

mg/kg, the rates of responding under the FI component were within the control range. During subsequent sessions, as the dose was increased to 20 times the original dose, rates of responding fell below those of controls infrequently. During some sessions, however, administration of Δ^9 THC did increase the rates of responding relative to the control rates of responding after Triton X 100. Similar rate increases during the FI component of a mult FI FR schedule have been observed after daily injections of morphine and methadone in pigeons (6), but rate increases have not been observed with pigeons for Δ^9 THC when injections were widely spaced during the determination of dose-effect curves (2), although rate-increasing effects of tetrahydrocannabinols also have been observed in monkeys when shock-avoidance procedures were used (10).

Doses of Δ^9 THC of 10 mg/kg or higher were given for 8 days after the 28 days shown in Figs. 1 and 2, and then administration was discontinued. Although small changes in the rates of responding were observed when the drug was withdrawn, no gross behavioral symptoms suggesting a withdrawal syndrome could be detected, nor did the general health of the pigeons seem to be impaired during or after long-term administration. Bird 6512 was given 10 mg/kg (from the same sample of Δ^9 THC used previously) after 4 weeks during which no injections were given. Much of the tolerance to this dose had disappeared during the 4-week period, since bird 6512 responded at a rate of 0.07 response per second during the FI component and at a rate of 0.18 response per second during the FR component.

During the course of these experiments, the purity of the Δ^9 THC was established both by gas chromatography and by injections of the solutions used into birds (6640 and 5117) that had not previously received Δ^9 THC. Table 1 shows the effects of 5.6 mg/kg in bird 6640. The injection was drawn from the same sample used to inject the two pigeons in the tolerance study. The table shows that the 5.6 mg/kg dose, which did not decrease responding under either schedule component in the tolerant birds, completely eliminated the responding of bird 6640 2 hours after injection, and effects could still be seen 48 hours after injection. In another experiment, a dose of 36 mg/kg was given to bird 5117. Within

2 hours this bird could not stand, walk, or fly normally and refused food. At 8 hours after the injection, the bird lay on the cage floor with labored respiration. The bird did not stand up until 48 hours after the injection, and he did not eat until 72 hours after the injection. Yet this dose (36 mg/kg) had no effect on schedule-controlled behavior in the tolerant birds.

Our experiments demonstrated that a dose of Δ^9 THC which completely disrupts food-reinforced responding in pigeons for many hours can be increased more than 20-fold without disrupting this schedule-controlled behavior in tolerant birds. Since no behavioral effect was obtained at this very large dose, the 20-fold increase probably does not represent the limits to which tolerance to Δ^9 THC can develop. The degree of behavioral tolerance we obtained in these pigeons is more like that reported for morphine in animals (11) than like the lesser degree of tolerance which develops to the barbiturates in animals and man (12). The pattern of the development of tolerance to Δ^9 THC is similar to that seen with morphine and methadone in similar behavioral experiments with pigeons (6), both in the rate of the development of tolerance under the FI component and in the appearance of rate-increasing effects during long-term administration.

Previous failures to demonstrate development of tolerance to the effects of marihuana in man and animals (4, 5) may have been related to the route of administration, the purity of the drug preparation, or to the species. Although our data do not determine the relative importance of each of these

variables, and therefore limit any generalization of our results to man, they do indicate that a tolerance resembling somewhat that seen with narcotics, can develop in pigeons when Δ^9 THC is given parenterally at high doses.

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Many Responses per Food Reward with Free Food Present

Carder and Berkowitz (1) showed that, when ten lever presses were required to produce one pellet of food, rats ate freely available pellets almost exclusively and rarely pressed the lever. They also confirmed Jensen's (2) original finding that when each press was immediately reinforced with a pellet, rats frequently pressed a lever although free pellets were continuously available. In an extension of work previously reported (3), I found that pigeons behaved in essentially the same way. With free grain present, pigeons responded to a disk if the fixed ratio of responses

to grain reinforcements was less than 5 : 1 but did not respond significantly if the ratio was greater than 10 : 1.

Under a different procedure, however, the pigeons pecked a disk more than 40 times for each food reinforcement while free identical food was available. Three male White Carneaux pigeons, with previous experiences in a variety of operant-conditioning experiments, were maintained at 80 percent of their normal weights. The subjects received 15 preliminary sessions on a 1-minute variable-interval schedule of reinforcement. On the average of

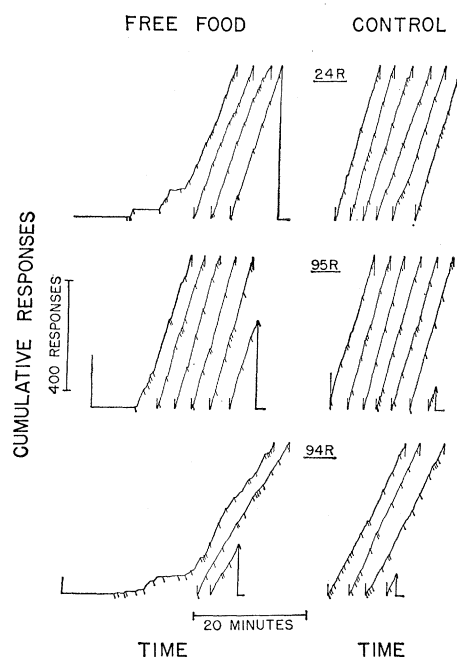


Fig. 1. Cumulative response records showing the second free-food session (24R), the third free-food session (95R), and the last free-food session (94R). Paired control sessions preceded the free-food sessions by one day. Slash marks indicate the presentation of grain in the hopper.

once per minute, a peck to a lighted response disk produced 4 seconds of access to grain in a lighted hopper (see 3). A session ended when the bird obtained 45 reinforcements. During the first "free food" session, the procedure was identical except that a cup filled with about 240 g of grain was placed in a rear corner of the chamber. Thus, there were now two sources of identical food. The apparatus was turned on (the response disk was lighted, and so forth) only after the bird began to eat the free grain. All birds behaved similarly. They ate the free grain continuously for a few minutes, then turned around and pecked the disk to produce hopper grain. During the next few minutes, the subjects occasionally returned to the cup of free food, but they then ignored the free food, pecked the disk at relatively high frequencies, and ate grain from the hopper until the programmed 45 reinforcements were obtained. The cup of free food was about half-filled with grain at the end of each session. After returning to 80 percent of normal weights (about 4 days later), the birds received one control session under the variable-interval schedule alone (no free food), followed the next day by a session with free grain again available. This same sequence was repeated three

more times. During the five free-food sessions, subjects 95R, 24R, and 94R responded on the average of 64, 40, and 26 times, respectively, for each reinforcement. The averages during the intervening control sessions were 69, 71, and 47 responses per reinforcement, respectively. Responding during the last free-food session (an average of 42 responses per reinforcement) was approximately the same as during the first free-food session (39 responses per reinforcement). Figure 1 shows representative cumulative response records of these performances. The birds responded despite an average gain in weight during free-food sessions approximately ten times greater than that during control sessions. Indeed, after some free-food sessions, one bird regurgitated grain in its home cage.

This study differs from previous experiments (1-4) in a number of ways. The birds were at 80 percent of their normal weights when sessions began; a variable-interval schedule of reinforcement was used; free-food sessions alternated with control sessions; and the subjects had considerable prior experimental experiences. The individual contributions of each of these, together with the durability of the effect, must be determined. My results indicate, however, that under some conditions animals respond many times to earn one food reward while identical food is freely available.

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Control of Acidic Mine Drainage

Singer and Stumm (1) have established the oxidation of Fe^{2+} as the rate-determining step and propose two means for control of pyrite oxidation—the highly impractical one of excluding oxygen from a mine, and the more likely one of introducing bactericides

to reduce the rate by destruction of the biocatalytic organisms presumably present in natural systems.

A third possibility exists—that of reducing the rate of a noncritical step to a very small value. About 1953, Patrick (2) found that small quantities of chromate ion were effective in inhibiting the oxidation of pyrite, both in laboratory tests and in the field. The mechanism is probably analogous to that of chromate in inhibiting the corrosion of metals.

Patrick's work was with sodium chromate, which of course leached rapidly from a wet mine face, and hence the effect was not long-lasting. Furthermore, this rapid leaching would cause significant if temporary pollution of the mine effluent. The amount of chromate necessary to afford virtually complete inhibition of iron in waters with a chloride concentration of 10 ppm is 100 ppm (3), but corrosion is reduced by 90 percent or more in systems where 5 ppm is maintained (4). Such concentrations can be readily attained on the mine face by the use of a slightly soluble chromate, such as calcium or strontium chromate, dispersed in an adherent, hydrophilic coating, such as a polyvinyl acetate. Although chromate is photochemically reduced in such systems, they should be stable inside a mine.

Some of the oxidation of pyrite in mines results from the percolation of oxidizing groundwaters through fracture zones, but much occurs at the mine face, where both oxygen and bacteria have free access, and it is this that chromates may be helpful in controlling. Only a small amount of chromate should appear in the mine effluent, and this will probably be reduced and precipitated not far below the effluent point.

In accord with Singer and Stumm (1), it is important to note that chromate is an effective biocide, having a low killing concentration for wood-destroying fungi (5).

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