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ABSTRACTS

*Color detection of bile acids using thin-layer chromatography. W. L. Anthony, and W. T. Beher. *J. Chromatog.* 13:567, 1964.

A method is described for identifying free and conjugated bile acids by the use of selective color detection reagents. The colors were well defined, and when the chromatoplates were covered with glass plates, the colors were stable for several hours and in some instances for days. All detecting reagents with one exception produced yellow color with those bile acids having a hydroxyl group at 12-carbon position.

Implications of involvement of small bowel in ulcerative colitis. J. Barron, and L. S. Fallis. *Dis. Colon Rectum* 7:290, 1964.

In a series of 99 patients operated upon for ulcerative colitis, 29 had ileal involvement. X-ray examination is not of great diagnostic value. At operation, gross external evidence of ileal involvement was present in only one third of the patients. Inspection of the opened ileum during surgical exposure is mandatory. The long-range mortality rate was five times greater in patients with ileal involvement than in those in whom the small intestine was not involved.

*Effect of hyocholic acid on cholesterol and bile acid metabolism in the mouse. W. T. Beher, G. D. Baker, W. L. Anthony, and D. G. Penney. *Proc. Soc. Exp. Biol. Med.* 116:442, 1964.

Hyocholic acid effectively prevented accumulation of dietary cholesterol in mice fed diets supplemented with cholesterol but had little or no effect on tissue cholesterol concentrations in mice fed normal diets. Treating mice with antibiotics largely reversed the effect of hyocholic acid, and permitted the accumulation of dietary cholesterol in hyocholic acid-treated mice. It was demonstrated that the hypocholesteremic effect is probably mediated by hyodeoxycholic acid, which arises from the action of intestinal bacteria on hyocholic acid. In animals which received hyocholic or hyodeoxycholic acid, cholic acid disappeared from the bile acid spectrum of the small intestine. Treatment with antibiotics restored cholic acid to the bile acid spectrum of hyocholic acid-treated mice but not to that of hyodeoxycholic acid-treated mice.

*Correlation of enzymatic activity and the appearance of the EPR signal at $g=1.94$ in NADH dehydrogenase and its thermal breakdown products. H. Beinert, G. Palmer, T. Cremona, and T. P. Singer. *Biochem. Biophys. Res. Commun.* 12:432, 1963.

This paper demonstrates for the first time that catalytic activities measured by enzymatic assays in the DPNH dehydrogenase segment of a mammalian respiratory chain correlate excellently with the rate of appearance and decay of the EPR (electron spin resonance) signal at $g=1.94$. This signal has been ascribed to a new species of non-heme iron, which is known to be present in high concentration in the highly purified DPNH dehydrogenase isolated in this laboratory. By suitable rapid mixing techniques, which permit the measurement of reaction velocities in the millisecond range, it has been possible to demonstrate that there is a gratifying agreement between the rate of appearance of the signal at $g=1.94$ and the turnover number of the enzyme measured by the ferricyanide assay in ultrarapid spectrophotometers. On conversion of the enzyme to DPNH — cytochrome reductase, a degradative process involving major changes in the structure of a protein and the transformation of the dehydrogenase to an artefactual cytochrome-reducing fragment, loss of catalytic activity and loss of substrate-reducible signal at $g=1.94$ occur at identical rates.

*From Edsel B. Ford Institute for Medical Research.

ABSTRACTS

Tumor imprints as a source of nuclear substrate for the detection of antinuclear factors. T. K. Burnham, G. Fine, and T. R. Neblett. *J. Invest. Derm.* 43:7, 1964.

Sera of patients with positive lupus erythematosus cell tests, scleroderma and various dermatoses were investigated for antibodies to skin components and antinuclear factors by the indirect fluorescent antibody technic. Speckled nuclear fluorescence in the epidermis was seen with several of the scleroderma sera. Epidermal nucleolar fluorescence occurred with one scleroderma serum, while homogeneous epidermal nuclear fluorescence was seen with several of the lupus erythematosus cell positive sera. Tumor imprints were far superior for the detection of antinuclear factors to the conventional blood smears and tissue sections. Nuclear fluorescence was much more conspicuous due to the greater number, size and delineation of nuclei and to the greater quantity of some of the nuclear antigens. We therefore suggest the routine use of tumor imprints as a rapid and practical screening test for antinuclear factors.

*Ultrastructure of the salamander thyroidectomy cell. R. R. Cardell, Jr. *J. Ultrastruct. Res.* 10:515, 1964.

Adult salamanders (*Diemyctylus viridescens viridescens* Rafinesque) were surgically thyroidectomized and 60 days later their pituitaries were removed, fixed for electron microscopy, and ultra thin sectioned. The pars distalis contained an abundance of enlarged "thyroidectomy cells." These cells were characterized by extensive development of the rough and smooth endoplasmic reticulum; the rough endoplasmic reticulum was usually highly vesiculated. The cytoplasm contained more mitochondria than are usually found in pituitary secretory cells, and the mitochondria were enlarged and many were branched. The Golgi complex was extensively developed, being found throughout the cytosome. Fine fibrils were frequently seen in the cytoplasm of the thyroidectomy cell, and many irregular osmiophilic bodies were observed in this cell.

*The lactic dehydrogenases of yeast. IV. D- α -hydroxy acid dehydrogenase. T. Cremona. *J. Biol. Chem.* 239:1457, 1964.

A method is described for purification of D- α -hydroxy acid dehydrogenase of anaerobic yeast. The enzyme is a flavoprotein which oxidizes a number of D- α -hydroxy acids in a reversible manner. Ferricyanide is the most satisfactory electron acceptor; 2,6-dichlorophenolindophenol and methylene blue are less active; cytochrome *c* is inactive. A number of L- α -hydroxy acids and α -keto acids are competitive inhibitors. The probable involvement of a metal ion, possibly zinc, in the catalytic activity is suggested by the reversible inhibition of the dehydrogenase by chelating agents. Evidence is presented that the function of the metal moiety may be one of substrate binding.

*Conversion of DPNH dehydrogenase to DPNH-cytochrome reductase by thiourea. T. Cremona, E. B. Kearney, and G. Valentine. *Nature* 200:673, 1963.

This paper deals with the demonstration that the so-called "DPNH-cytochrome reductase" preparation, isolated from heart mitochondria by the use of thiourea as an extracting agent and considered by its discoverers to be a native enzyme, is in fact a modification product of DPNH dehydrogenase. Artefactual degradation of the native enzyme to the derived cytochrome-reducing fragment is shown to occur under the direct influence of thiourea, the extracting agent.

*Labile flavin adenine dinucleotide of heart muscle preparations. T. Cremona, E. B. Kearney, J. Salach, and T. P. Singer. *Nature* 200:958, 1963.

This paper deals with the demonstration that the so-called "labile FAD" purportedly present in mammalian heart muscle and identified by its "spontaneous" breakdown to FMN is actually normal FAD linked to a protein component in a linkage which renders it labile to storage. On continued storage of heart muscle preparations in the cold a gradual release of free FAD occurs, which is subsequently enzymatically hydrolyzed to FMN. The source of this "labile FAD" is not mitochondria but cytoplasm and, therefore, conclusions in the literature concerning the non-existence of FAD in mammalian mitochondria are erroneous. It is shown that fresh mitochondria contained a constant proportion of FAD to FMN of approximately 15:85.

*From Edsel B. Ford Institute for Medical Research.

ABSTRACTS

Liquid spray-on plastic film as a skin drape for abdominal operations. C. P. Hodgkinson, J. N. Canton, J. W. Truant, H. R. Zuber, and M. A. Correll. *Western J. Surg.* 72:230, 1964.

The technic of applying a double spray-on plastic film to the operative site of the abdomen for the purposes of isolating and containing the skin bacteria from the incision has been described. The spray-on plastic film was compared with skin towels and adherent vinyl plastic sheeting as operative drapes and it was noted that the spray-on plastic film had unique physical advantages. Bacteriologic studies indicated that the combination of the spray-on plastic film and Tr. thimerosal was an effective barrier to the migration of deep skin bacteria and that the duration of action was at least 3½ hours. When spray-on plastic film and Tr. thimerosal were used in conjunction as a protective skin coating, the skin, as a potential contamination source, was of minor importance. Far more important were the operating personnel, the ambient operating room air, and in gynecologic procedures, the opened vagina.

Mechanism of action of quinidine on the sinus node studied by direct perfusion through its artery. T. N. James, and R. A. Nadeau. *Amer. Heart J.* 67:804, 1964.

Studied by direct perfusion of the sinus node through its artery, quinidine has three actions: direct, anticholinergic, and antiadrenergic. The direct action of quinidine is insignificant at concentrations below 10.0 µg per milliliter, but causes suppression of sinus activity at 100 µg per milliliter. The anticholinergic and antiadrenergic actions occur concurrently and are unrelated to the direct action; both of these effects increase in direct relation to the concentration of quinidine. Since the autonomic blocking effect includes both nerve stimulation and the administration of local neurohormones, this action of quinidine occurs at the receptor site and is not due to inhibition of local release of effector substance.

An etiologic concept concerning the obscure myocardopathies. T. N. James. *Progr. Cardio. Dis.* 7:43, 1964.

Medial necrosis leading to luminal encroachment of small coronary and pulmonary arteries is presented as a heritable trait on the basis of its observation in patients with Marfan's syndrome, progressive muscular dystrophy, "primary" pulmonary hypertension, Friedreich's ataxia and the syndrome of congenital deafness with fainting attacks and sudden death. Especially involved were the nutrient arteries of the sinus node and A-V node, which may account for the high incidence of arrhythmias and conduction disturbances reported in these diseases; a similar explanation is applicable to the clinical features of palpitations, fainting attacks and sudden death. The same lesions in small ventricular arteries may lead to repeated episodes of minute focal areas of ischemic degeneration and fibrosis, and ultimately cardiac dilation and failure. The possibility that a hereditary medial necrosis of small coronary arteries is also responsible for the cardiac pathologic disease in other obscure myocardopathies deserves further study.

Pathology of the cardiac conduction system in hemochromatosis. T. N. James. *New Engl. J. Med.* 271:92, 1964.

In each of the hearts of 5 patients with hemochromatosis there were iron deposits with associated tissue damage in the atrioventricular node but not in the sinus node. Heart block and arrhythmias, which have commonly been described in hemochromatosis, are probably related to this abnormality in the cardiac conduction system. It is not clear why the sinus nodes did not contain pathologic iron pigment.

Traitement chirurgical des anévrismes du ventricule gauche. (Surgical treatment of aneurysms of the left ventricle.) C. R. Lam, H. Gale, E. Drake, and J. van de Kerckhof, *J. Chir.* 88:5, 1964.

Six patients with large post-infarction aneurysms of the ventricle have been treated surgically. The aneurysms were excised during extra-corporeal circulation with an oxygenator of the De Wall type. Two patients did not survive. In these, the infarcts were very large and involved the interventricular septum. The four survivors have resumed their former activity. This experience as well as that of others reported in the literature indicates that the prognosis after surgical treatment of ventricular aneurysms is remarkably good.

ABSTRACTS

Diagnostic criteria for distinguishing cervical disk herniation from spondylosis in the neural compression syndrome. K. D. McGinnis, and A. B. Eisenbrey. *Radiology* 83:67, 1964.

Disk protrusion and spondylosis are clinically and radiographically distinct manifestations of degenerative change at an interspace. A disk protrusion is indicated when a lobulated defect is projected within the contrast column on the myelogram or when a myelographic defect is demonstrated without evidence of spondylosis on the plain films. Bony spurs from the area of the neuro-central joint frequently project medially into the contrast column, but the greatest diameter of the defect extrapolates lateral to the contrast material and to the disk protrusions observed. In the series here reported it was relatively seldom that this lateral spondylosis produced symptoms requiring surgical intervention. Both cervical spondylosis and disk protrusion produced superimposed central symptoms of spinal cord compression, in which case the results of therapy were less satisfactory than when the problem was radicular alone. It was, indeed, the poor results in these cases that inspired the study. This review of 120 cases indicated that the roentgen diagnosis of spondylosis is sufficiently accurate to permit investigation of treatment, such as primary anterior fusion, that does not necessarily explore the root area for tumor or disk protrusion.

Angiographic study of the left atrium in mitral stenosis. R. S. Ormond, E. H. Drake, and H. H. Gale. *Radiology* 83:277, 1964.

Left atrial angiography by cinegraphic technic with the injection of contrast material into the pulmonary artery is a convenient and reliable examination for the evaluation of left atrial thrombi in patients with mitral stenosis and auricular fibrillation. The failure of opacification of the atrial appendage is the *sine qua non* of an atrial thrombus.

Massive gastrointestinal hemorrhage secondary to tumors of Brunner's glands. J. L. Ponka, and A. K. Shaalan. *Amer. J. Surg.* 108:51, 1964.

Adenomas of Brunner's glands are rare, but in the occasional patient they cause serious sequelae. At least eighty-four cases of lesions of Brunner's glands are available for study in the literature. Massive gastrointestinal bleeding is the most common significant manifestation of such adenomas. Obstruction of the upper gastrointestinal tract is the second most important manifestation of lesions of Brunner's glands. Malignancy has not been reported in polypoid lesions of Brunner's glands. Duodenotomy and polypectomy are the treatment of choice for pedunculated adenomas of Brunner's glands. Cysts and hyperplasias of Brunner's glands may be associated with vague symptoms of epigastric pain, gnawing and burning. Treatment should consist of dietary management, antacids, antispasmodics and mild sedation. Two cases of lesions of Brunner's glands causing massive upper gastrointestinal hemorrhage are reported.

Changing aspects in surgery of diverticulitis. J. L. Ponka, and A. K. Shaalan. *Arch. Surg.* 89:31, 1964.

During a period of 20 years, 604 patients were treated for diverticulitis of the colon. During the decade from 1942-1951, 22 per cent, and during 1952-1961, 18.6 per cent required operation. In the first decade (1942-1951) the three-stage operation was employed in over half of the patients. During the second decade (1952-1961) the one-stage procedure had been used in nearly half of the patients. The length of segment resected varied greatly. When carcinoma was suspected, and in the presence of bleeding, the longest segments of colon were excised. Excision of the diseased sigmoid, especially the lower portion, was found to be of paramount importance. The three-stage procedure continues to be safe and in general promises excellent to good results. The operative mortality rate in the decade from 1942-1951 was 6.6 per cent, and in the period from 1952-1961 there was one death due to peritonitis (1.16 per cent). Surgery of diverticulitis is changing rapidly. The important concepts embrace the idea that we must operate upon more patients with diverticulitis before life-threatening complications develop.

Abnormal prothrombin consumption time in ulcerative colitis. J. A. Rinaldo, Jr., S. A. Johnson, and J. P. Abraham. *Amer. J. Dig. Dis.* 9:459, 1964.

The prothrombin consumption time was assayed in 40 patients suffering from ulcerative colitis and compared with that of 30 control patients who did not have clinical evidence of a hemorrhagic disease. Prothrombin time was also measured in each patient. Platelets were examined on a blood smear, and peripheral capillary fragility was evaluated in the diseased

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patients. Ulcerative colitis patients had abnormal prothrombin consumption times and prothrombin times. They had normal platelets and normal peripheral capillary fragility. The prothrombin consumption time was normal when ulcerative colitis was mild. Most abnormal prothrombin consumption times occurred in patients with severe ulcerative colitis.

*Further studies on the labile flavin adenine dinucleotide of heart muscle preparations. J. Salach, E. B. Kearney, and T. P. Singer. *Nature* 201:1027, 1964.

This paper follows up previous observations in this laboratory on the nature of the "labile FAD" of heart muscle preparations. It is shown that the apparently spontaneous conversion of protein-bound FAD to free FMN, which occurs on storage of heart muscle preparations in the cold, is actually an enzymatic process. The pathway involves denaturation of an unknown flavoprotein in heart cytoplasm, accompanied by liberation of FAD in the free state, which is then attacked by the enzyme nucleotide pyrophosphate, known to be present at a high concentration in heart cytoplasm.

Allergic emergency aftermath of modern therapeutics. J. H. Shaffer. *J. Kentucky Med. Ass.* 62:523, 1964.

Although newer diagnostic and therapeutic chemicals, drugs, and biologicals have revolutionized the practice of medicine over the past several decades, their widespread use has resulted in an ever-increasing number of allergic reactions which have complicated the practice of medicine. Diagnostic and therapeutic pitfalls are numerous. Care in selection of and route of administration of all drugs is necessary if we are to avoid serious and fatal allergic reaction. Metabolic, or, degradation products of drugs have the capacity to combine with tissue proteins. Such hapten-conjugates become antigenic and may form antibodies, which, when re-exposed to the antigen initiates the allergic reaction. Patients with a personal or family history of allergy are highly susceptible to reactions to drugs. This group of patients should be exposed to as few medications as possible. We should not, as some have intimated, be guilty of over-medicating our patients. General measures to be considered in the prevention and treatment of allergic emergencies which may occur in office practice are life saving. No clear-cut advantage is represented by many new drugs as compared to standard remedies. If high risk is involved, their use may not be justified.

*Problems and controversies in the field of the respiratory chain-linked dehydrogenases. T. P. Singer and T. Cremona. "Oxygen in the Animal Organism," Proceedings of a symposium on oxygen in the animal organism, London, 1963, Pergamon Press, 1964.

The examples cited in these few pages were intended to illustrate the many pitfalls which exist in this field, by which most workers active in it — including the present authors — have been trapped at one time or another. If there is a lesson to be learned from these instances it is that progress in the area of the respiratory chain-linked dehydrogenases has not been limited by the dearth of imaginative, sometimes inspiring, ideas but by technological and methodological advances. Few investigators consider it glamorous or even intellectually satisfying to improve available assay methods for a given enzyme or to develop a procedure for determining its concentration on the basis of its molecular properties, and yet, in each of the instances quoted it is precisely this type of seemingly pedestrian endeavour which has led to a solution of controversial problems. It may be that the closer we penetrate into the problem of mitochondrial enzyme systems, the more inadequate will become the methods carried over from studies of extracellular and cytoplasmic enzymes.

*Newer knowledge of the role of metals in metallaflavoproteins. T. P. Singer, and E. B. Kearney. *Proc. Fifth Intern. Cong. Biochem.* London, Pergamon Press 4:206, 1963.

This is an extensive review dealing with recent advances involving the catalytic and structural roles of metal components of metal-flavoproteins. Particular emphasis is placed on the role and chemical properties of the Zn component of Zn-flavoproteins, a newly discovered class of enzymes, which have been investigated *in extenso* in the Detroit laboratories.

*From Edsel B. Ford Institute for Medical Research.

ABSTRACTS

Femoral expansion in aging women: Implications for osteoporosis and fractures. R. W. Smith, Jr., and R. R. Walker. *Science* 145:156, 1964.

In femoral radiographs of 2030 aging women, the diameter of the midshaft periosteum increased as cortical thickness declined. Since the cortical area enlarged, periosteal accretion exceeded endosteal resorption. Since the section modulus increased more than did cortical area, the ratio of flexural failure resistance to crush resistance increased, in apparent contrast to the changes observed in the femoral neck. The great extent to which the human skeleton involutes with age is apparent in the high incidence of spontaneous vertebral and femoral fractures in elderly women. In studying the correlation between vertebral and femoral atrophy we obtained unexpected results in respect to femoral dimensions. If changes in the tibia and fibula are found to parallel those of the femur, they may reflect a progressive adaptation to the erect state in which flexural and longitudinal compression forces on leg bones from lifelong weight-bearing decline proportionately less than do predominantly flexural forces on the arms and predominantly compression forces on the spine.

Venous autografts in femoropopliteal arterioplasty. D. E. Szilagyi, R. F. Smith, and J. P. Elliott. *Arch. Surg.* 89:113, 1964.

The clinical experience with 34 femoropopliteal ("long") and 18 femorofemoral ("short") autogenous venous bypasses is described in the treatment of advanced (grade 2 and 3) femoral and popliteal occlusive disease. The operative technical steps and the postoperative observations during observation periods of from 1 to 30 months with respect to patency rates, wound healing, as well as angiographic and histologic changes in the grafts are discussed. The immediate postoperative patency rate was comparable to that seen with other graft materials and the patency rates (checked by angiography) during the subsequent observation periods were significantly superior; during the 6- to 30-month postoperative interval only one graft thrombosed. The scarcity of angiographic changes in the older venous implants and the histologic findings in three grafts recovered at 3, 6, and 13 months and showing excellent preservation of structure, suggest that these results will be much more durable than those observed with other types of arterial substitutes.

Comparison of 6 α -methyl-9 α -fluoro-17-acetoxy-21-deoxyprednisolone with fluoxymesterone and methylprednisolone in treatment of metastatic breast cancer. R. W. Talley, M. J. Brennan, V. K. Vaitkevicius, E. L. San Diego, M. L. Reed, and G. A. Leighton. *Cancer* 17:1063, 1964.

6 α -Methyl-9 α -fluoro-17-acetoxy-21-deoxyprednisolone (oxylone acetate) was compared in a randomized double-blind study with fluoxymesterone (Halotestin) in the management of metastatic breast carcinoma. Oxylone acetate induced regressions in 6 of 23 patients (26 per cent) and Halotestin induced regressions in 3 of 23 patients (13 per cent). These differences are not significant. In a second study, oxylone acetate was compared in a randomized double-blind study with methylprednisolone (Medrol) in patients previously treated with 1 hormonal agent. Objective regressions were obtained in 3 of 13 Medrol-treated patients, and in 3 of 14 oxylone acetate-treated patients. Objective responses were obtained with these 2 glucocorticoid drugs in 4 out of 9 patients who had responded to previous hormonal therapy, but in only 2 of 18 who had failed an initial trial on either an endrogen or estrogen. Oxylone acetate at a dose of 25 mg. twice daily, produced moderately severe hypercorticoid changes. Vaginal bleeding was observed following withdrawal in several, supporting the progestational activity demonstrated in experimental animals. Oxylone acetate at this dose level does not appear to have any advantages over other hormonal agents in the treatment of metastatic breast carcinoma in the postmenopausal woman.

Localized amyloidosis (amyloid tumor) of the urethra. A. S. Ullmann, G. Fine, and A. J. Johnson. *J. Urol.* 92:42, 1964.

A case of amyloid deposition in the male urethra is reported and the literature has been reviewed for similar cases. Elevation of serum gamma globulin and increased number of adult type plasmacytes in the bone marrow were found but are not considered to be indicative of systemic amyloid deposition, multiple myeloma or Waldenstrom's macroglobulinemia.

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Submerged deciduous molars; familial tendencies. W. F. Via, Jr. *J. Amer. Dent. Ass.* 69:128, 1964.

In a study of children with submerged deciduous molars, the condition appeared to be a familial tendency and indicated that it is probably a heritable trait. There was no evidence of its being sex-linked. Siblings of children with the characteristic had a 44 per cent incidence of submerged deciduous molars, whereas nonsiblings had only a 1.3 per cent incidence.

*Utilization of ammonia nitrogen, administered by intragastric, intraperitoneal, and subcutaneous routes; effects of growth hormone. T. G. Vitti, R. Vukmirovich, and O. H. Gaebler. *Arch. Biochem.* 106:475, 1964.

Incorporation of N^{15} from ammonium citrate into proteins of liver, heart, kidney, spleen, and 3 fractions of quadriceps muscle, was studied in untreated and growth hormone-treated hypophysectomized rats. Three successive lots of animals received the same dose of N^{15} per unit of body weight, by the intragastric, intraperitoneal, and subcutaneous route, respectively. Changing the route of administration drastically altered the distribution of N^{15} between α -amino, amidine, and amide nitrogen of organ proteins. Subcutaneous injection apparently facilitated contact between labeled ammonia and the widely distributed glutamine synthetase system. When this route was used, heavy labeling of amide nitrogen in both control and growth hormone-treated rats reduced the difference between the two groups, with respect to total N^{15} incorporation. This was particularly true for liver protein, where labeling of α -amino and amidine groups decreased. When N^{15} -labeled ammonium citrate was given intragastrically or intraperitoneally, labeling of arginine, glutamic acid, and other amino acids of liver protein, was extensive, and growth hormone augmented total N^{15} incorporation into all proteins examined. Effect of the hormone on ammonia utilization appears to be related to its effect on utilization of amino acids to which ammonia is transferred.

*Studies on the respiratory chain-linked reduced NADH. IV. Transformation of the dehydrogenase into cytochrome *c* reductase-diaphorase by the action of acid-ethanol. H. Watari, E. B. Kearney, and T. P. Singer. *J. Biol. Chem.*, 238:4063, 1963.

Criteria which have been used in the literature to distinguish previously described reduced nicotinamide adenine dinucleotide (NADH)-cytochrome *c* reductases from heart have been re-examined. Several of these criteria (molecular weight based on flavin content, iron to flavin ratios, specific activity, kinetic constants for electron acceptors) were found to be unreliable, and other criteria, previously used or introduced in the present study (sedimentation velocity, absorption spectra, substrate specificity, Michaelis constants for substrates, fluorescence, identity of flavin, activation by flavin mononucleotide, and response to inhibitors), fail to distinguish these preparations. Upon exposure of highly purified NADH dehydrogenase preparations, which are virtually free of cytochrome reductase and diaphorase activities, to the acid-ethanol treatment or to prolonged incubation at 37°, under the conditions used in the literature for the extraction of cytochrome reductases, the characteristic high NADH-ferricyanide activity of the dehydrogenase is lost, and cytochrome *c* reductase and diaphorase activities emerge. The product of acid-ethanol degradation has been isolated and shown to be essentially indistinguishable from cytochrome reductases in the literature in terms of the criteria discussed above. This transformation appears to entail major changes in molecular and catalytic properties. Thus a high molecular weight enzyme is transformed to one of approximately 80,000 molecular weight; the flavin moiety becomes labile; sensitivity to inhibition by mercurials is acquired; the substrate specificity and K_m values for substrates and the absorption spectrum are changed; and the majority of the nonheme iron present is lost. Purified preparations of the mammalian respiratory chain have very little NADH-cytochrome reductase activity. The majority of this low reductase activity is antimycin A- and Amytal-sensitive and thus may represent an interaction between external cytochrome *c* or c_1 component of the chain. On treatment with acid-ethanol at 42°-44°, a large increase in cytochrome reductase activity is created with concomitant disappearance of NADH-ferricyanide activity. On subsequent digestion with phospholipase A, as in the extraction of the respiratory chain-linked NADH dehydrogenase, little or no dehydrogenase is extracted. If the dehydrogenase is first extracted with phospholipase A, however, subsequent exposure of the residue to acid-ethanol fails to elicit cytochrome reductase activity. Thus the reductase appears to originate from the dehydrogenase and does not occur, as such, in intact respiratory chain preparations. On the basis of these findings, it is concluded that the NADH-cytochrome reductases from heart described in the literature are produced by breakdown of the respiratory chain-linked NADH dehydrogenase under the conditions used in their isolation.

*From Edsel B. Ford Institute for Medical Research.

ABSTRACTS

*Recent electron microscopy of human small intestine mucosa in Whipple's disease. J. H. L. Watson, and W. S. Haubrich. Third European Regional Conference on Electron Microscopy, B:437, 1964.

In 1960 the authors described unique morphological manifestations of Whipple's disease in human small intestine mucosa and demonstrated for the first time in electron micrographs clusters of minute cylindrical bodies both within and without large histiocytes (previously referred to as "sickle-form particles containing SPC cells") exclusively and specifically within the lamina propria. This has since been confirmed by others. Our recent study of ultrathin sections has revealed the complex structure of these "Whipple's bodies" in greater detail and has given support to our earlier suggestion that they could be bacillary. Their relationship to the histiocytes suggests that they are being phagocytized and destroyed by them. Electron micrographs are shown which illustrate the major conclusions from the recent investigations, including evidence for the reproduction of the organisms by binary fission. Differential staining with uranyl acetate supports the conclusion that the interior of these organisms has a high DNA content in the unphagocytized state.

*The effects of aging and concentration upon the growth of FeOOH crystals which form Schiller layers. J. H. L. Watson, W. Heller, and L. E. Poplawski. Third European Regional Conference on Electron Microscopy, A:315, 1964.

Accounts were given earlier of the growth and structure of β FeOOH crystals in slowly hydrolyzing, FeCl₃ solutions as a function of the starting concentration, C₀, in millimoles of Fe per liter. A report is given here of how the growth of these crystals is affected by time as well as by C₀. Schiller layers were contained in the first four systems. Growth is very rapid during the first weeks in any system but becomes asymptotic after a few months. The crystal length increases with both concentration and time. There is also a distinct increase in crystal length with increasing C₀ at any given age. There are (i) a modest but consistent increase in axial ratio with increasing C₀ at any given age and (ii) no change in axial ratio with increasing age at low C₀ but a modest increase with age at higher C₀. Thus, a given crystal at low C₀ at all ages tends to grow uniformly in the *a*, *b* and *c* directions after its initial rapid growth in the *c* direction, while at higher C₀ it grows a little more rapidly preferentially in the *c* direction. The distribution curves for the crystal lengths are everywhere negatively skewed. Electron micrographs and a table illustrate the observations in detail.

Acute fatal fibrinolysis with gastric carcinoma. J. K. Welborn, M. J. Brennan, and J. C. Hathaway, Jr. Amer. J. Surg. 108:344, 1964.

Clinically recognizable hemorrhagic states due to fibrinolysis are uncommon. There are a number of case reports, however, in which bleeding associated with a variety of diseases has been attributed to fibrinolysis. These patients have exhibited marked hypofibrinogenemia and, in some instances, additional coagulation defects. It is stated that, in a study of patients with hemorrhagic complications only one patient was found whose primary clotting defect was fibrinolysis. Several others with bleeding initiated by other mechanisms also showed evidence of fibrinolysis as a contributing factor. A report of acute fatal fibrinolysis with gastric carcinoma is presented. Seven cases of gastric carcinoma associated with severe hemorrhagic states are reviewed. Possible etiologic factors are discussed. Presumptive evidence suggests that a proteolytic enzyme may activate plasminogen to initiate the fibrinolytic system.

Meaning of five-year cure in cancer of the breast. D. G. Whitney, and D. E. Szilagyi. Arch. Surg. 88:637, 1964.

Among a group of 512 radical mastectomies there were 238 five-year survivors. Survival for five years after radical mastectomy represents a probability of living an additional length of time. Survival beyond the initial five-year period carried a probability of 0.786 for 5 years, 0.579 for 10 years, and 0.164 for 20 additional years. Patients may still die of cancer of the breast after 30 postoperative years. The presence of axillary metastases at operation reduces the chance for five-year survival by 60 per cent. Postoperative radiotherapy has not increased long-term survival rates. The true salvage rate is small; in terms of 15-year survival it constitutes about 8 per cent. However, since results of this order of success have not been achieved by any other means the rationale of the operation remains sound.

*From Edsel B. Ford Institute for Medical Research.

AUTHOR INDEX

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