*Summary.* *In vitro* clearing activity has been measured in samples of human plasma and thoracic duct lymph before and after heparin administration. When administered in amounts sufficient to cause lipid clearing activity in plasma, heparin does not produce clearing activity in thoracic duct lymph.

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Received March 11, 1960. P.S.E.B.M., 1960, v104

## Depot Fat Mobilization in Spinal Cord Sectioned and Restrained Rats.* (25751)

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The work of Goering(1), Wertheimer(2), Hausberger(3), Boecke(4) and others supports the concept that metabolism of adipose tissue is influenced by neural factors. Thus, autonomic nervous system may alter movement of fat to and from storage depots(3, 5-8). Our previous work showed that certain autonomic blocking agents prevented mobilization of fat from epididymal depots of adrenalectomized rats during fast. Surgical intervention within the nervous system eliminates ambiguities of the mechanism of blocking drug action. Therefore, spinal cord section was used as alternative tool. Since paralysis induced by this procedure alters activity of animal and the energy expended, restraining cages were used to immobilize equally both control and cord sectioned animals.

*Methods.* Male rats of Holtzman strain, weighing 90-110 g, were used. The epididymal fat pad was utilized as index of peripheral depot mobilization. Fat body removal was performed as previously described(9). Total lipids were extracted and weighed according to Bloor's method(10). The first fat depot was removed just prior to beginning of 24-hour fast. The second pad was excised upon termination of starvation. The difference between amount of extracted fat in the 2 epididymal depots determined extent of fat mobilization. Initial depot removal was altered from side to side throughout experiments. All spinal cord sections and sham operations were performed under ether anesthesia. A midline incision was made over region of thoracic vertebrae 2-4. Laminectomy was performed and spinal cord exposed, which was then severed. Muscles were sutured and skin closed with wound clips. Only those animals with complete cord transection, as determined on autopsy, were used. Sham operations consisted of cord transection procedure without actual cutting of the spinal cord. Fasting began with end of surgery. Restraint was accomplished by confining the rat within a wire screen cylinder. This prevented most bodily activity and allowed only slight movement of head. Restraint immedi-

* This investigation made with assistance of grant from Committee on Research, Council on Drugs, A.M.A. and from Eugene and Agnes Meyer Research Fn.

TABLE I. Effect of Spinal Cord Transections ($T_2$–$T_1$) and Restraint on Body Weight and Epididymal Fat Mobilization during a 24 Hour Fast.

| Procedure | No. of rats | Body wt ± S.E. | | | Epididymal fat wt ± S.E. | | | |
|---|---|---|---|---|---|---|---|---|
| | | Initial, g | Final, g | Diff., g | Initial, mg | Final, mg | Mobiliz., mg | Mobiliz., mg % |
| Intact | 91 | 99.8 ± .21 | 82.6 ± .26 | 17.2 ± .12 | 108.9 ± .8 | 87.1 ± .9 | 21.8 ± .5 | 20.0 ± .4 |
| Sham spinal cord section | 23 | 97.4 ± .83 | 81.0 ± .57 | 16.4 ± .40 | 99.1 ± 2.8 | 71.5 ± 2.6 | 27.6 ± 1.6* | 27.8 ± 1.6* |
| Spinal cord section | 24 | 96.8 ± .60 | 88.8 ± .68 | 8.0 ± .36§ | 112.4 ± 3.6 | 81.2 ± 3.2 | 31.2 ± 2.5* | 27.8 ± 2.6* |
| Intact + restraint | 21 | 97.3 ± .77 | 78.3 ± .90 | 19.0 ± .41 | 93.7 ± 2.5 | 71.6 ± 2.6 | 22.1 ± 2.0 | 23.5 ± 2.0 |
| Sham spinal cord section + restraint | 23 | 98.7 ± .70 | 78.8 ± .83 | 19.9 ± .30 | 93.6 ± 2.5 | 51.2 ± 3.1 | 42.4 ± 3.3† | 45.1 ± 3.4† |
| Spinal cord section + restraint | 24 | 96.5 ± .63 | 90.6 ± .79 | 5.9 ± .47‖ | 106.3 ± 3.5 | 92.5 ± 2.6 | 13.8 ± 1.6‡ | 12.9 ± 1.7‡ |

* $p < .01$ compared to intact.
† *Idem* , sham cord section and intact plus restraint.
†† " , spinal *Idem*
§ $p < .01$ compared to all other procedures.
‖ *Idem*

ately followed any surgical procedure and marked the onset of fasting.

*Results.* Initial mean *body weights* were approximately the same in all procedures (96.5-99.8 g). Spinal cord sectioned animals lost significantly less body weight than did intact rats during the 24-hour fast. When lesioned rats were restrained, their body weight loss was even less than that observed due to cord section alone. However, sham cord section alone and with restraint, and restraint alone resulted in weight loss comparable to that demonstrated by unrestrained intact rats (Table I).

*Fat mobilization.* Since initial epididymal fat body weights varied (93.6-112.4 mg), amount of lipid mobilized is expressed not only as absolute weight lost but also as mg% initial fat weight. Amount of fat moved out of the depots during fasting period, was increased significantly ($p < 0.01$) over control values in both sham operated and cord sectioned animals. This is not consistent with total body weight changes. Rats which were restrained but did not have sectioned cords (intact or sham operated) showed about the same degree of fat mobilization as did control animals. Combination of sham operation and restraint resulted in marked increase of movement of lipids from these fat bodies ($p < 0.01$); whereas, cord section plus restraint produced significant inhibition of fat mobilization despite fasting state (Table I).

*Discussion.* Decreased loss of body weight in cord sectioned rats is not explained only by inactivity, since restraint alone in intact and sham operated preparations did not alter total body weight loss during this short fasting period. It is impossible, however, to determine relative amounts of energy expenditure using this crude technic. Smaller body weight loss of cord sectioned rats probably reflects mainly water retention.

The acute effect of either manipulation of spinal cord (sham) or actual transection augmented fat movement out of epididymal depots. Both procedures produce an immediate firing of peripheral nerve impulses. This may account for changes observed in fat mobilization in unrestrained animals.

On this basis, it is difficult to account for inhibition of fat mobilization in animals that were restrained after cord section and for pronounced increase in fat mobilization in sham operated restrained animals. Neural excitation initiated by manipulation of intact cord seems aggravated by muscle tension produced by restraint. This cannot occur in lesioned animals where muscle tonus is eliminated. Alteration in fat mobilization has been produced by these procedures and chronic experiments are planned to elucidate mechanisms involved.

*Summary.* Male rats were subjected to spinal cord section and restraint during 24-hour fast. Both sham operation and cord section increased movement of fat from epididymal depots. Sham cord section plus restraint resulted in even greater rate of lipid movement; whereas, section plus restraint inhibited fat mobilization.

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Received March 14, 1960. P.S.E.B.M., 1960, v104.

## Fluorinated Pyrimidines XII. Effects of Simple Nucleotides on Transplanted Tumors.* (25752)

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Previous work demonstrated potent tumor inhibitory properties(1,2) of 5-fluorouracil (FU)(3) and its nucleosides, 5-fluorouridine (FUR) and 5-fluoro-2′-deoxyuridine (FUDR). Although it seemed improbable (4) that nucleotides could enter cells without breakdown, nevertheless the finding that 5 - fluoro - 2′ - deoxyuridine - 5′ - monophosphate (FUDRP) is a potent inhibitor of thymidylate synthetase(5,6) pointed to the desirability of testing this compound, as well as corresponding ribonucleotide, 5-fluorouridine-5′-monophosphate (FURP), against transplanted mouse tumors. FURP was prepared enzymatically by Dahl *et al.*(7), and chemically by Farkas *et al.*(8). However, the method of Gilham and Tener(9) appeared more convenient, and we have prepared gram quantities of FURP and FUDRP by this procedure. The synthesis will be described elsewhere, and we are greatly indebted to Dr. Tener for making the details available to us prior to publication. The 2 nucleotides have been tested at various dosages against 3 transplanted mouse tumors, and compared with equimolar amounts of the corresponding nucleosides. We are not aware of any published reports on tumor-inhibitory activity of nucleotides of purine or pyrimidine analogs.

*Methods.* Nucleosides, FUR and FUDR, were kindly supplied by Dr. Robert Duschinsky of Hoffmann-LaRoche, and were converted chemically into nucleotides, FURP and FUDRP(9). Female Swiss mice were obtained from A. R. Schmidt Co., Madison, Wis., and used for Sarcoma-180 and EF Ehr-

* This work supported in part by grant from Am. Cancer Soc.; National Cancer Inst. and from Hoffmann-LaRoche