

ability of glucose to regenerate reduced pyridine nucleotide during oxidation of phosphoglyceraldehyde to phosphoglyceric acid, where the hydrogen transfer likewise proceeds by way of diphosphopyridine nucleotide, may explain its effectiveness in stimulating fatty acid synthesis.

It may be worthwhile mentioning that as end products of fermentation in worms, which consume six times as much glycogen in fermentation than in respiration, in addition to lactic acid, large amounts of higher fatty acids have been found<sup>18</sup>. It is also tempting to correlate the striking accumulation of lipid in the cytoplasm of healthy growing chondrocytes with the high glycolysis present in cartilage. In conclusion, a reducing system appears to be essential for efficient lipogenesis. Excess glucose increases both glycolysis and fat accumulation in cultured cells. Augmentation of lipid vacuoles observed in cultures treated with high concentrations of hydrocortisone appears to be connected with increase of glycolysis (and depression of respiration) by hydrocortisone in high concentration.

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Zusammenfassung

Fettsäuresynthese wird durch die Anwesenheit eines glykolytischen reduzierenden Systems gefördert. Die auffallende Tendenz normaler Geweskkulturzellen zur Fettanhäufung im Zytoplasma scheint mit dem charakteristisch hohen Fermentationsstoffwechsel der Geweskkulturen zusammenzuhängen. Die Steigerung der Fettbildung durch Hydrocortison in hoher Konzentration mag auch in Zusammenhang stehen mit dessen Eigenschaft, Spaltungsstoffwechsel zu fördern.

<sup>18</sup> W. R. SLATER, *Biochem. J.* **19**, 604 (1926). – T. V. BRAND, *Erg. Biol.* **10**, 37 (1934).

\* Supported by U. S. Public Health Service grant.

Effects of Cortisone  
and Ethylenediamine-Tetraacetic Acid on  
Deposition of Promethium (Pm<sup>147</sup>)

In this investigation cortisone, which has been reported to affect bone metabolism<sup>1</sup>, was administered with the calcium salt of ethylenediamine-tetraacetic acid (CaEDTA)

<sup>1</sup> R. H. FOLLIS, JR., *Proc. Soc. exp. Biol. Med.* **76**, 722 (1951).

to enhance its effects on retention of promethium (Pm<sup>147</sup>) in skeleton and other tissues of rats.

Twelve and one-half µc of Pm<sup>147</sup>Cl<sub>3</sub> (half-life, 2-6 years) in 0.25 ml of dilute NaCl solution, pH 3, were injected intravenously into 20 young female Wistar rats (wt. range, 160–185 g). Of these rats three groups of five animals each were subsequently treated with CaEDTA and/or cortisone acetate according to the schema shown in Table I. Five rats received no treatment and served as controls.

The animals were maintained *ad libitum* on a standard stock diet throughout the 72-hour experimental period. Liver, spleen, kidney, and one femur from the killed animals were muffled and the residual ash dissolved in N/10 HCl. Samples of whole plasma, and of plasma proteins obtained by alcohol precipitation, were taken from the animals. An undecalcified femur from each animal was longitudinally transected and prepared for contact autoradiography. The sections were exposed for 72 hours at 4° C on No-screen x-ray film.

Concentrations of Pm<sup>147</sup> in aliquots of the samples were measured in a gas counter. After correcting for self-absorption the radioactivity present in the samples was compared to aliquots of the original injection solution.

*Tissue Distribution.* The concentrations of Pm<sup>147</sup> in the samples were found to be independent of the organs' weights. These data are expressed as per cent of administered dose per organ in Table II. This table also presents Pm<sup>147</sup> concentrations in plasma and plasma proteins.

In each of the animal groups the liver contained the largest fractions of the injected Pm<sup>147</sup>, in agreement with an early study<sup>2</sup>. As in a recent study<sup>3</sup> the amount of Pm<sup>147</sup> in liver was decreased by 20% by CaEDTA treatment, a difference which was statistically valid at the 99% level of significance. No effects of CaEDTA treatment on retention of Pm<sup>147</sup> in spleen, kidney or femur were detected.

In contrast to the marked localization of Pm<sup>147</sup> in liver only small amounts were found in spleen. This suggests correspondingly that there was little uptake of radio-colloidal Pm<sup>147</sup> by the reticuloendothelial components of the spleen. By inference much of the injected and circulating Pm<sup>147</sup> may have been relatively diffusible.

The table shows that, in contrast to its depressant action on early uptake by spleen and enhancement of femur uptake of radioyttrium<sup>4</sup>, cortisone treatment had no effect on Pm<sup>147</sup> uptake by these tissues. However, these

<sup>2</sup> J. G. HAMILTON, *Rev. Mod. Phys.* **20**, 718 (1948).  
<sup>3</sup> H. FOREMAN and C. FINNEGAN, *J. Biol. Chem.* **226**, 745 (1957).  
<sup>4</sup> B. KAWIN, *Nature* **179**, 871 (1957).

Table I  
Sequence of treatments following intravenous Pm<sup>147</sup> injection (a)

Time Treatment group	1	2	21	22	45	46	69	70	72
	Hours after Pm <sup>147</sup> injection								
Controls . . . . .			– No treatments –						
Cortisone <sup>(b)</sup> . . . . .	Cortisone		Cortisone		Cortisone		Cortisone		Sacrifice
CaEDTA <sup>(c)</sup> . . . . .		CaEDTA	CaEDTA		CaEDTA		CaEDTA		Sacrifice
Cortisone-CaEDTA . . .	Cortisone	CaEDTA	Cortisone	CaEDTA	Cortisone	CaEDTA	Cortisone	CaEDTA	Sacrifice

(a) Pm<sup>147</sup> Cl<sub>3</sub>, carrier-free, half-life 2-6 years. Dose: 12.5 µc/0.25 ml/animal, pH 3, in dilute NaCl.  
(b) Cortisone acetate. Dose: 50 mg/kg body weight, as 'Cortone' (Merck), 25 gm/ml with added suspending agents and 1.5% benzyl alcohol as preservative.  
(c) Calcium salt of 'Sequesterene' (Alrose Chemical). Dose 50 mg/0.5 ml/animal, pH 7.4.

Table II  
Effects of Cortisone and CaEDTA on distribution of Promethium (Pm<sup>147</sup>)

Treatment Group \ Tissue <sup>(a)</sup>	Liver	Kidney	Spleen	Femur <sup>(b)</sup>	Plasma	Plasma Proteins
	Per cent Pm <sup>147</sup> /tissue				Per cent Pm <sup>147</sup> /ml	Per cent Pm <sup>147</sup> /g
Controls, untreated . . . . .	46.6 ± 4.6	0.82 ± 0.11	0.06 ± 0.05	1.13 ± 0.26	0.60 ± 0.51	0.03 ± 0.02
Cortisone . . . . .	48.5 ± 11.8	1.00 ± 0.40	0.16 ± 0.07	1.08 ± 0.50	3.30 ± 1.62	0.05 ± 0.004
CaEDTA . . . . .	37.5 ± 2.9*	1.22 ± 0.55	0.12 ± 0.08	0.98 ± 0.37	4.08 ± 1.25*	0.06 ± 0.01
Cortisone-CaEDTA . . . . .	43.7 ± 12.0	1.03 ± 0.27	0.06 ± 0.05	1.06 ± 0.24	3.92 ± 2.23	0.001 ± 0.002

<sup>(a)</sup> Values are means from five animals expressed as per cent of administered dose of Pm<sup>147</sup> ± standard deviation of the mean.  
<sup>(b)</sup> Corrected for a measured mean value of 25 per cent for marrow weight.  
\* Compared to control group these differences were statistically significant with *P* ≤ .01.

differences may be accounted for by dissimilarities in (a) duration of experimental periods, (b) cortisone administration-sacrifice interval, and (c) chemical natures of these radioelements.

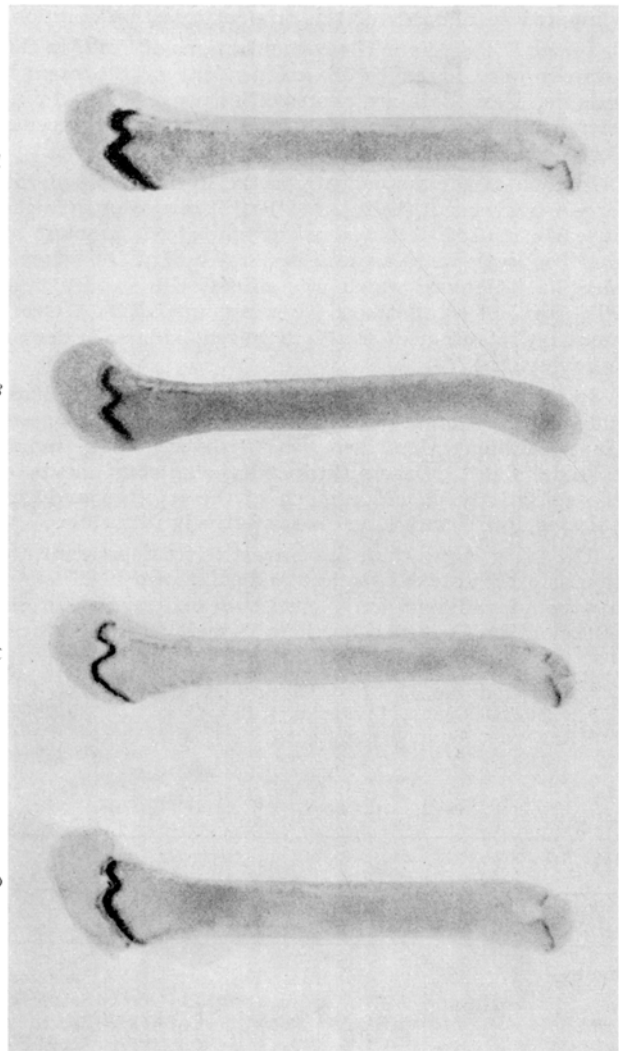


Fig. 1.—Autoradiograms of femurs from adult rats injected with promethium (Pm<sup>147</sup>) and sacrificed at 72 hours (×10). Exposed 72 hours at 4° C on Noscreen X-ray film. A, untreated controls; B, CaEDTA treated; C, cortisone treated; D, CaEDTA-cortisone treated.

In each of the treated groups plasma concentration of Pm<sup>147</sup> was increased several-fold compared to the control group. The Pm<sup>147</sup> concentrations of the plasma proteins which accompanied these increases did not vary significantly from the control group values. Thus the enhanced plasma concentrations may have been dependent on increased concentrations of Pm<sup>147</sup> not bound by plasma proteins.

**Femur Localization.** Autoradiograms of bones representative of each animal group are shown in Figure 1. In these figures the densities of deposited Pm<sup>147</sup> were not quantitated, but the resolution obtained by equal times of exposure permits comparison of the localization of this radioelement.

The localization of Pm<sup>147</sup> in a femur from the control group, shown in Figure 1 (A), is very similar to those reported earlier for other lanthanide elements<sup>2</sup>. The most intense deposition appeared to be in the zone of provisional calcification and in the region of the cancellous bone of the proximal epiphysis. These concentrations of Pm<sup>147</sup> appeared to be separated by a band of much lower concentration in the region of the cartilaginous plate. In the region of the distal epiphysis Pm<sup>147</sup> was concentrated to some extent in a single narrow transverse band. Throughout the femur shaft Pm<sup>147</sup> was diffusely distributed in marrow and in the regions of the endosteal and periosteal surfaces. Deposition of presumably radiocolloidal Pm<sup>147</sup> in the marrow region may have resulted in part from its uptake by reticuloendothelial cells<sup>5</sup>. However, the low spleen uptake of Pm<sup>147</sup> suggests that this factor may account for only a small fraction of the distribution in marrow, as compared to its apparently greater role in bone marrow uptake of colloidal radio-lanthanum<sup>6</sup>.

The autoradiogram obtained from the CaEDTA treated animals is shown in Figure 1 (B). It indicates a localization of Pm<sup>147</sup> very similar to that shown in the control femur autoradiogram.

After cortisone treatment alone Figure 1 (C) shows that the zone in the region of the epiphyseal plate in which Pm<sup>147</sup> was localized appeared to be narrowed to some degree compared to the control femur localization. This slight modification of the Pm<sup>147</sup> deposition is suggestive of the narrowing of the cartilaginous area of the epiphysis produced by cortisone administration, but establishment of a more definite relationship would require further investigation.

<sup>5</sup> C. W. ASLING, J. G. HAMILTON, D. J. AXELROD-HELLER, and B. J. LOUIE, *Anat. Rec.* 113, 285 (1952).  
<sup>6</sup> D. LASZLO, D. M. EKSTEIN, R. LEWIN, and K. G. STERN, *J. Nat. Cancer Inst.* 13, 559 (1952).

The autoradiogram obtained after CaEDTA administration with cortisone, shown in Figure 1 (D), indicates a localization of Pm<sup>147</sup> closely similar to that of the control femur.

The autoradiographic observations indicate no marked effect of cortisone and CaEDTA treatments on localization of Pm<sup>147</sup> in femur. The concurrent lack of overall effect on the total amounts of Pm<sup>147</sup> in the several tissues indicates that neither cortisone nor CaEDTA have significant therapeutic value for removal of internally deposited promethium from rats.

This paper is based on work performed under contract for the U.S. Atomic Energy Commission. Portions of the material in this paper were presented at the Fall Meeting, American Physiological Society, Rochester, N. Y., September 4-7, 1956.

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*Zusammenfassung*

Junge erwachsene weibliche Ratten, welche Einspritzungen von radioaktivem Promethium (Pm<sup>147</sup>) erhalten hatten, wurden mit dem Kalziumsalz von Äthylendiamintetraessigsäure (CaEDTA) und/oder Cortison behandelt. Die Behandlungen vergrößerten die Blutkonzentrationen von Pm<sup>147</sup> ein wenig. CaEDTA-Behandlung verkleinerte die Menge von Promethium in der Leber um 20%, aber in anderen typischen weichen Zellgeweben und im Schenkel veränderte keine der Behandlungen die allgemeine Verteilung von Pm<sup>147</sup>. Das autoradiographische Bild zeigt, dass die örtliche Verteilung von Pm<sup>147</sup> derjenigen von anderen lanthaniden Elementen ähnlich ist.

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**The Electrophoretic Distribution of Protein-Bound Carbohydrates in Asthma Bronchiale**

To investigate the electrophoretic distribution of protein-bound carbohydrates (PBC) in cases with bronchial asthma, we studied 26 patients with this disease. For each case, electrophorograms of serum-proteins (stained with bromphenilblue) and of PBC (stained with P.A.S. according to Köiw<sup>1</sup> with our modification) were performed, together with the absolute eosinophil count. The routine laboratory results (blood count; sedimentation rate, urine, etc.) were normal.

<sup>1</sup> E. Köiw and A. GRÖNWALL, Scand. J. clin. Lab. Invest. 4, 244 (1952).

No difference of interest was found in the serum protein patterns, but the analysis of the electrophoretic distribution of the PBCs gave unusual results. In 12 cases out of 26, the PBCs of the albumin-fraction were found to be definitely increased, while 11 of these cases had an eosinophil count of over 6% relat. The PBCs of the  $\alpha$ -2-globulins were also increased in 12 cases, in no correlation to the eosinophilia. A (possibly compensatory) decrease of the  $\beta$ - and  $\gamma$ -globulin PBS fractions was observed. Our results are presented in the table.

The frequency of the so-called albuminotropic type of PBC distribution is evident. This observation offers a new point of view in the allergic etiological conception of asthma bronchiale. Usually, the antibodies (in allergies and infections) are supposed to travel with the  $\gamma$ -globulines. This is the case in urticaria, where increased protein-bound hexoses in this fraction are found<sup>3</sup>.

The albuminotropic type is rather rare and can be seen in gravity<sup>2</sup> and in a few infectious diseases<sup>4</sup>, for example typhus abdominalis, where it is considered as a sign of anergy or loss of defence powers of the organism. As a rule, in asthma bronchiale, a slight increase of the protein-bound hexoses and serum mucoproteins is found<sup>5</sup>.

As asthma bronchiale can be considered a powerful and long-lasting stress, exhaustion of the suprarenal (corticoid) activity is found very often. A low excretion of neutral 17-ketosteroids and reducing corticosteroids is usual<sup>6</sup>. Such a relative hypocorticism can be the cause of the albuminotropic (or anergic, exhaustive) type in the PBC distribution.

The difference between asthma bronchiale and other allergic conditions with regard to the therapeutic effect of antihistaminic drugs could possibly be explained by the electrophoretic differences in the antibodies.

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*Zusammenfassung*

Bei Asthma bronchiale wurde in annähernd der Hälfte der Fälle die Verteilung der Polysaccharidproteine nach dem «albuminotropen Typ» gefunden. Derselbe ist in der Regel bei allergischen Zuständen nicht vorhanden und kann als elektrophoretische Abweichung der Antikörper interpretiert werden.

<sup>2</sup> F. ALLERGRA, Arch. ital. dermatol. sifilogr. venerol. 28, 36 (1956).  
<sup>3</sup> Z. STARY, Hoppe-Seylers Z. 288, 55 (1956).  
<sup>4</sup> Z. STARY, F. BURSA, O. KALEOGLU, and M. BILEN, Med. Mschr. 7, 497 (1953).  
<sup>5</sup> F. GALLETTI and G. GELLI, G. Pneumologia I, 3, 265 (1957).  
<sup>6</sup> H. LEUBNER, F. GABL, and I. RABL, Allergie und Asthma 3, 79 (1957).

Fractions	Electrophoretic patterns										Eosinophil count
	of proteins					of PBC					
	Albumin	$\alpha_1$	$\alpha_2$ globulins	$\beta$	$\gamma$	Albumin	$\alpha_1$	$\alpha_2$ globulins	$\beta$	$\gamma$	
No. of cases											
Increased . . . . .	2	4	3	2	5	12	9	12	1	2	14 (>6%)
Decreased . . . . .	2	2	2	5	2	3	3	2	9	8	
Normal . . . . .	22	20	21	19	19	11	14	12	16	16	12