and degree of binding of the EAE globulins corresponded to the distribution of myelin in the sections stained with Luxol blue, thus suggesting that the presence of myelin is required for binding to occur.

In control studies, the sera of animals with "allergic" encephalomyelitis did not bind to sections of rabbit liver or kidney. Prior absorption of EAE sera with rabbit spinal cord removed the specific fluorescence, whereas similar treatment with rabbit liver had no effect. Specific fluorescence was not obtained with any of the sera from rabbits injected with liver or bovine serum albumin in combination with Freund's adjuvant or from rabbits injected with the adjuvant alone. Negative results were also obtained with the sera of rabbits with acute nephrotoxic nephritis and with the potent anti-rabbit-kidney serum (chicken) used to produce the nephritis. Fluorescein-labeled anti-chicken gamma globulin was used for detection of the latter.

There is considerable evidence, as summarized by Waksman (*4*), that the pathological lesions of "allergic" encephalomyelitis are a manifestation of delayed hypersensitivity and associated with cell-bound antibodies. However, it is likely that circulating antibodies may play some role in its pathogenesis. Bornstein (*2*) demonstrated in vitro a circulating toxic factor, and Paterson *et al.* (*5*) have recently presented evidence for a circulating factor in the serum of rats that have recovered from "allergic" encephalomyelitis which, when passively transferred, protects other rats against developing the disease. This factor may be an anti-brain antibody, with properties similar to the "enhancing" factor demonstrable in tissue-transplantation studies, which appears to protect the transplant against rejection by the host animal (*6*). The sera of our rabbits with experimental "allergic" encephalomyelitis possessed a factor capable of binding specifically to myelin. This serum factor exhibits all the properties of an organ-specific antibody. The localization of the antibody to myelin assumes added significance in view of the fact that the encephalitogenic antigen is considered to be a myelin constituent (*4, 7*).

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Effect of Estradiol on the Transfer Rate of Small Molecules into the Rat Uterus

Abstract. The uterus-to-serum distribution ratio has been studied for urea-C^{14} as a function of time, and for sucrose-C^{14} at an early time after injection of the substance into rats. For both substances, estrogen influences the rate of passage between plasma and uterus.

One mechanism proposed for the biological action of estrogens has been an effect on the permeability of the uterus. There has been little experimental work that bears directly on this theory, largely because of the many variables present when the target organ is studied in its natural environment. At least three physical changes occur in the rat uterus soon after estrogen treatment: there is an increase in water content (*1*); there appears to be an increase in capillary permeability (*2*); and there is an increase in blood-flow rate (*3*). In a recent paper (*4*), Halkerston *et al.* concluded that no changes in permeability of the uterus could be found 1½ hours after injection of estradiol into ovariectomized, nephrectomized, and adrenalectomized rats. Their measurement of "permeability" was the distribution ratio (tissue to plasma) of C^{14}-labeled materials (including sucrose-C^{14}) 90 minutes after the injection of the tracer. Since their work has been quoted in the recent literature (*5*), it seems worth while to re-examine the problem before the proposed effect on permeability is discarded.

The critical process is really the "flux" (*6*) of a substance across a biological barrier, and not the "steady-state" relation between levels in blood and tissue which is achieved some time after the tracer is injected. Since the small molecules used in this type of study enter the uterus very rapidly, it is almost impossible to obtain tissue levels that increase with time; the die-away curve in plasma is so steep that a downhill gradient may exist between tissue and plasma which favors loss of the tracer material from the tissue. Nevertheless, one can get tissue-to-plasma ratios quite early after the administration of a tracer substance and examine these as a function of time.

Ovariectomized Long Evans rats weighing 200 to 250 g were given 2 μg of estradiol in saline intravenously 1 hour before sacrifice; the controls received saline. Experimental and control animals were anesthetized with pentobarbital (50 mg/kg, injected intraperitoneally) and then given urea-C^{14} intravenously (3 to 5 μc) from 0 to 10 minutes before sacrifice. In one set of experiments rats received 3 to 5 μc of sucrose-C^{14} 3 minutes before sacrifice. At the time of sacrifice a blood sample was obtained by heart puncture, the aorta was severed, and the uterus was removed. The serum was collected from each blood sample, the serum proteins were precipitated with 75-percent ethanol, and a sample of the supernatant was saved for assay of radioactivity. After weighing, the uterus was placed into a vial containing 1 ml of distilled water, and the vial was stored overnight in the refrigerator. A sample of the water from this vial was used to assay for radioactivity in the uterus. (It was demonstrated that equilibrium between tissue and aqueous phase had occurred by homogenizing

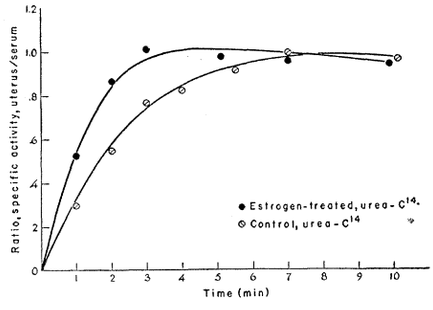

Fig. 1. Distribution ratios between uterus and serum for urea-C^{14} as a function of time after injection of tracer. Open circles, animals that received saline 1 hour before time of sacrifice; solid circles, animals that received estradiol 1 hour before time of sacrifice.

Table 1. Uterus-to-serum ratios of urea-C^{14} and sucrose-C^{14} 3 minutes after injection. The differences between means for each substance (controls as against experimental group) is significant at $P = .01$ for urea and at $P = .001$ for sucrose. There were six rats in each group. The ratios for sucrose distribution are less than those for urea; this is due to the larger volume of distribution of urea.

Group	Mean ± S.E.
Urea-C^{14}	
Control	0.69 ± 0.09
Estrogen	1.02 ± 0.04
Sucrose-C^{14}	
Control	0.38 ± 0.01
Estrogen	0.46 ± 0.01

the tissue and precipitating protein; supernatant from this procedure was assayed for radioactivity and found to yield the same results as that obtained by the "diffusion" method outlined above.) Counting of radioactivity was performed in a liquid scintillation counter.

In Fig. 1, the ratio counts per minute per milligram of uterus to counts per minute per microliter of serum is plotted as a function of time after the injection of urea-C^{14} in animals that were injected with estradiol or saline 1 hour before sacrifice. It is apparent that there is no clear difference in the tissue-to-serum ratio after about 5 minutes. It is also clear that there is a steeper slope toward a ratio of unity for the estrogen-treated animals than for controls.

It was the purpose of the next set of experiments to evaluate this estrogen effect in quantitative terms. For this purpose all animals were killed 3 minutes after the injection of a trace amount of urea-C^{14} or sucrose-C^{14}, and 1 hour after estrogen or saline administration. Results for these two tracers, studied in separate groups of animals, are given in Table 1. The results show a significant difference between control and experimental groups for each radioactive substance. The tissue-to-serum ratios are higher in each case where the rats had received estrogen.

On the basis of the foregoing results it is contended that there is an increased rate of equilibration of small molecules between uterus and serum as early as 1 hour after estradiol treatment. Examination of plasma levels of each tracer as a function of time after injection revealed no apparent difference in the die-away curves for estrogen-treated and control animals. The results do not prove that there is enhanced permeability of the uterus, since we have been unable to determine the influence of changes in blood flow. Even the "increased capillary permeability" mentioned above may be a reflection of an increased blood-flow rate. In an earlier report it was demonstrated that uterine blood flow is markedly enhanced 4 hours after estradiol administration (*3*); in a few experiments we have found an increased blood flow as early as 1 hour after estradiol injection.

It thus appears that there is no basis for a categorical dismissal of a proposed estrogen effect on permeability of the uterus at the present time. At the same time the point should be made that the rate of access of small molecules into the uterus is enhanced by this hormone (*7*).

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Potassium-Argon Age of Devils Tower, Wyoming

Abstract. Devils Tower consists of columnar phonolite porphyry which contains large phenocrysts of orthoclase. Potassium-argon determinations on the orthoclase indicate an age of 40.5 million years ± 4 percent. This is consistent with the geologically accepted Tertiary age.

Devils Tower, located in the northeastern corner of Wyoming, stands about 1800 m above its immediate surroundings and has a diameter of about 2400 m at its base (*1*). Vertical columnar jointing causes its steep sides to be fluted (Fig. 1). The tower itself and the talus surrounding its base have been classified as phonolite porphyry (*2*).

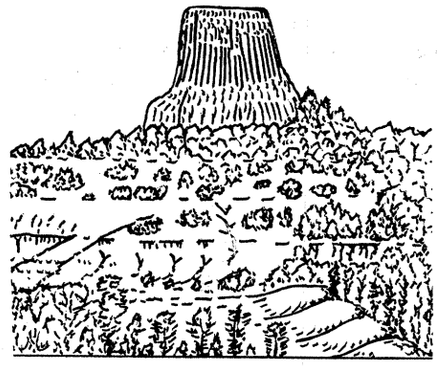

Fig. 1. Devils Tower, Wyoming, from the south. [P. F. Kerr]

Soda-rich orthoclase phenocrysts range from 6 to 12 mm across and offer suitable material for potassium-argon age determinations.

Devils Tower lies in a region of Triassic and Jurassic sedimentary strata. In Fig. 1 the flat valley in the foreground is the Gypsum Spring formation (Triassic), and the cliffs in the middle distance are members of the Sundance formation (Jurassic). The tower itself is considered to be Tertiary on geological evidence (*3*).

A sample of phonolite porphyry was crushed and sized, and the orthoclase phenocrysts were separated from the rest of the rock by means of an isodynamic magnetic separator. The potassium content of the orthoclase was found, by flame photometric determinations, to be 4.88 percent. Two mass spectrometric determinations of the argon-40 by the isotope dilution method gave 8.04×10^{-6} and 7.86×10^{-6} cm^3/g (STP). Ages calculated from these values with constants $\lambda_e = 0.585 \times 10^{-10}$ yr^{-1} and $\lambda_\beta = 4.830 \times 10^{-10}$ yr^{-1} (*4*), are 41.0 million years and 40.0 million years, respectively. The average of these two values places the probable age of the Devils Tower phonolite porphyry at about 40.5 ± 1.6 million years (*5*).

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