Ferguson's principle could be applied—namely, substances that are present at the same proportional saturation in a given medium have the same degree of biological action—and indication could be obtained regarding the presence or absence of structurally specific or nonspecific action. This principle has already been fruitful in biological investigation; for example, in studies of action of narcotics (*10*). Future experiments are being designed with this in mind.

SUMMARY

1) Spectra in the ultraviolet and visible regions have been obtained on samples of malononitrile under different conditions. The samples were manufactured by several companies in America and Sweden.

2) The spectral analysis has demonstrated that the compound used by Hydén and Hartelius is not the same as that employed by American investigators. If, however, an aqueous solution of the American product is allowed to stand at room temperature for a long enough time, it develops the same spectral characteristics as the Swedish solution.

3) Future studies will concern themselves with attempts to identify the active substance and to examine its effect on neuronal nucleoproteins.

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Stimulus Control of Food- and Shock-Maintained Behavior

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This paper presents a technique for maintaining behavior in a rat that is alternately under the control of shock avoidance and food reinforcement (*1*).

Sidman described a conditioning procedure that maintained a constant rate of bar pressing when each bar press postponed a brief electric shock (*2*). Techniques have also been developed for maintaining lever pressing by following lever-pressing responses intermittently with food. Moment-to-moment rate changes have been generated that are both reproducible and a function of how reinforcement is made contingent upon the bar press (*3–5*). Under both of these techniques, the momentary rate, as well as the day-to-day level of responding, are sensitive base lines for the study of the control of behavior by noxious stimuli and food reinforcement.

Alternate periods of buzzer and no buzzer were used. When the buzzer was off, the Sidman-avoidance procedure was in force. Each lever press postponed a 1/5-sec electric shock by 30 sec. If no bar presses were made, the shock recurred every 30 sec. After 8 min of avoidance procedure, the buzzer was turned on, the shocking circuit was disconnected, and the first lever press occurring after 8 min was followed by a pellet of food. The buzzer was then turned off, the program reverted to the shock-avoidance procedure, and the cycle was repeated. Two cumulative recorders operating in tandem recorded the lever presses that occurred during these alternate periods of buzzer on and buzzer off.

Figures 1 and 2 are cumulative response curves after 120 hr of the avoidance and food behavior. The rat behaved appropriately to the food- and shock-avoidance schedules. When the buzzer was off and the shock-avoidance procedure was operating, the bar pressing occurred at a constant rate of 6 responses/min. When the buzzer was on and the food-reinforcement procedure was operating, the rate of lever pressing was zero for 1 to 2 min after the receipt of a food pellet; during the remainder of the 8-min period, the rate increased gradually to a terminal rate of about 60 responses/min. The diagonal marks on the food record indicate where a food pellet was delivered. Similar curves were recorded for two other rats.

The behaviors under the two schedules show little effect upon each other. The constant rate of emission

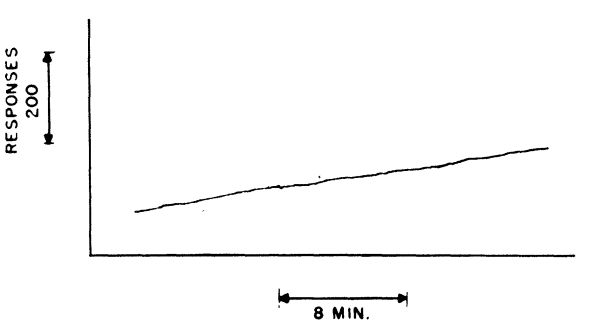

Fig. 1. Each bar press postpones a brief electric shock for 30 sec.

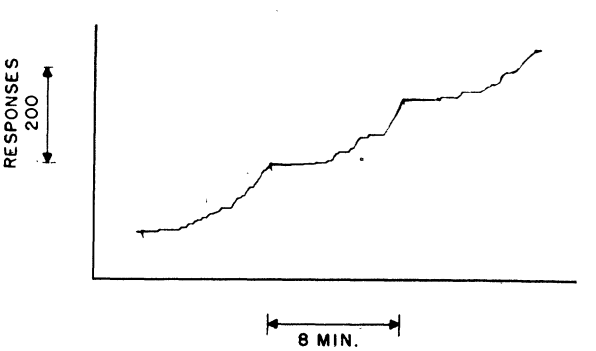

Fig. 2. The first bar press after 8 min produces a pellet.

of the avoidance responses within each experimental period and day-to-day reproducibility confirm Sidman's results. The food curve in Fig. 2 is similar to records of pigeons and other rats after extended training on this kind of procedure. The interaction between the two schedules can be determined by manipulating each schedule in turn and observing the effect on the behavior under the control of the other schedule. For example, if the food reinforcement were not delivered at the end of the 8-min period, the rate of bar pressing would eventually fall to zero whenever the buzzer was on. Any concomitant change in the shock-avoidance behavior would be a consequence of an interaction from the food-maintained behavior. The different character of the rate changes generated by the two schedules of this experiment simplifies the identification of the interactions between them.

More complicated behavioral processes, such as discrimination procedures or other schedules of food reinforcement, could also be used alternately with the avoidance procedure to serve as base lines for the emotional by-products of the avoidance behavior or side effects of analgesic drugs.

References and Notes

1. This experiment is part of a research program carried out under contract N5ori-07631 between Harvard University and the Office of Naval Research, U.S. Navy (project NR 143-943, report PPF-4), directed by B. F. Skinner.
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Filament Formation in *E. coli* Induced by Azaserine and Other Antineoplastic Agents

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Azaserine (0-diazoacetylserine) is a new antibiotic that has limited activity against microorganisms but is of great interest because of its ability to inhibit certain experimental neoplasms (*1–3*).

A remarkable effect of azaserine on the growth of *Escherichia coli* was the induction of the formation of greatly elongated filaments, as are shown (*4*) in Fig. 1. Examination of these filaments in the phase microscope indicated that they were apparently multinucleate and nonseptate. The length of the filaments varied from a few times to as much as 100 times the length of a normal cell, depending on the time of observation after exposure to the inhibitor. Short filaments could be observed only 30 min after inoculation into azaserine-containing medium.

In contrast to certain other observations on inhibitor-induced filament formation (*5, 6*), there was no critical level of azaserine at which the phenomenon occurred. Although detailed correlation of filament length with azaserine level has not yet been made, it was obvious that filaments appeared whether the inhibition was barely significant or almost complete.

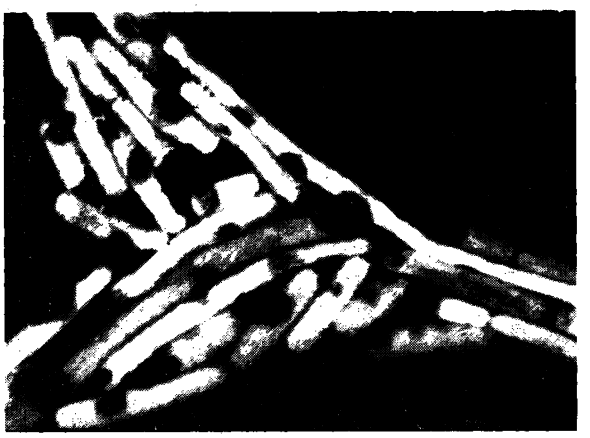

Fig. 1. Electron photomicrograph of filamentous *E. coli* after 5-hr exposure to 0.025 gamma/ml of azaserine. Several organisms of normal length may be seen (×4800).

The striking nature of this morphological aberration led to the examination of other inhibitors and antineoplastic agents. For most of the growth studies, a salts-glucose medium (*7*) was employed, but observation of filament formation could be repeated in nutrient (neopeptone) medium. *Escherichia coli* (Parke, Davis Culture Bureau No. 03489) was maintained in the synthetic medium. A 0.1-ml inoculum from an over-night growth was added to 9.9 ml of the medium at 37°C containing the desired constituents, and nephelometric determinations of cell mass were made at hourly intervals for 7 hr. Phase microscopic examinations were made of cultures that were inhibited in the range of 30 to 70 percent.

Under these conditions, the following inhibitors did not cause the formation of nonseptate filaments: chloramphenicol, chlortetracycline, oxytetracycline, streptomycin, sulfanilamide, aminopterin (*8*), a-methopterin (*8*), 8-azaguanine (*8*), glycidol, 2,6-diaminopurine, 6-mercaptopurine (*9*), ethionine, β-2-thienylalanine, 6-methyltryptophan, isobutyl diazoacetate (*9*), and diazomalonic ester (*9*). The following compounds were found to be as potent as azaserine in inducing filament formation: methyl-bis(2-chloroethyl)-amine, triethylenemelamine (*8*), and 5-diazouracil. Filaments induced by penicillin were characterized by large sphere-shaped vesicles (*10*), a feature that was never seen in filaments produced by the other inhibitors.

Since this study was made, another report has appeared with illustrations of the filaments induced by nitrogen mustard (*11*). It has been known for many years that gamma-irradiation of *E. coli* results in filament formation (*12*).

It has been observed in this laboratory, as well as in another (*13*), that inhibition of *E. coli* in synthetic mediums by low levels of azaserine may be reversed by aromatic amino acids. Higher levels of azaserine