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## Publications of the Staff

of the Henry Ford Hospital and the  
Edsel B. Ford Institute for Medical Research

### Titles and Selected Abstracts

Edited by G. B. Bluhm, M.D.

**Interaction of aminonucleoside-8-C<sup>14</sup> with subcellular fractions of rat kidney cortex.** P. D. Bartlett, J. F. Bossart, and C. J. Podsiadly. *Life Sciences* 8:1299-1307, 1969.

Attempts to duplicate *in vitro* experiments the *in vivo* effects of the potent nephrotoxic aminonucleoside of puromycin on mitochondrial systems involved in cellular bioenergetics have met with little success in this laboratory. To explore: (1) the possibility that this might be attributable to failure of aminonucleoside to interact with normal rat kidney mitochondria removed from their intracellular milieu; and (2) the possibility of the existence of some preferential site of binding of aminonucleoside to kidney cortex subcellular fractions, studies were undertaken of the *in vivo* and *in vitro* binding of aminonucleoside-8-C<sup>14</sup> to nuclei, mitochondria and microsomes. Utilizing a combination of equilibrium fractionation and equilibrium dialysis procedures, it was established that aminonucleoside-8-C<sup>14</sup> interacts with all three of the above fractions isolated from normal rat kidney cortex. Emphasizing the general nature and non-specificity of the binding, aminonucleoside-8-C<sup>14</sup> also interacted with normal rat kidney cortex cell membranes and with recrystallized serum albumin. During the course of induction of the nephrotic syndrome, both the specific and relative specific activities of the nuclear fraction remained constant in kidney cortex of rats treated for eight days with aminonucleoside, while activities of the mitochondrial and microsomal fractions virtually doubled. Although preferential interaction of the labeled aminonucleoside with the microsomal fraction is suggested by these results, further confirmation is required. Interaction of aminonucleoside with normal rat kidney cortex mitochondrial and cell membrane fractions is largely reversible by the simple mechanical procedure of washing.

**Carcinoma of the thyroid after external radiation to the neck in adults.** M. A. Block, J. M. Miller and R. C. Horn, Jr. *Amer J Surg* 118:764-9, Nov 1969.

Of a total of 296 patients with thyroid carcinoma, 14% were found to have received previously external radiation therapy to the neck region and nearly one-half of the patients were over 21 years of age when the therapy was administered. Of the last hundred patients, 21% had previously been given external radiation therapy to the neck region when the

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diagnosis of thyroid carcinoma was made. This suggests, therefore, that external radiation has been clinically important in the pathogenesis of thyroid carcinoma in patients of all ages. The average interval between the radiation therapy and recognition of thyroid carcinoma was 13 years, with the range being 3 to 30 years. The characteristics of the thyroid carcinomas following external radiation therapy corresponded to those usually recognized for this malignancy. Coexisting benign thyroid nodules were present in 30% of the patients. Although benign thyroid nodules can be related also to external radiation therapy, patients with thyroid nodules should be queried for such a history. Surgery appears urgent for thyroid nodules in patients who have previously received radiation therapy.

**The practical application of dose fractionation to clinical radiotherapy.** L. A. DuSault. *Radiology* 93:181-3, Jul 1969.

If radiotherapy treatments could be given two or three times a week instead of five, equipment and personnel could handle more patients and the patients would find it easier to make fewer trips to the therapy department. There is radiobiological evidence and clinical data are accumulating which suggest this is practical and effective. For instance, if the overall time of the treatment series is not changed, a 10% to 12% decrease in total dose when treatment is given three times a week instead of five will result in the same reactions, both in tumor and in normal tissues. If the change is from five to two times a week, the total dose should be reduced 18% to 20%. These statements are based on the assumption that all parts of the irradiated volume are treated at each session. Therapists are not always precise in describing their technique. "Treatment was given five times a week" may mean that the patient was treated five times a week, but various areas were irradiated in rotation. Under such conditions a much greater reduction in total dose would be required if normal tissue reactions were not to increase markedly.

**Pustular psoriasis of the scalp.** H. T. Eisenman and G. R. Mikhail. *Arch Derm* 100:598-600, Nov 1969.

A patient with a relapsing pustular eruption of the scalp with alopecia is presented. The course and histologic findings were characteristic of pustular psoriasis. Localized pustular psoriasis is known to involve the palms and soles and may occur without classical lesions of psoriasis. The case reported is of particular interest because of the exclusive involvement of the scalp, a site which, heretofore, has not been affected by chronic pustular psoriasis.

**Inhibition of horse liver alcohol dehydrogenase by L-3,3',5'-Triiodothyronine.** M. J. Gilleland and J. D. Shore. *J Biol Chem* 244:5357-60, Oct 1969.

Triiodothyronine was found to be a very potent inhibitor of liver alcohol dehydrogenase. The inhibition was strictly competitive with coenzyme (NAD or NADH) in either reaction direction. Multiple inhibition studies indicated that the triiodothyronine was competing for the site on the enzyme responsible for binding the adenine ring of the coenzyme. The high affinity of triiodothyronine for adenine binding sites may be related to its physiological mechanism of action.

**Uterine production of renin in normal and nephrectomized dogs.** A. A. Hodari, O. A. Carretero and C. P. Hodgkinson. *Obstet Gynec* 34:358-62, Sept 1969.

This experimental study demonstrates the presence of a reninlike substance in the uterus of nonpregnant dogs, increase of this substance per gram of uterine tissue during pregnancy, a higher concentration of it in nephrectomized, pregnant dogs, and higher postpartum levels in the uterus of non-nephrectomized and nephrectomized dogs than in the uterus of non-pregnant animals. These findings indicate that the uterus is the probable source of the enzyme.

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**Follicular papulopustular syphilid.** G. R. Mikhail and T. A. Chapel. *Arch Derm* 100:471-3, Oct 1969.

A case of generalized follicular papulopustular secondary syphilis is reported. The spread of infection to the central nervous system was detected by laboratory tests. The cutaneous and cerebrospinal fluid changes regressed promptly after the institution of penicillin therapy. Histological study of the cutaneous lesions showed a perifollicular tuberculoid granuloma, and necrosis with abscess formation in the outer root sheath of hair follicles. On reviewing the literature, no microscopic illustrations of this type of lesion could be found. Because syphilis may simulate many skin diseases, the value of exercising a high index of suspicion in the detection of this disease is stressed.

**Effect of long-acting parenteral corticosteroids on adrenal function.** G. R. Mikhail, C. S. Livingood, R. C. Mellinger, T. N. Paige and H. L. Salyer. *Arch Derm* 100: 263-8, Sept 1969.

The extent and duration of suppression of the pituitary-adrenal axis after single injections of three commonly used derivatives of 9-alpha-fluoro-prednisolone were studied in 13 normal subjects and 22 patients with inflammatory skin diseases. Levels of plasma cortisol and urinary 17-hydroxycorticosteroids (17-OHCs) were determined before and at few-day intervals after injection of the synthetic corticosteroid analog for six to seven-week periods. The drugs tested were triamcinolone acetonide (Kenalog IM®: TCA), triamcinolone diacetate (Aristocort Forte®: TCDA) and betamethasone acetate-phosphate mixture (Celestone®-Soluspan® Suspension: BAP). TCA in 40 mg doses decreased the plasma cortisol and the urinary 17-OHCs for as long as four weeks after injection, whereas 50 mg of TCDA and 9 mg of BAP had adrenal suppressive effects for only one week. These periods closely correlate with the duration of the clinical therapeutic effect observed with each of these preparations. The data obtained indicate that in selecting a depot-type corticosteroid for injection, it is important to take into consideration the relatively prolonged adrenal suppression that occurs with TCA as compared to TCDA and BAP.

**Growth hormone in hypersecretory diseases of the adrenal gland.** L. B. Morrow, R. C. Mellinger, J. J. Prendergast, and A. R. Guansing. *J Clin Endocr* 29:1364-8, Oct 1969.

The plasma growth hormone (GH) response to insulin hypoglycemia was assayed on 25 occasions in 12 patients with adrenal hypercorticism before and after treatment. Six of eight patients with bilateral adrenal hyperplasia were studied before treatment. GH responses were normal in four and impaired in two. Following treatment, all patients with hyperplasia augmented GH secretion normally except one who had a pituitary tumor. Growth was arrested in three patients with hyperplasia despite normal GH levels suggesting a peripheral antagonism of GH. Two patients with adrenal adenomas and one with adrenal cancer had impaired GH response. The adenoma patients reverted to normal following adrenalectomy but the cancer patient did not. The patient with virilizing adenoma had normal GH levels. The GH suppression occurred in both the high and low ACTH types of Cushing's syndrome and correlated best with the clinical severity of the disease. GH unresponsiveness following treatment may indicate pituitary tumor.

**Effects of buffer systems on the interaction of the potent nephrotogenic aminonucleoside of puromycin with rat kidney cortex microsomes.** C. Podsiadly and P. D. Bartlett. *Biochem Biophys Res Commun* 37:464-9, Oct 1969.

Study of the effects of pH on the interaction of the nephrotogenic aminonucleoside of puromycin with rat kidney cortex microsomes clearly indicates that microsomal binding of aminonucleoside is sharply reduced in equilibrium dialysis experiments conducted in the presence of the Good series of buffers, of glycylglycine and of phosphate buffers. In seeking

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a common mechanism to explain the interference of such structurally unrelated buffering systems with the binding of aminonucleoside to the microsomes, it is postulated that the interaction involves a positively charged site on the microsomes and a negatively charged functional group on aminonucleoside and on the buffering compounds. Thus, in experiments conducted in the presence of BICINE, TRICINE, TES, and HEPES buffering systems (all of which contain one or more  $-\text{CH}_2\text{OH}$  functional groups), interference with binding may be partially explained by the negatively charged  $-\text{CH}_2\text{O}^-$  grouping and similar functional groups on aminonucleoside competing for a positive site on the microsomes. However, in the case of MES, glycylglycine, and phosphate buffers, it is postulated that negatively charged sulfonic acid, carboxyl, and phosphate functional groups are mechanistically involved in such interference. These observations emphasize the necessity of being alert to side effects of buffering compounds on biochemical and biophysical parameters, and focus attention on the importance of the proper selection of buffer in *in vitro* attempts to confirm *in vivo* effects of drugs or other chemical agents on a specific reaction system.

**Some controversial topics in vascular surgery.** D. E. Szilagyi. *Amer J Surg* 118:406-12, Sept 1969.

Although the surgical procedures used in the treatment of vascular disease have gradually become more standardized over the past few years, variations continue to exist in surgical indications and in the preferences for surgical technique. Three problems in whose management some differences of opinion can still be found are discussed. The author's choices of treatment are as follows: (1) The use of autogenous (saphenous) vein graft as a bypass from groin to calf is favored in the treatment of femoro-popliteal occlusive disease. (2) In aorto-iliac occlusive involvement, bypass grafting with a Helanca-Dacron prosthesis is preferred since its ten-year results are at least as good as those with endarteriectomy and it has a much wider applicability. (3) An aggressive attitude is advocated in the treatment of asymptomatic abdominal aortic aneurysms; neither small size nor advanced age is judged to contradict surgical treatment as long as the patient's physiologic state is good enough to support aneurysmectomy.

**Solution absorptiometry with beta excited sources by means of balanced filters.** W. S. Toothacker and L. E. Preuss. *Advances in X-ray Analysis*, Vol 12, Plenum Press, 1969, pp 439-45.

The use of beta excited x-ray sources in solution absorptiometry has been reported by this laboratory. These sources produce characteristic K x-ray lines superimposed upon a bremsstrahlung continuum. The work previously reported made use of the entire beta excited spectrum. The resulting plots of  $\ln(I_0/I)$  versus concentration of solute were not straight lines, ( $I_0$  is the intensity of the x-rays after passing through the solvent, and  $I$  is the intensity after passing through both the solvent and solute), but curved downward, as is characteristic of polychromatic sources due to preferential absorption of the low energy photons. The use of a monochromatic source has two advantages for solution absorptiometry. First, the sensitivity is much greater since the K peak is of lower energy than the bremsstrahlung continuum. Secondly, the plot of  $\ln(I_0/I)$  versus solute concentration is a straight line, thus simplifying calibration. To use only the monochromatic K energy from these beta excited sources, we have applied the method of balanced filters. These monochromatic K x-rays, with the remainder of the continuum filtered out, have been employed in solution absorptiometry. The resulting plots of  $\ln(I_0/I)$  versus solute concentrations are straight lines with very good sensitivity. Using this technique, a very wide range of monochromatic energies is available for use in solution absorptiometry.

**Salary planning guide for electron microscopists.** J. H. L. Watson. *Laboratory Management* 7:26-8, Oct 1969.

Three times, in 1958, 1962 and in 1968, as Statistical Officer of the Electron Microscopy Society of America the author has collected data concerning salaries paid to electron microscopists in the United States for a number of categories of areas of work, training and

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experience. This paper summarizes pertinent sections of the statistical report for the most recent of these surveys to provide laboratory managers with a general guideline on salaries for electron microscopists. In addition to presenting the tabular data, certain important observations are emphasized concerning them. The first is the striking difference between salaries paid to males and to females in all categories and at all levels. The second is the fact that the significantly higher salary paid to those engaged in electron microscopy who have their M.D. or the Ph.D. degrees is more a function of the higher salaries paid to M.D.'s generally than it is a result of their connection with electron microscopy. A third observation concerns the relative attractiveness of the emolument for technicians in the field, a fact which, coupled with the great demand for technicians in a field with a bright future and interesting work, should encourage young people to enter it and educational institutions to provide them with the training necessary.

**Bone formation in osteoporosis.** K. Wu and H. M. Frost. *Arch Path* 88:508-10, Nov 1969.

By means of tetracycline labeling the appositional rate of new bone formation, an index of bone formation at the cellular level was determined in 50 patients with symptomatic osteoporosis. The activity proceeded at 67% of normal on Haversian, and 57% of normal on cortical-endosteal surfaces of rib biopsies taken from these patients.