dose distribution. Details of the construction of isodose curves are given with several samples of such curves.

IMPORTANCE OF THE LATERAL VIEW IN THE EVALUATION OF LEFT VENTRICULAR ENLARGEMENT IN RHEUMATIC HEART DISEASE. W. R. EYLER, D. L. WAYNE, AND J. R. RHODENBAUGH. Radiology 73:56, 1959.

In patients with rheumatic lesions of the mitral valve, the detection of left ventricular enlargement in the lateral view has been the most reliable single roentgen indication of the presence of mitral insufficiency or of an aortic valve lesion. All four views as well as fluoroscopy should be used. The ratio of the length of the segment of the heart which intersects the left leaf of the diaphragm to the internal diameter of the chest has been determined on a lateral view of the chest. Those cases

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with a ratio of 0.42 or less have usually not had enlargement of the left ventricle. In those with a ratio above 0.42 the left ventricle has usually been enlarged. When the left ventricle was enlarged, it has in most cases projected behind the shadow of the inferior vena cava for a distance of 15 mm. or more. Patients with a giant left atrium or deformity of the left hemidiaphragm cannot be evaluated by this method. All roentgen signs must be combined; when the roentgen information agrees with the clinical, further study such as left heart catheterization is not required.

STAINING OF FRESH, UNDECALCIFIED, THIN BONE SECTIONS. H. M. FROST. *Stain Technol.* 34:135, 1959.

Fresh, undecalcified bone sections can be reproducibly and reliably stained by any of the following procedures: (A) Basic fuchsin, 1% in 30% alcohol, 48 hr, 22°C. (B) AgNO₃, 0.033 M, 48 hr, 22°C.; washing 48 hr in a large volume of distilled water; exposure to light to develop the color. (C) Metallic sulfides (Co⁺⁺, Pb⁺⁺, Hg⁺⁺, Cu⁺⁺): the nitrate of the metal, 0.033 M, 48 hr, 22°C; then Na₂S, 0.033 M, 48 hr, 22°C. (D) Alizarin Red S, 0.1% solution in distilled water, 48 hr, 22°C; differentiated 48 hr at 22°C in weakly alkaline water, pH about 8. (E) KMnO₄: boiling 8-10 min. in a 0.1 N solution. With the exception of D the surface stain must be ground off the section for microscopic examination of its interior. Stain concentration, time and temperature can be altered to suit specific needs.

STOKES-ADAMS ATTACKS COMPLICATING ACUTE MYOCARDIAL INFARCTION; THEIR TREATMENT WITH CONTINUOUS INTRAVENOUS INFUSION OF ISOPROPYLNOREPINEPHRINE. H. H. GALE AND H. L. ENFROY. *New England J. Med.* 260:1229, 1959.

A case of Stokes-Adams syndrome is presented in which the use of a continuous intravenous infusion of isopropyl norepinephrine was successful in overcoming the bouts of asystole that we had been unable to prevent with either oral administration or subcutaneous, intramuscular or intermittent intravenous injections of the drug.

METAPHYSEAL CHONDRODYSPLASIA OF JANSEN. P. B. GRAM, J. L. FLEMING, B. FRAME AND G. FINE. *J. Bone & Joint Surg.* 41-A:951, 1959.

A case is described for which the name metaphyseal chondrodysplasia of Jansen is suggested. Biochemical changes were found simulating those caused by hyperparathyroidism, but different and distinctive roentgenographic findings were also evident. Parathyroid exploration was negative for hyperplasia or adenoma. It is postulated that the metabolic changes — hypercalcaemia and hypophosphataemia — may have been secondary to the underlying bone defect.

ANTIBIOTIC CONCENTRATIONS IN DISCS USED FOR SUSCEPTIBILITY TESTING OF STAPHYLOCOCCI. J. E. GREER, R. R. MENARD AND P. F. LESNEY. *Antibiotics Annual* 1958-59, p. 818.

The distribution of minimum inhibitory concentrations among susceptible and resistant strains of *Staphylococcus aureus* tested by both broth dilution and disc (agar diffusion) techniques with eight antibiotics is reported. These data show these values to be mostly at either extreme, susceptible or resistant. Thus, two discs are sufficient to classify staphylococci as susceptible, moderately resistant, or resistant,

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since few intermediates occur. One disc is sufficient if concentrations and zone sizes are properly standardized. Some reasons for inaccurate discs are discussed.

*STUDIES ON SUCCINIC DEHYDROGENASE. X. REACTIVITY WITH ELECTRON CARRIERS IN RESPIRATORY CHAIN PREPARATIONS FROM HEART. XI. INACTIVATION BY CYANIDE AND ITS MECHANISM. A. GIUDITTA AND T. P. SINGER. *J. Biol. Chem.* 234:662, 1959.

The characteristics and mechanism of action of the cyanide inactivation of succinic dehydrogenase activity in particulate preparations have been investigated. The soluble enzyme isolated from heart is insensitive to cyanide regardless of the method of assay. Particulate preparations are inactivated by incubation with cyanide to the following maximal extent: oxidation of succinate by cytochrome *c*, methylene blue, brilliant cresyl blue, and dichlorophenolindophenol, 100 per cent; succinate-ferricyanide reaction, 65 to 70 per cent; succinate-phenazine methosulfate reaction, 50 per cent; fumarate-leucomethyl viologen reaction, 50 percent; fumarate-reduced riboflavin 5-phosphate reaction, 0. In confirmation of the results of Tsou it was found that the inactivation by cyanide progresses as a reaction of first order, of which the rate depends on temperature and cyanide concentration. Contrary to Tsou's report, the rate was found to vary markedly with pH, and the pH-dependence is not the same in the inactivation of the succinate-methylene blue and succinate-phenazine methosulfate assays. The inactivation is characterized by two distinct effects: loss of activity at infinite concentration of electron carrier (V_{max}) and loss of affinity for electron carriers. Both of these effects are prevented by compounds which reduce succinic dehydrogenase (succinate, hydrosulfite, reduced diphosphopyridine nucleotide) but only the second effect is reversed by reducing agents. Although reduced diphosphopyridine nucleotide prevents the action of cyanide on succinic dehydrogenase, cyanide does not abolish the oxidation of reduced diphosphopyridine nucleotide in heart muscle preparations. The cyanide inactivation described has been encountered only in heart preparations; it is not observed in brain or yeast. The possible mechanism of the cyanide inactivation and its implications on the organization of the respiratory chain in sarcosomes have been discussed.

IRIDENCELEISIS; TECHNIQUE AND RESULTS IN NINETY-FIVE CONSECUTIVE OPERATIONS. M. W. HAISTEN AND J. S. GUYTON. *A.M.A. Arch. Ophth.* 61:727, 1959.

The operative technique employed, the results obtained, and the complications encountered in 95 consecutive iridencleisis over a three-and-one-half-year period are presented. A successful result was obtained in 84% of the cases (acute congestive, chronic open-angle, and chronic narrow-angle glaucoma). We believe iridencleisis is the operation of choice in those cases of acute congestive glaucoma in which permanent embarrassment of the outflow mechanism has occurred. It would appear that iridencleisis and cyclodialysis are of comparable effectiveness for chronic primary noncongestive glaucoma of either the open- or narrow-angle type (with the exception of those cases occurring in the Negro race, in which we would prefer cyclodialysis). We do not feel that iridencleisis is indicated in aphakic or other secondary glaucomas.

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METHODS OF FIXATION IN MANDIBULAR BONE GRAFTS. F. A. HENNY AND W. D. McCLELLAND, JR. *J. Oral Surg., Anes. & Hosp. Dent. Serv.* 17:34, 1959.

A new appliance is described which can be used quickly, easily and effectively to retain mandibular segments in their correct anatomic relationships after partial resection of the mandible. The device consists of a Kirschner stainless steel pin, 9 inches long and 3/32 inch in diameter, threaded for its entire length. Two nuts and washers are provided with each pin. Both insertion and removal are rapid and simple.

SUBTOTAL RECONSTRUCTION OF THE THUMB; TUBED-PEDICLE FLAPS WITH TACTILE RESTORATION. A. P. KELLY, JR. *A.M.A. Arch. Surg.* 78:582, 1959.

The tubed-pedicle flap and bone graft can effect a satisfactory restoration of the amputated thumb. This method can be utilized for a loss through the proximal phalanx or metacarpal. I feel, however, that it is most suitable for losses through the metacarpophalangeal joint or proximal phalanx. I believe that the major disadvantage of the tubed-pedicle flap, its lack of stereognosis, can be combated by the neurovascular pedicle flap or the proximally based palmar flap. Two illustrative cases are presented.

CHLOROTHIAZIDE AND HYDROCHLOROTHIAZIDE IN THE TREATMENT OF CONGESTIVE HEART FAILURE. J. W. KEYES, G. M. BRENNEMAN, AND H. ALVAREZ, JR. *Internat. Rec. Med.* 172:454, 1959.

In the past two years, a new class of potent oral diuretic agents, derived from the aromatic sulfonamides and belonging to a group known as benzothiadiazines, has been introduced to the medical profession. The first major breakthrough in producing a nontoxic and highly active oral diuretic resulted in the development of chlorothiazide, 6-chloro, 7-sulfamyl, 1, 2, 4-benzothiadiazine-1, 1-dioxide. Since then, a second and more powerful derivative, hydrochlorothiazide, has been synthesized; it is designated as 6-chloro-7-sulfamyl-3, 4-dihydro-1, 2, 4-benzothiadiazine-1, 1-dioxide. Both of these compounds are very active saluretic agents, causing the excretion of large amounts of sodium, chloride, and, to a lesser extent, potassium. It is to this activity that the drugs owe their effectiveness in the management of edema states, particularly congestive heart failure. Hydrochlorothiazide differs from chlorothiazide in having no double bond in the heterocyclic ring and appears to be several times more effective in its diuretic activity mg. for mg., as will be shown later. Chlorothiazide and hydrochlorothiazide were administered to separate series of patients with congestive failure. Both drugs were potent oral diuretic agents for the short- and long-term management of these patients. One of these drugs (hydrochlorothiazide) was also effective by intravenous administration. Dosage and toxicity of the two drugs are discussed.

RECENT DEVELOPMENTS IN CARDIAC SURGERY. C. R. LAM. *Chicago M. Soc. Bull.* 62:68, 1959.

There is so much change and expansion in the field of surgery of the heart it is interesting to prepare a report on recent developments. It is common knowledge

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that the most dramatic advances have been made because of the break-through into open heart technics by Lillehei and the group at the University of Minnesota. It is now almost five years since their first successful by-pass of the heart and lungs by means of cross circulation with a human donor. Within a year, they were able to eliminate the donor by utilizing a bubble type of oxygenator and open heart surgery took its place in surgical practice. Also, the test of time has been applied to some of the earlier cardiac operations so that we now know if they have shortcomings and of their "durability." The surgical management of the following conditions is discussed, patent ductus arteriosus, coarctation of the aorta, mitral stenosis and insufficiency, aortic stenosis, aortic insufficiency, pulmonic valve stenosis, atrial septal defect, ventricular septal defect, tetralogy of Fallot, and coronary artery insufficiency. In spite of the progress in heart surgery which has been reported, many problems still challenge the investigative surgeon. A successful operation for transposition of the great vessels still has to be devised, and there are other congenital and acquired lesions which demand attention. With continued intense interest, further improvements in the near future are inevitable.

EFFECT OF ANTIBIOTIC THERAPY ON THE EMERGENCE OF RESISTANT STAPHYLOCOCCI IN CUTANEOUS BACTERIAL INFECTIONS. C. S. LIVINGOOD, J. E. GREER, R. E. BURNS, AND R. R. MENARD. *J. Invest. Dermat.* 32:485, 1959.

Our experience regarding the emergence of antibiotic-resistant *Staph. aureus* in skin lesions of patients with cutaneous bacterial infections, following therapeutic trials with tetracycline ointment, erythromycin ointment, neomycin ointment (or lotion), bacitracin ointment, or neomycin-bacitracin ointment, or after oral administration of tetracycline, erythromycin, or novobiocin is reported. A total of 354 patients met the following criteria for inclusion in this study: 1) Presence of an apparent clinical primary or secondary cutaneous bacterial infection. 2) Isolation from involved sites, before therapy, of *Staph. aureus* susceptible to the antibiotic which was administered systemically or applied topically. 3) Availability of follow-up cultures after varying periods of time following the antibiotic therapy. There was a change from a sensitive to a resistant antibiogram in 16 of 136 patients treated with either tetracycline or erythromycin ointment. Of the 109 patients treated topically with either neomycin, bacitracin, or the combination of neomycin-bacitracin, there was either no change in the antibiogram or *Staph. aureus* was not isolated following treatment. Emergence of antibiotic-resistant *Staph. aureus* was noted in 17 of 92 patients with skin infections, treated systemically with tetracycline, erythromycin or novobiocin. The problem of emergence of antibiotic resistant *Staph. aureus* following the use of topical and systemic antibiotic therapy for the treatment of cutaneous bacterial infections is of greater significance in in-patients than in out-patients. Our present policy regarding the use of systemic and topical antibiotic therapy for the treatment of bacterial infections of the skin is summarized.

ALTERED PROGNOSIS WITH CARDIAC MASSAGE; CARDIAC RESUSCITATION IN ACUTE MYOCARDIAL INFARCTION — REPORT OF TWO SUCCESSFULLY TREATED CASES. S. N. NICKEL AND H. H. GALE. *J.A.M.A.* 170:23, 1959.

In two instances patients with previous symptoms of myocardial infarction

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collapsed suddenly and became pulseless. Artificial respiration was given by insufflation, and immediate thoracotomy was performed to permit rhythmical compression of the heart, which was in a state of asystole. Intracardiac injection of 0.5 cc. of 1:1,000 aqueous solution of epinephrine was followed by ventricular fibrillation. Normal cardiac rhythm was restored by use of an electrical defibrillator in each case, and both patients survived without signs of injury to the brain. This is in accord with other published data indicating that these methods of resuscitation, if applied without delay, greatly improve the prognosis of patients with acute myocardial infarction.

LIPOID NODULES IN CHRONIC RHEUMATOID ARTHRITIS; NODULOS LIPOIDE IN CHRONIC ARTHRITIS RHEUMATOIDE. R. K. NIXON, JR., AND R. H. DURHAM. *Arthritis & Rheumat.* 2:27, 1959.

A case of advanced rheumatoid arthritis with multiple lipoid nodules is presented. No conclusions as to the particular significance of lipoid nodules are attempted, but their recognition as an unusual feature associated with chronic rheumatoid is stressed. The origin of lipoid nodules from ordinary rheumatoid nodules is reviewed. They are concluded to be probably identical to so-called calcium cysts previously reported in rheumatoid patients with vitamin D intoxication. The etiologic role of vitamin D, however, is questioned.

BLEEDING, PLATELETS, AND MACROGLOBULINEMIA. M. R. PACTER, S. A. JOHNSON, T. R. NEBLETT, AND J. P. TRUANT. *Am. J. Clin. Path.* 31:467, 1959.

Two cases of primary macroglobulinemia of Waldenström were exhaustively evaluated from the standpoint of modern methods on coagulation. The literature regarding the hemorrhagic diathesis is reviewed and evaluated. A coating of the platelets by macroglobulins as a cause of bleeding in macroglobulinemia of Waldenström is hypothesized and substantiated on the basis of coagulation, immunochemical, and electron and fluorescent microscopic studies. A potential deleterious effect of macroglobulins on erythrocytes and leukocytes is indicated. The relation between the macroglobulin and cellular surface is discussed.

ACUTE APPENDICITIS; AN ANALYSIS OF COMPLICATIONS IN 551 PATIENTS. J. L. PONKA, H. L. SHIELDS, AND D. M. EVANS. *J. Michigan M. Soc.* 58:415, 1959.

The fact that early appendectomy has long been established as the curative procedure for acute appendicitis needs emphasis. Antibiotics are not effective in the treatment of appendicitis associated with appendicular obstruction. Complications of appendicitis are much too common, (16.46 per cent in this series) and are the result of delays in diagnosis and surgical treatment. Antibiotics, surgical drainage, gastro-intestinal tract decompression and blood transfusions are life saving adjuncts in the treatment of complications. The public and the profession as well need to be reminded that appendicitis can be disabling, as well as fatal, if neglected.

PERIODONTICS FOR THE GENERAL PRACTITIONER. Z. A. READER. *J. Michigan Dent. Assoc.* 40:179, 1958.

Most patients that have had extensive periodontal treatment should return

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approximately every three or four months for thorough oral prophylaxis and for examination of gingival health, pocket depth, tooth mobility, etc. If necessary, returning periodontal problems can be treated and the occlusion readjusted. Complete dental films should be taken annually. The patient must never be told that his case has been cured but rather he should be told that the case is controlled and it will only remain controlled in the future through his cooperation by proper home care and periodic examination and treatment by the dentist. Because periodontal diseases are so universal the general practitioner must recognize and treat them. The cases which are too involved may be referred to a periodontist. After the periodontal work is finished the periodontist may make suggestions to the referring dentist for mouth rehabilitation. The general practitioner should be especially interested in the prevention of periodontal disease with the same zeal which he has had in the prevention of dental caries. This can be accomplished only by patient education and immediate treatment of incipient periodontal alterations.

***STUDIES ON CHOLINE DEHYDROGENASE. I. EXTRACTION IN SOLUBLE FORM, ASSAY, AND SOME PROPERTIES OF THE ENZYME. G. RENDINA AND T. P. SINGER. J. Biol. Chem. 234:1605, 1959.**

The assay of choline dehydrogenase activity in mitochondrial as well as soluble preparations with phenazine methosulfate as acceptor has been described. Electron acceptors employed in the past for the assay of this enzyme (cytochrome *c*, ferricyanide, methylene blue, and 2, 6-dichlorophenolindophenol) either do not react directly with the dehydrogenase and consequently measure a variable part of its activity, or they are unreliable because of the extensive dependence of the measured activity on dye concentration. Choline dehydrogenase has been brought into solution in good yield by a mild procedure involving treatment of mitochondria or acetone powders thereof with certain snake venoms. Evidence has been presented that the active component in liberating the dehydrogenase in soluble form is phospholipase A. The process appears to depend on the point of attack and on the structural specificity of the particular phospholipase, since plant phospholipase D and the phospholipase A of certain venoms are inactive, whereas the phospholipase A of other venoms is active in dissolving the dehydrogenase. Upon treatment with phospholipase A the reactions of the dehydrogenase with cytochrome *c* and ferricyanide are abolished, probably as a result of the uncoupling of the enzyme from the factors linking it to these acceptors in respiratory chain preparations. The enzyme extracted by this means does not sediment at $144,000 \times g$ for 1 hour and does not precipitate on repeated freezing and thawing or on prolonged dialysis. Contrary to claims in the literature, choline dehydrogenase is not stimulated by flavin adenine dinucleotide or diphosphopyridine nucleotide, even after extensive dialysis, in either soluble or mitochondrial preparations. The apparent stimulation of the dehydrogenase by added diphosphopyridine nucleotide in assays involving the respiratory chain (choline oxidase) has been explained as an indirect effect involving the activation of betaine aldehyde dehydrogenase, with consequently increased rate of O_2 uptake and removal of the aldehyde which is inhibitory to choline dehydrogenase. Some properties of the soluble dehydrogenase have been described.

*From Edsel B. Ford Institute for Medical Research.

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MALABSORPTION SYNDROME AND DIARRHEA; A PANEL DISCUSSION. D. J. SANDWEISS, D. ADLERSBERG, A. B. FRENCH, R. H. MARSHAK, H. L. BOCKUS, AND R. J. PRIEST. *J. Michigan M. Soc.* 59:772, 1959.

THERAPY OF PRIMARY MALABSORPTION. ROBERT J. PRIEST.

Although clinical and symptomatic improvement has been observed in this recent series of patients, the period of observation has been of too short duration to permit conclusions. Sprue has been a disease renowned for its chronic remitting course. Spontaneous remissions are not infrequent. The importance of the psychological effect of a new management regime must be evaluated. In fact, an important measure in the management of primary malabsorption is attention to the factors of nervous stress and fatigue. We have seen one patient who did not secure any symptomatic relief from the gluten-free diet during a period of time when she had problems in the family situation. Six months later, after resolution of the situational factors, and an opportunity for an extended vacation, she responded promptly when the gluten-free diet was again attempted. Many patients should be encouraged to take short periods of rest during the day and to avoid nervous or physical fatigue. Therapy of primary malabsorption must be directed towards improving the patient's nutrition and correction of the deficiency states. No single drug nor dietary program can be given complete reliance. The gluten-free diet offers promise of a valuable adjunct to the previous dietary management. The corticosteroids are an important adjunct in the control of patients who have not responded to therapy with vitamin and mineral supplements.

LOCALIZATION OF ACETYLCHOLINESTERASE IN THE COCHLEA. H. F. SCHUKNECHT, J. A. CHURCHILL, AND R. DORAN. *A.M.A. Arch. Otolaryng.* 69:549, 1959.

We have previously published the results of studies showing that acetylcholinesterase is present along nerve fibers and in dense accumulations at the bases of the hair cells in the organ of Corti of the cat. In the present study fresh cat cochleas were perfused with acetylthiocholine in the presence of cupric ions, the solutions passing from the round window through the helicotrema and out the oval window. The cochleas were fixed, decalcified, sectioned, and counterstained. The copper sulfide deposits resulting from activity of acetylcholinesterase were found to be markedly decreased in six cochleas in which the olivocochlear bundle had been successfully sectioned in the medulla. Acetylcholinesterase was not decreased in any of the control ears or in the two ears in which the olivocochlear bundle had not degenerated after unsuccessful section. The esterase remained in the neighborhood of hair cells that had been destroyed by streptomycin in three cats. It was concluded that the presence of acetylcholinesterase in the cochlea was dependent upon the integrity of the olivocochlear bundle. The evidence revealed that fibers of the olivocochlear bundle terminate upon or very close to the cochlear hair cells, and that these fibers are cholinergic. Acetylcholine liberated at the endings of the olivocochlear tract fibers may alter the excitability state of the hair cells or the acoustic nerve endings. The amacrine cells of the retina, which are known to contain acetylcholinesterase, may subserve a function similar to that of Rasmussen's bundle in the cochlea. Perhaps other sensory end-organs should be investigated for cholinergic efferent nerve fibers.

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TYMPANOPLASTY. H. F. SCHUKENCHT AND S. OLEKSIUK. *Laryngoscope* 69:614, 1959.

Tympanoplasty surgery is an exercise in micro-surgical technique which requires good judgment, great patience and an understanding of the physiological principles of sound transmission. Success depends upon meticulous removal of diseased tissues and reconstruction of the tympanic space so as to accomplish a columella effect and/or a pressure differential at the windows. It is most important that the mucosa of the tympanum, medial tympanic wall and round window area be cautiously preserved and that the skin graft, preferably full-thickness from the post-auricular sulcus, be trimmed, fitted and packed into place with great care. Ten per cent of the patients were made worse by 5 db or more, but several of these losses were less than 15 db and have been corrected subsequently by surgical revision. The percentage of good cases increases with time as our surgical technical ability has improved. The two main reasons for tympanoplasty failure are: 1. partial graft necrosis, and 2. scarring of the graft into the hypotympanum. Four of the patients have had a significant unexplained loss of bone conduction thresholds. An analysis of the results of 160 tympanoplasties reveals that a 30 db level was acquired by 82 per cent of Type I cases, 70 per cent of Type II cases, 48 per cent of total plastic cases (Type III-A and IV-A) and 70 per cent of minor plastic cases (Type III-B and IV-B). Our experience has shown that damage to ossicles and tympanic membranes was less in the younger age group and the success of tympanoplasty operation depends in part upon early intervention in chronic irreversible suppurative middle ear disease.

EFFECT OF ANTIBACTERIAL AGENTS ON CLEAN WOUNDS. C. K. SERGEANT, J. L. PONKA, AND B. E. BRUSH. *A.M.A. Arch. Surg.* 78:480, 1959.

It was found that the antibacterial agents tetracycline (Achromycin), chlortetracycline (Aureomycin), bacitracin, chloramphenicol (Chloromycetin), neomycin, polymyxin B, and oxytetracycline (Terramycin) generally do not retard or accelerate the rate of wound healing, with the exception of chlortetracycline, which was found to retard routinely the time for healing from two to six days.

TRAUMATIC EPIDERMOID CYSTS INVOLVING DIGITAL BONES; EPIDERMOID CYSTS OF THE DISTAL PHALANX. J. C. SIERACKI, AND ALEX P. KELLY, JR. *A.M.A. Arch. Surg.* 78:597, 1959.

Epidermoid cysts in the digital bones generally follow trauma and represent a distinct clinicopathologic entity. The clinical, roentgenologic, and histologic features allow the correct diagnosis in all cases. Surgical treatment is curative, and will allow preservation of the distal phalanx in the majority of cases. A significant degree of pseudoepitheliomatous hyperplasia in the cyst wall was found in four out of the nine cases presented in this series.

CURRENT PROBLEMS IN PERIPHERAL ARTERIAL SURGERY. R. F. SMITH. *Heart Center Bull.* 15:1, 1958.

An angiographic survey is essential in evaluating the type of arteriosclerotic occlusive disease present in patients so afflicted and greatly assists the vascular surgeon in choosing those individuals in whom an appropriate angioplastic procedure may be employed with reasonable success. As the disease process has a variety of pathological

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manifestations, one must be selective in establishing the indications for an operation and utilize a procedure suitable for the specific circumstances. The guiding principle should be to avoid any surgery that could further embarrass the circulatory status of an extremity. We are currently favoring a long bypass of elastic Dacron for the management of femoro-popliteal occlusions with the hope that a greater degree of late patency will be achieved than with arterial homografts.

PRESENT STATUS OF ARTERIAL SUBSTITUTES. R. F. SMITH AND D. E. SZILAGYI. *J. Michigan M. Soc.* 58:77, 1959.

As yet no truly ideal arterial substitute has been developed. Further investigation and clinical trial will be necessary before this goal is achieved. Autogenous vein grafts are readily available, especially in emergency circumstances, but are limited as to their dimensions. Experimentally, heterografts have been shown to be completely unreliable. Both venous and arterial homografts, because of their lack of durability, should be limited to the occasional instance where the technical difficulties in the case require their superior ability to remain patent under adverse conditions or in older individuals where the need for long-range function is not great. All the rigid synthetic plastic prostheses suffer from the disadvantage of kinking when bent, making their clinical usefulness quite limited. Elastic nylon tubes satisfactorily overcome the problem of kinking but show progressive deterioration of tensile strength which drastically limits their clinical application. In almost all instances we have found an elastic Dacron prosthesis to function very satisfactorily without loss of tensile strength, and we feel that this is the most suitable type of arterial substitute at the present time.

OSSIFICATION OF REGENERATED MEDIAL SEMILUNAR CARTILAGE. S. S. STANISAVLJEVIC. *Acta Orthop. Scandinav.* 28:224, 1959.

The first instance of post-traumatic ossification of a regenerated medial meniscus with limitation of flexion of the knee joint was observed. The meniscus was removed and hydrocortisone was injected into the cavity of the joint. The treatment restored the normal use of the leg.

CHLOROTHIAZIDE THERAPY IN OBSTETRICS AND GYNECOLOGY. L. B. STEVENSON, AND C. P. HODGKINSON. *Am. J. Obst. & Gynec.* 77:1286, 1959.

After appraisal of the reasons for elevation of blood uric acid from the administration of chlorothiazide, it was observed that this occurred in both obstetric and gynecologic patients. Hyperuricemia was not caused by hemoconcentration since uric acid levels rose out of proportion to the other constituents of the blood. The reason for the increase in uric acid concentration is not established by this study and whether this resulted from altered renal excretion of uric acid or dysfunction of metabolism is not known. While the clinical importance of hyperuricemia resulting from chlorothiazide treatment appears to be minimal, its obstetric import lies in the confusion which may result from using serum uric acid levels as aids in diagnosis and prognosis in toxemia. Results of this study suggest that chlorothiazide is a potent diuretic agent that is relatively free of toxicity. The equimolar excretion of sodium

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and chloride makes the drug comparatively safe for administration during pregnancy. Although the drug does not cure toxemia of pregnancy, our findings would put chlorothiazide in the group of drugs used as adjunctive in its treatment. These conclusions are similar to those of Finnerty and associates who used chlorothiazide in patients with toxemia of pregnancy.

ANTEROMEDIAL APPROACH TO THE POPLITEAL ARTERY FOR FEMOROPOPLITEAL ARTERIAL GRAFTING. D. E. SZILAGYI, J. G. WHITCOMB, AND R. F. SMITH. *A.M.A. Arch. Surg.* 78:647, 1959.

An approach is described to the popliteal artery that makes it possible to insert long femoropopliteal bypass implants in an uninterrupted technical sequence. Bridging, in this manner, a longer segment of diseased artery, this operation promises to reduce the late failure rate of grafting operations for occlusive disease of the femoropopliteal area.

HEMODYNAMIC FACTORS IN ARTERIAL GRAFTING: AN EXPERIMENTAL STUDY OF ANASTOMOTIC TYPES, GRAFT SIZE AND GRAFT SURFACE CHARACTERISTICS. D. E. SZILAGYI, J. G. WHITCOMB, P. WAIBEL, AND W. SCHENKER. *S. Forum* 9:319. 1959.

Measurements of blood volume-flow with the bubble flow-meter in the iliac arteries of the dog have shown that: A properly constructed end-to-end anastomosis is almost as efficient in transmitting blood as the intact artery. An end-to-side anastomosis is less efficient hemodynamically than an end-to-end anastomosis, but its efficiency to a large extent depends on the size of the angle between the component channels. By making the angle small the performance of this type of anastomosis can be made to come very close to that of an end-to-end anastomosis. A graft placed as a bypass is less efficient hemodynamically than a direct replacement of the same size but the difference can be markedly reduced and even eliminated by appropriate surgical technique. An increase in the diameter of a vascular graft by a factor of up to 2 brings about an increase in blood volume-flow which, however, is not proportional to the dimensional increase. An increase in diameter above a factor of 2 results in a decrease in volume flow. A prosthesis with rough or corrugated (crimped) luminal surface is less efficient than a prosthesis whose wall is uncorrugated and smooth.

PRIMARY ALDOSTERONISM DUE TO ADRENAL HYPERPLASIA; OCCURRENCE IN A BOY AGED 10 YEARS. B. THERIEN, R. C. MELLINGER, J. R. CALDWELL, AND P. J. HOWARD. *A.M.A.J. Dis. Child.* 98:90, 1959.

The details of a case of primary hyperaldosteronism occurring in a child 10 years of age have been presented. This hyperaldosteronism was proved to be due to bilateral adrenal hyperplasia chiefly involving the zona fasciculata. It is postulated that this hyperplasia was congenital in origin. Hyperaldosteronism should be considered in the differential diagnosis of any case of "essential" hypertension or of unexplained polyuria in children. The determination of serum potassium and urinary pH are useful screening tests in these patients. When hyperaldosteronism is caused by adrenocortical hyperplasia, bilateral total adrenalectomy is recommended. Maintenance of the patient postoperatively with adrenocortical hormones has been completely satisfactory.

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GLUCAGON FOR TREATMENT OF INSULIN HYPOGLYCEMIA: ITS USE IN THE PATIENT WITH DIABETES. F. W. WHITEHOUSE, AND H. G. BRYAN. *Am. Pract. & Digest Treat.* 10:1326, 1959.

Hypoglycemic reactions in the diabetic using insulin are alarming to the patient and the family. In establishing a program of control, hypoglycemic reactions make the course more labile with rebound hyperglycemia from use of glucose to control the reactions. Thus, the substance produced by the alpha cells of the islets of Langerhans, and now available in crystalline form as glucagon, having a hyperglycemic effect, has potential uses in labile diabetics. Though the material is not on the market, the studies detailed here are nevertheless of interest. Glucagon for the relief of insulin hypoglycemia has been used successfully over one hundred times during the past year. Generally it has been given subcutaneously in a dosage of 10 to 40 mcg./Kg. body weight. No toxicity has occurred. Its advantages and disadvantages are discussed.

BOOK REVIEW

ENCYCLOPEDIA OF MEDICAL SYNDROMES. BY ROBERT H. DURHAM, M.D. F.A.C.P. Chief Physician, Division of General Medicine, Henry Ford Hospital. New York, Paul B. Hoeber, Inc., 1960.

It has been a privilege to review this fascinating volume which contains such a variety of subjects, including as it does a comprehensive discussion of nearly 1,000 medical syndromes. The collection of this unprecedented number of syndromes is an impressive achievement and obviously required a widespread search of the world literature. Although some of the subject titles are readily recognized and others are vaguely familiar, many are unusual and rare.

The general plan and arrangement of the book are excellent. The various syndromes as well as their eponymic and descriptive synonyms are arranged alphabetically. Conveniently listed with each subject title are associated or interrelated syndromes. As a typical example:

PICKWICKIAN SYNDROME.

Synonyms: Cardiopulmonary-obesity syndrome, reversible obesity-cardio-respiratory syndrome, alveolar hypoventilation-obesity syndrome.

See also *Gelineau's syndrome: Kleine-Levin syndrome; postural syndrome; hypoventilation syndrome.*

The text of the individual syndromes is presented in a well organized editorial style of summarization and includes both the lesser known as well as the better known facts concerning each subject. Pertinent comments are made concerning historical data, genetic relationships, hereditary, congenital and familial factors, the reported incidence and sex ratios. Recorded in sequence are clinical manifestations, laboratory and pathologic findings, differential diagnosis, the clinical course, prognosis and known therapy and therapeutic results. These amassed facts are condensed into a brief but comprehensive summary without any evidence of a stereotyped pattern or repetition of style.

Book Review

The composite result is a vast amount of factual information concerning a large number of associated clinical patterns or relationships. Many of these syndromes have not before been incorporated into text; at least no similar complete reference source has previously been available.

There is an index arranged by classification under the various body systems. The alphabetization of subject titles provides an adequate cross reference of related syndromes.

Aside from the educational import of this book as a factual reference source, it commands attention for other basic reasons. This reviewer foresees for it two potential significant influences: (1) That it will accelerate a developing trend by means of which syndromes may to an increasing degree supplant diseases as a definitive medical term. During the past decade it has become increasingly evident that the number of new diseases is becoming more limited, although a larger number of medical syndromes is becoming apparent. (2) That both eponymic and descriptive syndromes, hitherto largely omitted in the index of text-books and almost completely ignored in other standard reference indexes, will command more recognition in these index reference sources in the future. This book will undoubtedly be a contributing influence in these two directions.

Aside from being a splendid contribution to medical needs, this volume is timely, and in many respects, timeless. It is without question the most comprehensive and authoritative source pertaining to medical syndromes ever published in the English language. With equal certainly the scope and character of its subject matter will make it an indispensable text for many years to come. As a further attest to the high standard of excellence with which this scholarly compendium is regarded in critical circles, the Foreword is by T. R. Harrison, eminent medical author and teacher.

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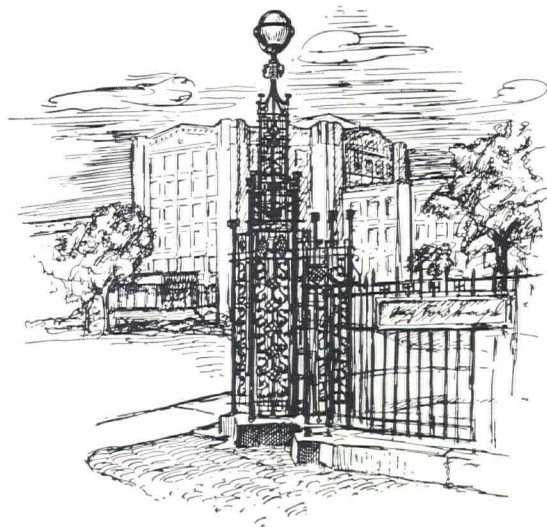
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