Abstracts

Two cases of rupture of a papillary muscle of the left ventricle are presented. We believe that these are the two longest recorded survivals of this complication of acute myocardial infarction—14 months and 11 months. A presumptive clinical diagnosis is possible from the characteristic history of sudden deterioration together with the development of a loud apical systolic murmur. The differential diagnosis and the possibility of corrective surgery in a patient who survives the acute event are discussed.


The use of insulin correctly is imperative for the assurance of good health of the diabetic patient who needs insulin. When insulin-dependent diabetes begins during adulthood, satisfactory control can generally be accomplished with a single daily dose of an intermediate insulin. We prefer Lente insulin in this situation because: there is no added foreign protein; if an adjustment of the time-action of the insulin is necessary, the ratio of slow to fast-acting insulin, using the Lente family, can be altered without abandoning the single daily injection; the regular use of a single type of insulin strengthens the confidence of the physician in its use. The physician should become proficient in the use of a minimal number of suitable preparations of insulin. Skill with a few preparations of insulin is preferred to inexperience in the use of all available preparations.


While the author was engaged in a study of the ultrastructure of the cercarial tail of Himasthla quissentensis, many observations were made on the body ultrastructure of this larval trematode. These observations have been extended, and it is the purpose of this report to describe these findings and to integrate them with observations made on the ultrastructure of the excretory system of the miracidium of Fasciola hepatica and observations on protein crystals in Lumbricus terrestris. The protonephridial excretory system of the cercaria consists essentially of a flame cell with cytoplasmic “starlike extensions” at one end of the cell and cilia projecting into the lumen of the protonephridial tubule. The mechanism of the formation of the excretory fluid is unclear, but one author has presented strong structural evidence that a filtration occurs through the cap-membrane, undoubtedly aided by the beating of the cilia which would form a current flowing from the flame cells through the protonephridial tubules. Evidence presented in this report of finger-like extensions from the internal surface of the excretory tubule would greatly increase the surface area of this internal lining and would lead one to believe that perhaps a selective reabsorption occurs in the protonephridial tubules thus allowing some control of the nature of the excretory fluid. It is to be emphasized that the only evidence presented is of a structural nature and conclusive physiological evidence is needed.


Isolation of 6-aminopenicillanic acid, the nucleus of the penicillin molecule has been recognized as an important discovery. It is now possible by modification of the side chain to prepare a wide variety of semisynthetic penicillins having differing biological and pharmacological characteristics. This report presents certain observations concerning the effect of bovine albumin and pooled human serum on the antimicrobial activity of nine penicillins, and the results of pharmacological studies on five of the nine agents. Knowledge of the fate of an antimicrobial agent in vivo is largely incomplete. It becomes apparent that reliance on determination of serum concentration and antimicrobial activity of any given antimicrobial agent by conventional methods is at best a crude index of the potential therapeutic efficacy of the agent. In lieu of more precise testing methods, it behooves the clinical investigator to carefully equate the actual effect of these agents in disease states.

Forty-three patients with suspected restenosis of the mitral valve are reported. Forty of these occurred in a series of 672 mitral commissurotomies. A significant degree of recurrent stenosis was found in 40 of the 43 cases at the time of the second operation. The clinical features and findings in these patients are discussed, as well as the probable etiologic factors. Left heart catheterization is indicated in many of these cases to define precisely the hemodynamic status, particularly in those individuals with suspected concomitant mitral incompetency or myocardial disease. Open-heart surgery should significantly improve the results of a repeat mitral commissurotomy.


Dose-response curves for cure of spontaneous mammary adenocarcinomas in C3H mice by radiation maintain their slope for over-all times of 18 days and 25 days, and also for fractions given daily, three times a week, and twice a week. Cure rates can be explained qualitatively in terms of treatment dose size, but quantitative examination shows that a given treatment dose becomes more effective with repetition. Among other possible explanations for this, the oxygen effect is suggested. A possible optimum occurs for small treatment doses given three times a week.


The effect of manganese chloride on the amelogenesis of the incisors was studied in groups of rats, guinea pigs, and hamsters. The experimental animals received subcutaneous injections of manganese chloride, and the control animals were injected with sodium chloride solutions or remained untreated. The erupting incisors were observed periodically for the appearance in the oral cavity of any defects. Only in respect to the rats were sections prepared for a histologic examination. The histologic and clinical studies revealed that defects developed in 100 per cent of the manganese chloride-treated rats. The hypoplastic enamel lesions observed clinically made their appearance in the oral cavity between the thirty-fifth and fiftieth days postinjection. No morphogenic alterations occurred. Hypoplastic enamel defects became evident clinically in the guinea-pig incisors between the fifty-sixth and seventy-third days postinjection. These faults developed in 100 per cent of the surviving animals. Only four of the upper incisors remained free from hypoplastic damage. However, all the incisors exhibited a dual grooving. These grooves manifested a disturbance of morphogenesis. In each instance, the hypoplastic pitting developed in relation to the grooves.


Primary extragenital choriocarcinoma is known to occur in both sexes, but the incidence is greater in male subjects. The primary site of the neoplasm is often difficult to establish since spontaneous regression occurs and clinically unrecognized small choriocarcinomas and teratomas of gonadal origin can metastasize. The pathologic and clinical aspects of a choriocarcinoma primary in the mediastinum of a man are described. The world literature has been reviewed and summarized with particular emphasis on the endocrine aspects of the disease; because of use of analytic methods of questionable reliability by current standards, many of the reports can be given only qualified acceptance.


Three patients with an unusual skeletal disorder are reported. In roentgenograms of the axial skeleton of all three, a bizarre coursening and disorientation of the trabecular pattern is observed. The bones of the appendicular skeleton appear to be normal roentgenologically, in marked contrast with the affected bones. Abnormal histologic changes, consisting of an increased number of widened osteoid seams compatible with osteomalacia, are present in open biopsies obtained from the iliac crest in each patient. However, the
characteristic changes in serum chemical values for calcium, inorganic phosphorus and alkaline phosphatase observed in osteomalacia are lacking. The authors consider the cases described to represent a newly recognized skeletal syndrome. The significance of the clinical findings in the condition is discussed insofar as these findings are related to concepts of bone-remodeling activity. The suggestion is made that there may be primary osteomalacic diseases caused by local cellular defects in the skeleton in addition to the known secondary osteomalacic conditions accompanied by serum depressions of calcium, inorganic phosphorus, or both.


In human lamellar bone, mineralization begins in a plane, termed the zone of demarcation, which separates osteoid seams from mineralized bone. Permanently fixed tetracycline antibiotics are deposited in the zone of demarcation in vivo, and in no other locus in lamellar bone. When certain criteria are fulfilled, precise measurements of new bone formation may be made on material labelled for known duration at known times. The tetracycline label is, in every way, comparable to labels obtainable with radiocalcium or alizarin but without any of the defects of these agents. In particular, there is no adverse effect of the drug on human bone formation and mineralization, although there may be some such effect in certain animals.


The term "humoral hypertension" was coined in the context of hypertension which follows the administration of desoxycorticosterone acetate (DOCA), pituitary extracts, and exposure to nonspecific toxins. The term is used more loosely in this report to include hypertension related to known and suspected metabolic and endocrine disturbances. The endocrine glands known to be of significance in the establishment and maintenance of blood pressure levels include the pituitary, adrenal, thyroid and gonad, all of which, with a few other factors, are analyzed.


Intractability, denoting the recurrence of progressively frequent and intense ulcer distress despite medical treatment, is the commonest primary indication for partial gastrectomy in the management of peptic ulcer disease. A majority of intractable peptic ulcers have been found to exhibit changes in pathological anatomy characterized by deepening penetration as evidenced by dense fibrous adhesion or confined perforation into contiguous structures. The complication of penetration can be predicted by an appreciation of altered symptom features, which include reference of ulcer pain to the back, the occurrence of night pain distortion in a previously established, rhythmic pattern of ulcer distress, changes in the location, spread, and intensity of anterior abdominal pain, and an increasing refractoriness to agents formerly yielding prompt relief of distress.


A case illustrating a pancreatic islet cell neoplasm associated with gastric hypersecretion and steatorrhea is described. During successive test periods, the fecal loss of fat was eliminated when all acid gastric secretions were aspirated, and was practically normal when all gastric aspirates were neutralized and returned to the duodenum. A year of remission of diarrhea followed a subtotal gastrectomy. It is postulated that the steatorrhea in this syndrome derives from an inactivation of essential digestive enzyme systems in the lumen of the small intestine.


It has been known for more than 20 years that sulfonamides are capable of producing drug eruptions and that in the production of these eruptions a photosensitivity mechanism is frequently involved. Recently, several members of the sulfonylurea group of drugs,
related to the sulfonamides by similarities in chemical structure, have enjoyed widespread usage because of their antidiabetic effect when given orally. The three sulfonylurea derivatives which in turn have been popular are carbutamide, tolbutamide (Orinase), and most recently, chlorpropamide (Diabinese). Photosensitivity-type drug eruptions produced by carbutamide and tolbutamide have been reported previously. The purpose of this communication is to report such a reaction following the administration of chlorpropamide.


With the remarkable advances in our knowledge of the physiology and biochemistry of blood coagulation in recent years, little attention has been directed at the morphology of blood clots. Notable exceptions have been studies of the structure of normal platelet-fibrin clots and the effect on structure by alteration of chemical constituents of blood. Microscopic study of platelet-plasma clots has demonstrated certain structural defects in clots from patients with diseases manifest by abnormal coagulation. Abnormally formed clots were found from patients with polycythemia vera, macroglobulinemia, Christmas disease, AC-globulin deficiency and fibrinolytic syndrome. Some of the problems imposed by the method are discussed.


On the basis of lesions observed in the arteries supplying the sinus node and A-V node in three patients with primary pulmonary hypertension it is suggested that dysfunction of these critical cardiac centers may account for the syncope and sudden death which are commonly observed in this disease.


Closure of acute and chronic wounds of the leg and foot have been discussed. The thigh has been excluded, as we have not encountered any thigh wounds that could not be effectively closed by use of skin grafts or local tissue. We have utilized common problems necessitating pedicle flap wound closure and attempted to indicate the general principles involved in the use of such flaps. We believe that the crossed extremity flap is an excellent method of obtaining pedicle flap tissue in large amounts at minimal risk. Its disadvantages are joint stiffness which is akin to that seen after major long bone fractures.


The historic and philosophic steps toward heart surgery are reviewed. The presently known heart operations are described and illustrated and the author's style is illustrated by the following quotation: "Many problems in heart surgery remain to be solved. Only a few of them can even be defined at this time. One of the most obvious is the problem of coronary artery disease. It is very likely that when anatomic localization of the arterial block is more precise and operative technique more refined, the surgeon will be able to do a great amount of good before the hardworking investigators are able to tell us how to prevent atherosclerosis. Durable plastic parts for the heart are practically with us. Transplantation of the heart may become physiologically possible when the secrets of antibody formation are known, but by that time we shall probably have an implantable plastic pump with built-in atomic power. The artificial electrical excitation of the heart with 'block' is already possible in a crude way, but small pacemaker units that can be recharged by induction are almost ready for placing in human cases."


Whole blood cannot be treated with sterilizing concentration of beta-propiolactone and ultraviolet irradiation without destroying its components. However, when the component
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parts are treated separately absolute sterilization can be obtained without appreciable loss of the physiological properties. The work with erythrocytes is most promising but requires further study. Plasma sterilization, however, has been brought to a much more satisfactory level. The laboratory studies and the clinical evaluation of treated plasma indicate complete sterilization in large volumes. It must be emphasized that the problem of sterilizing plasma was not one of inactivating the bulk of the virus. A number of methods can accomplish this, even to the destruction of 99.99% of the virus activity. It is the remaining 0.01% (or less) that keeps the plasma infective when used in transfusion volumes. It was not until we combined beta-propiolactone and ultraviolet irradiation that we were able to eliminate these trace quantities of virus and maintain a satisfactory plasma product. We feel that the results obtained with the combined procedure warrant a renewal of the human volunteer studies. It is not until this is done that we can conclusively establish the efficacy of this sterilization procedure. A word of caution must be made about the grade of beta-propiolactone used for the sterilization of plasma and other biological products. Only the "Specially Purified Grade" must be used as this contains at least 99% of the active lactone structure, whereas commercial grades may contain as much as 18% impurities and only 82% of the lactone structure.


The lesion in streptomycin and dihydrostreptomycin toxicity is limited to the inner ear. Streptomycin sulfate and dihydrostreptomycin both damage the vestibular end-organ. They do so in a selective manner in the cat, where the cristae appear to be less resistant to toxic changes than do the maculae of the saccule and the utricle. Dihydrostreptomycin toxicity is associated with a delayed permanent loss of hearing which can occur several weeks to several months following treatment with the drug.


Clinical, laboratory, and radiographic studies of 50 patients with hypertensive disease who had upper abdominal murmurs have been presented. In 66% of these cases, renal artery disease was found at lumbar aortography. Renal artery disease has been emphasized as an important cause of hypertension in man. This investigation of upper abdominal murmurs has shown a surprising incidence of renal artery disease in a selected group of patients with hypertensive disease. The known onset of hypertension in the age range for so-called "essential hypertension" was found in 51% of our cases with renal artery disease. When an abdominal murmur of high pitch is found in a patient with hypertension, even though the intravenous pyelogram is normal, renal artery stenosis is a good possibility. With intravenous pyelogram abnormalities, the presence of a high-pitched abdominal murmur is almost pathognomonic for renal artery disease in the patient with severe hypertensive disease. There is evidence that turbulence may affect the localization and formation of atheroma. Abdominal murmurs serve as a valuable clinical parameter of either actual or potential disease of the aorta or its branches.


A method is described for obtaining x-ray diffraction patterns of methacrylate-embedded specimens. This technique is useful in determining if the specimen has undergone any molecular change during the embedding procedure. Diffraction patterns, before and after embedding in methacrylate, of tungstic acid monohydrate (H₂WO₄·H₂O), ferric monohydroxy oxide (α-FeoOH) and human bone are presented. The results show no molecular changes occurred.


During the transition from the paleolithic to the neolithic period, with the expanding art of chipping, flaking and shaping of flints and stones giving man more ingenious sharp-edged, pointed weapons and tools for defending himself, obtaining and storing food, as well as making more instruments, we have the earliest evidence of a daring surgical
operation. Thus, before more advanced civilization developed in the river valleys of the Nile, Tigris, Euphrates and Indus from the tenth to the fifth millennium B.C. neolithic man roamed the western parts of Europe and left behind the single impeccable sign of prehistoric medical practice—trepanation of the skull. After many years of studying this subject, it is believed that the operation was not of a magical nature but represented an attempt to cure wounds and other painful afflictions of the head. Although many skulls operated on show evidence of previous injury or fracture, not all do. Indeed, the majority do not and are intact other than for the trepanations. A description is included of 19 skulls, and reference to 75 more (Part II will include the known technical aspects of trephining and a discussion of why it was done.)


Ultrastructural platlet dysfunction should be suspected in those patients of either sex who present with increased purpuric susceptibility after minor trauma, or with abnormal bleeding from the mucous membranes, when their platelet counts are found to be normal or elevated, and no deficiencies of their plasma coagulation factors are demonstrable. The findings that the platelets of such a patient support poor prothrombin consumption leads to a preliminary diagnosis of qualitative platelet disease. Confirmation rests, in increasing order of difficulty: in the demonstration of abnormal thromboplastin generation with the patient’s platelets as the test platelets; in the identification of deficient platelet factor 3 activity utilizing the two-stage prothrombin determination, again with the patient’s platelets as the test platelets, together with electron microscopic differentials of the suspected platelets as direct evidence of ultrastructural platelet abnormality.


There is no single “treatment” or “routine” therapy for rheumatoid arthritis, no magic pill or potion that can be substituted for thoughtful consideration of the individual patient by the interested physician. There is ample evidence that the disorder is potentially reversible, and the fact that 15 to 20 per cent of patients will have progressive disease in spite of concerted efforts should not discourage us from doing everything possible to help the 80 to 85 per cent whose condition can be improved. The plan of management suggested should produce encouraging results in the majority of cases, but only with dedicated determination on the part of both patient and physician. The plan of management is presented with a consideration of multiple general factors, chrysotherapy, steroids, intra-articular steroids, antimalarial drugs, and phenylbutazone.


Hyperparathyroidism is generally characterized by decreased bone density, mottling, granularity, and cyst formation. Osteosclerotic bone changes in both primary and secondary hyperparathyroidism are, however, not rare. Cases demonstrating such changes with dense, thick bone in the lumbar spine, pelvis, and skull are presented.


Corneal disease caused by strains of the genus Pseudomonas is a severe problem in ophthalmology. The organism is usually inoculated into the corneal layers with small metalic foreign bodies or is a contaminant in the solutions used at the time of foreign body removal. Pseudomonas finds the human corneal stroma to be a hospitable medium, and the resulting ulcer may become an unmanageable keratitis in 24 to 48 hrs. The continuous introduction of new antimicrobial agents which may be suitable for the treatment of corneal Pseudomonas infection has made imperative the development of techniques for testing these preparations. In vitro studies of some 400 strains of Pseudomonas demonstrated that polymyxin B is superior to other available agents. Therefore, the experiments reported here were designed to test its in vivo efficacy and to compare it with other drugs.

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Vincaleukoblastine (VLB), an indole-indoline alkaloid isolated from a tropical variety of the common, decorative, periwinkle plant (*Vinca rosea* Linn) was shown to be effective against mouse leukemias P1534, L1210, and AKr or ascites tumor Ehrlich and, to some extent, against the transplanted and spontaneous C3H mammary tumor as well as transplanted leukemia IRC 741 in Fischer rats and human choriocarcinoma maintained in hamster cheek pouches. In humans, VLB produced regressions in 5 of 8 amethopterin (Methotrexate)-resistant choriocarcinoma patients. A significant number of leukemia and lymphoma patients benefited from this therapy, as did a small number of patients with solid tumors. Vincaleukoblastine (VLB) was used in the management of 52 patients with solid tumors. Objective and clinically worthwhile tumor regressions were seen in cases of Hodgkin's disease and carcinomas of the lung, colon, ovary, upper airways, and stomach. There was no demonstrable correlation between the response to VLB and the response to other chemotherapeutic agents. Clinical toxicity and the effect on mitosis produced by VLB is strikingly similar to that of colchicine—but unlike that, it can be modified by concomitant administration of L-glutamic acid. The metaphase inhibition in the biopsied tumors occurred to the same degree in "VLB sensitive" and in "VLB resistant" tumors.


With the use of insulin, came the problem of hypoglycemia. While hypoglycemia has never been responsible, in the patient with diabetes, for the morbidity and mortality attendant to the chronic vascular complications, it has caused much anxiety in both the patient and the physician. Too often the spectre of its presence has permitted inadequate control of the diabetes. Yet physicians must realize that there is evidence that good control of the diabetes prevents or postpones the serious vascular complications; that the morbidity and mortality from these vascular complications far exceed those of hypoglycemia; and that hypoglycemia can be prevented without compromising the status of metabolic regulation. Currently the physician uses the oral hypoglycemic agents (tolbutamide, chlorpropamide, phenformin) as well as insulin. Chlorpropamide is the most potent oral hypoglycemic agent. However, exogenous insulin is responsible for over 99 per cent of the problems with hypoglycemia. Hypoglycemia is rare with the use of the sulfonylureas and does not occur with the use of phenformin.