pass through the blind spot and the spot corresponding to the blind spot of the other eye.

The intensity of the stimulus light may be set for purposes of replication by adjustment so that the average reaction time is, for example, 144 msec at 15° on the temporal retina on the horizontal meridian. When RT is plotted against retinal location a curve can be obtained throughout a wide range of intensities, but the stimulus must be neither excessively bright nor very dim (*2, 3*).

Two observers, WP, 29 years, and JA, 24 years, reacted to the stimulus by initiating a fixed 2-second foreperiod and then by lifting a stylus as soon as the stimulus appeared. Visual reaction time was measured in milliseconds and automatically recorded on printed paper tape. The observer was given access to a switch which enabled him to nullify any error of response which he felt he may have made. The observer was seated in a black room with a background illumination of 0.03 millilambert. His head was held steady by a combination chin and cheek rest. The two observers using each eye made 30 RT's on each of four running orders at each of 32 retinal locations (Fig. 1).

The data obtained from the two eyes were so similar that averaging was warranted. Approximately 95 percent of the means would be expected to fall within these limits if the experiment were repeated.

The lowest RT's are found on the spot corresponding to the blind spot of the other eye and on the upper retina (where objects on the ground are seen). Long RT's are found about the 50° and 240° half-meridian. This is interesting since the count of rods and cones in the human eye, as judged by the count on one eye of a teenage boy in 1935, disclosed that the number of rods decrease most rapidly along the meridian from 45° to 225° (*4*). The average of the RT's at the 270° half-meridian is significantly shorter than the average of the surrounding RT's. Increased sensitivity along this half-meridian might be helpful in protecting the human head from objects above. Retinal locations along the meridian from 90° to 270° are serviced by both lobes of the brain, but no decrease in RT at 90° is noted.

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Depression of Circulating Interferon Response in Balb/c Mice after Urethan Treatment

Abstract. *Urethan, when given to female Balb/c mice, impaired the capacity of these animals to produce circulating interferon. The effect appeared rapidly after a single injection of either 1 or 1.5 milligrams of urethan per gram of body weight and was of short duration. The possibility that this inhibition of the production of interferon plays a role in the enhancement of viral leukemia by urethan should now be considered.*

The resistance of mice to some viral infections can be decreased significantly by treating the animals with urethan (ethylcarbamate). For example, by administering urethan, Mirick *et al.* (*1*) could increase the severity of infection with mouse pneumonia virus in Swiss albino mice, while Braunsteiner and Friend (*2*) increased the susceptibility of mice of different strains to infection with mouse hepatitis virus. Similar results have been obtained with leukemia viruses. Induction of leukemia by Graffi virus in adult C57Bl mice was greatly enhanced if the animals were injected intraperitoneally with urethan after having received the virus (*3*); and treatment with urethan also increased the susceptibility of C57Bl mice to radiation leukemia virus (*4*).

There are no indications as to the mechanism by which urethan can influence the host-virus relation in favor of the latter. The phenomenon is an important one, since urethan is also a carcinogen (*5*) and, in our opinion, the possibility exists that its properties of inducing (*6*) or promoting (*7*) leukemia are related to its capacity to impair defense mechanisms against virus infection. We investigated the possibility that urethan decreases interferon production in mice; interferon is an antiviral protein appearing in animals during virus infection (*8*), and other carcinogens, such as polycyclic aromatic hydrocarbons, decrease the synthesis of this virus inhibitor in tissue culture (*9*).

Mice for our experiments belonged to the inbred Balb/c strain. The capacity of these animals to produce interferon was determined by injecting 0.2 ml of a suspension of either Newcastle disease virus (NDV) or Sindbis virus intravenously, by way of the orbital sinus (*10*). Between 0.4 to 0.6 ml of blood was withdrawn 5 hours later from the orbital sinus of each animal. The samples were left in the syringes and were allowed to coagulate overnight in the icebox; they were then centrifuged for 30 minutes at 3000 rev/min in the sealed cylinders of the plastic syringes. Individual serums were collected and stored at –20°C until the time of titration for interferon. Titration was carried out as follows: serial fivefold dilutions of either each serum separately or of pooled serums were made in tissue culture medium and put on monolayers of L cells (*11*) grown in plastic petri dishes. Two or three cultures were incubated overnight with each serum dilution. The challenge virus, consisting of approximately 80 plaque-forming units of vesicular stomatitis virus (VSV), Indiana strain, was then added. Cultures were covered with a nutrient starch gel (*12*) 1 hour after the addition of the challenge virus; 48 hours later VSV plaques were counted. The interferon titer of the serum was expressed in units, one unit corresponding to the amount of inhibitor necessary to decrease the number of challenge plaques by 50 percent. Viral inhibitory activity of these serums could be destroyed by trypsin; it was not diminished when high-titered antiserums, made against the interferon-inducing virus, were added to the test system. Furthermore, antiviral activity was species specific, since no activity was found when serums were assayed against VSV in chick embryo fibroblast cultures. These properties indicate that the inhibitor we were measuring belonged to the class of interferons (*8*).

Adult Balb/c females, weighing between 20 and 25 g, were injected intraperitoneally with urethan (*13*) dissolved in phosphate buffered saline (PBS). Four groups of mice received a dose corresponding to 1 mg per

Table 1. Effect of urethan on interferon induced by Newcastle disease virus. A first group of six control animals was injected with phosphate-buffered saline (PBS) at the same time that the 72-hour group was injected with urethan; a second group of six control animals was injected with PBS at the same time that the 24-hour group was injected with urethan. Each serum pool was derived from the serums of four different animals, except for the control groups, in which six animals were used.

Time after urethan injection (hr)	Interferon titer of serum pools (unit/1.6 ml)	Percent of control value*
Controls (1st group)		
	4750	
Controls (2nd group)		
	4170	
Urethan-treated animals (1 mg/g)		
12	725	16
24	1380	31
48	4800	107
72	3500	78
Urethan-treated animals (1.5 mg/g)		
12	870	19
24	360	8
48	3500	78
72	4750	106

* Mean titer of the two control groups was taken as the 100-percent value.

gram of body weight, and four groups received 1.5 mg; two groups were injected with 0.2 ml of PBS only. Urethan injections of the different groups had been spaced in such a way that the interferon-inducing virus could be given simultaneously to all animals, at a time corresponding to 12, 24, 48, or 72 hours after the urethan. At this time, the animals of all ten groups were injected with NDV, and the interferon appearing in the circulation was determined for each group, with the use of pooled serums. Results of this experiment (Table 1) show that pretreatment with urethan significantly decreased the amount of circulating interferon that appeared after injection of NDV; the effect was most pronounced when the virus was given 12 and 24 hours after administration of the urethan and had practically disappeared after 48 hours.

In the foregoing experiments, the interferon content of the blood was measured between 5 and 6 hours after injection of the virus, since preliminary studies and work by others (*10*) had shown that at this period concentrations of interferon in the circulation are maximum. However, the possibility could not be excluded that, for some unknown reason, the peak of circulating interferon in the urethan-treated animals appeared at a time different from that in normal animals. In this case, the lower concentrations of interferon found in urethan-treated animals would not be a reflection of an impaired capacity to produce interferon, but simply a result of different kinetics of its release into the circulation. To investigate this possibility, we carried out an experiment in which concentrations of serum interferon of control and urethan-treated animals were followed during 48 hours. A group of adult female Balb/c mice were injected intraperitoneally with urethan (1.5 mg per gram of body weight), and the control mice were injected with PBS only; 15 hours later, all animals were injected intravenously with NDV. Four urethan-treated and four control animals were bled 2, 6, 12, 24, and 48 hours after the injection of virus, and the interferon content of the serum was determined separately for each animal (see Table 2). The kinetics of the appearance of circulating interferon were identical in control and urethan-treated mice, the maximum amounts being found in both groups 6 hours after injection of the virus. The concentrations of interferon in serum were consistently lower in the urethan-treated animals. This allows us to conclude that the diminished production of interferon in urethan-treated animals, observed in the first experiments, is real, since in both groups the titer of circulating interferon was determined at its highest level.

The results obtained with NDV were subsequently confirmed when Sindbis virus was used, instead of NDV, as an inducer of interferon formation. The amount of circulating interferon produced by urethan-treated animals (1.5 mg per gram of body weight) was reduced to approximately 36 percent of control values 12 hours after injection of the carcinogen. The effect, however, was of shorter duration than when NDV was used, since 24 hours after the injection of urethan the capacity to produce interferon was returning to normal (Table 3).

Results of our experiments demonstrate clearly that a single injection of urethan, at a dose of either 1 or 1.5 mg per gram of body weight, is capable of decreasing the amount of interferon produced by Balb/c mice upon injection of either NDV or Sindbis virus. The inhibitory effect appears quite rapidly, being most pronounced 12 and 24 hours after injection of the carcinogen, for Sindbis and NDV, respectively. Furthermore, this effect is of short duration, the production of

Table 2. Kinetics of interferon appearance after injection of Newcastle disease virus. Each value represents the mean titer of four different animals. The highest and lowest titers of each group are given in parentheses.

Time after injection of virus (hr)	Interferon titers of serum from mice (unit/1.6 ml)	
	Control	Urethan-treated
2	200 (110, 300)	150 (70, 250)
6	1270 (1050, 1660)	360 (260, 560)
12	890 (525, 1820)	300 (200, 380)
24	130 (0, 200)	0
48	0	0

interferon in the animals having returned to essentially normal values 48 hours after administration of the carcinogen. The mechanism by which urethan decreases the formation of interferon in vivo was not examined. We are considering, as a possible explanation, the well-documented cytolytic effect of urethan (*14*), which could cause a destruction of interferon-producing cells; an elucidation of the nature of these cells is now being attempted.

Interferon has been shown to protect animals against the induction of tumors with polyoma (*15*) or Rous sarcoma virus (*16*) and to inhibit malignant transformation by SV40 virus in vitro (*17*). In these studies, the protective effect was obtained by giving the interferon prior to the virus; much less information is available concerning the influence of interferon made during the course of an infection with a tumor virus on the outcome of this infection. Therefore, at the present time, only a hypothetical role can be ascribed to the inhibition of the produc-

Table 3. Effect of urethan on interferon induced by Sindbis virus. Each value represents the mean titer of four different mice. Highest and lowest titers of each group are given in parentheses. The dose of urethan was 1.5 mg per gram of body weight.

Time after injection of urethan (hr)	Interferon titer of serum (unit/1.6 ml)	Percent of control value
12	250 (125, 440)	36
24	330 (160, 440)	48
48	610 (400, 800)	88
Controls	690 (480, 870)	

tion of interferon as part of the mechanism by which urethan exerts its enhancing effect on viral leukemia. It will be possible to judge the validity of this hypothesis only when sufficient information about the interaction of endogenous interferon and leukemia viruses is available.

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Training without Reward: Traditional Training of Pig-Tailed Macaques as Coconut Harvesters

Abstract. Macaca nemestrina, *the pig-tailed macaque, is the only monkey regularly and extensively used for work. For centuries it has been trained in Southeast Asia to pick coconuts and other fruits. The training is based exclusively on punishment and avoidance of punishment.*

Macaca nemestrina is found in southern Burma, Tennasserim, the Malay Peninsula, and on the islands of Banka, Sumatra, Java, and Borneo. The monkeys are used to pick coconuts wherever the height of the trees makes the work uneconomical and dangerous for men. They provide the only contemporary example of an infra-human primate being trained as an agricultural laborer. Wild macaques, preferably males 1 or 2 years of age, are trapped in the jungle and kept tied in or near the house. They are not truly domestic animals, as their breeding is not controlled. The monkeys are generally trained during their third year, when they are less emotional than infants and easier to handle than adults, yet when they are capable of almost as much concentration as adults. During their fourth year the males begin to grow canines which may become as long as 6 cm. Their strength increases and their temperament becomes somewhat unreliable. Most of the animals who are trapped as adults do not learn to work and must be released or sold.

For 10 days in February 1966 I observed the training of two pig-tailed macaques and the work of three others in four villages in southern Thailand. The training is divided into three stages in which the subject learns: (i) to spin the coconut so as to twist the rough stem, which weakens the fibers enough to enable him to bite through them, (ii) to climb up a tree, work, and climb down according to the trainer's commands, and (iii) to distinguish various stages of ripeness of the coconuts so as to detach only the required type.

The most difficult part of the training is the first stage. The main problem consists in keeping the monkey interested in the coconut, which is too hard to bite or to eat. To induce the monkey to maintain contact with the coconut, the trainer ties him to a wall with a leash so short that the monkey must remain standing. The trainer sits facing him, with his legs on either side, in a position to unbalance the monkey with his feet. He passes the leash around his neck and holds it between his toes; this enables the trainer to increase the pressure on the collar of the monkey by shortening the leash. If the monkey struggles or attempts to escape, he can punish him by unbalancing him, choking him, and sometimes also by beating him. A coconut or other hard inedible fruit is suspended between the monkey and the trainer. When unbalanced or choked, the monkey tends to grab at the fruit for support. The trainer rotates the coconut so that the monkey feels the circular movement beneath his hands; then he holds the hands of the monkey and makes him spin the coconut. This is repeated until the monkey begins to rotate the coconut by himself. As soon as he does so, the trainer gives him more leash and moves away from him. The trainer makes the monkey practice; at the same time he cuts the string occasionally, so that the monkey associates the fall of the coconut with the twisting motion. If the monkey stops spinning, the trainer points at the coconut with his whip, a threat which generally results in the resumption of training. The monkey is also taught to spin the fruit backward, and to bite the stem on command. He first bites the stem, as well as other nearby objects, spontaneously and often just after he has been punished. This may be redirected aggression. Whenever the monkey bites the stem, the trainer says "Bite," and the word becomes associated with the act so that the monkey learns to bite the stem when the trainer gives the order. A few other commands are continually repeated beginning with the first lesson.

After the monkey has learned to twist the coconut, he is taken to a long pole from which a coconut is suspended. He learns to go up and down the pole on command, and to twist off the coconut while clinging to the pole (Fig. 1). This is the easiest part of the training and is often mastered in one lesson. The monkey climbs up willingly—indeed it is quite a natural thing for a pig-tailed monkey to do. The monkey is more reluctant to come down, but he has learned that he cannot resist a strong pull on his chain, and he usually does not attempt to do so. Monkey and trainer then climb up a small tree. The monkey is usually confused because he is faced with a compact cluster of nuts instead of a single one. He also may try to escape, since he is in a tree for one of the few times since his capture. Even though he was very obedient on the ground or on the pole, he may go as far away from the trainer as the chain will permit, jump around, or cling to a palm and refuse