changed AIA was extracted with ethylene dichloride. These metabolites migrated in the isooctane, acetic acid system with an R_F of 0.15. The PB treatment caused a twofold increase in the amount of AIA metabolites in the whole liver as compared to the saline treatment. Moreover, these metabolites were preferentially located in the microsomal fraction (Fig. 3).

Confirmation in vitro of this hypothesis was obtained by the following experiment. Microsomes (equivalent to 1.0 to 1.5 mg of protein) from PB-treated and control rat liver (eight rats per group) were incubated at 37°C with reduced nicotinamide adenine dinucleotide phosphate (NADPH) (0.67 μmole), tris buffer, *p*H 7.5 (35 mmole) in a final volume of 0.81 ml. After the addition of AIA (5 μmole) to the reaction vessel, oxygen consumption was measured polarographically with a Clark oxygen electrode (*10*). Hepatic microsomes of the PB-treated rats oxidize AIA at an increased rate as compared to control microsomes (mean of 4.6 compared to 2.5 μmole of O_2 consumed per minute per milligram of protein, respectively).

These data indicate that inducers of chemical porphyria are detoxified by drug-metabolizing enzymes of hepatic endoplasmic reticulum and that augmentation of this detoxification so reduces the amount of inducers that they are no longer effective. This has the following implications.

The first is that enzyme induction is influenced by the rate of biotransformation of the inducer in a target organ, as has been suggested (*11*). The second is the relevance of these findings to the human disorder. It is possible that the biochemical abberation in human genetic porphyria may be modified by reduced metabolism of circulating inducers of porphyrin biosynthesis. Indeed, observations in our laboratory and by others (*12*) have indicated that in human hepatic porphyria, endogenous inducers may be present in the blood in increased quantities, particularly during acute attacks. Thus, the rate of metabolism of these naturally occuring substances may be an important factor in the regulation of hepatic δ-aminolevulinic acid synthetase in the human disease.

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Pigeon Control by Chemosterilization: Population Model from Laboratory Results

Abstract. *Reproductivity of pigeons is inhibited with mestranol incorporated in a synthetic grit; continual erosion releases daily doses. Young squabs may be permanently sterilized when fed crop milk by treated birds. A theoretical model of pigeon population dynamics using laboratory-obtained data shows the advantages of chemosterilization over killing as a means of pigeon control.*

The feral pigeon, *Columba livia*, has become a problem in several areas, mainly by virtue of its numbers and unsanitary habits of dwelling in cities and parks, and harassing the feed lots and graneries of rural areas. Reproductive inhibitors have been tried for population control of pigeons (*1*), but the same problems always arise—how to get the inhibitor into the animals, and how to obtain more than a temporary effect.

Laboratory experiments to test dosage effects of the synthetic steroid mestranol [17α-ethynyl-3-methoxyestra-1,3,5(10)-trien-17β-ol] for avian inhibition of reproduction were run by Wentworth (*2*) and by Wentworth, Hendricks, and Sturtevant (*3*), with the Japanese quail (*Coturnix coturnix*) used as the experimental animal. The natural estrogen, ethynyl estradiol, is methylated to give the orally active estrogen mestranol. Once this synthetic estrogen, mestranol, enters any biological system, from microflora or -fauna to the human being, demethylation occurs to give, again, the natural steroid ethynyl estradiol. The half-life of available mestranol in a biological system is less than 6 hours (*4, 5*). Thus there is no retention or accumulation of mestranol in the ecosystem, hence no danger of contamination of the environment from mestranol.

Previous experiments on Japanese quail with mestranol (*2, 3*) indicated a potential use for control of pigeon populations. In 1968 I began laboratory testing of mestranol incorporated in synthetic grit on pigeons (*6*). Pigeons were fed pelleted pigeon food containing the synthetic grit, which then eroded in the gizzard. The rate of mestranol release through grit erosion was approximately 183 μg daily per treated bird, a dosage high enough to reduce the fertility of the first clutch of eggs after treatment to 26.4 percent and that of the following two clutches to 67.0 percent, as compared with 90.3 percent fertility of the controls.

When parental pigeons were treated with mestranol in grit approximately 4 days after laying a fertile clutch of eggs, the young hatched from these eggs were fed crop milk by the parents (a natural phenomenon) and some grit was passed to the young during feeding. Macroscopic changes in the reproductive tracts of adult F_1 birds receiving crop milk or grit or both from their parents the first several days posthatch were evident in 26.0 percent of all first-clutch birds; depressed fertility was statistically significant in males. Thus mestranol or its metabolites were passed to the young in crop milk or the grit or both (*6, 7*). The potential of F_1 sterilization is evident; I believe the results would be even more positive, however, if the level of mestranol in grit were increased.

A concurrent experiment was run in

which males and females were treated by gavage with grit containing mestranol and then paired with control mates. Fertility of first-clutch eggs from both types of mating (treated males and females, mated with control birds) was reduced; no other clutches from treated females and control males were significantly depressed in fertility, while all clutches from treated males and control females were significantly lower in fertility as compared with controls. This indicates that the sterilizing effect of mestranol in pigeons is more potent in adult males than in adult females.

Reproductive behavior appeared to be no different in treated birds as compared with controls in all experiments.

A second experiment in which pigeons' eggs were treated topically with 5 μg of mestranol in 5 μl of oil at day 5 of incubation was divided into two parts: in the first, eggs were artificially incubated after laying and squabs were autopsied at hatching; in the second, eggs were naturally incubated after laying and birds were autopsied at 6 months (maturity). There were no differences in hatchability, mortality, or sex ratio between treated and control birds. All male squabs had two oviducts, and usually the left testis morphologically resembled an ovotestis. All female squabs had two oviducts; most oviducts were incomplete and would have been nonfunctional at sexual maturity. Treated birds were easily distinguished from control birds at hatch, approximately 12 days after treatment, by the reproductive tract changes. Oviducts were invariably present in egg-treated males at maturity, the vasa deferentia were involuted, and histologically the left testis was an ovotestis. The right testis was not examined histologically. Mature females from treated eggs always had two incomplete oviducts, and ovaries were either immature or contained resorbing follicles with no internal ovulations evident. Females laid no eggs.

These laboratory experiments show that low dosages of the estrogen mestranol permanently sterlize pigeons if given when the neural-hormonal system of the squab is undifferentiated (during incubation or for a short time after hatching) or temporarily sterilize them if given by daily erosion from grit in an adult. (For a review of avian chemosterilization and more detailed data of effects of mestranol on pigeons, note references *2, 3, 6,* and *7.*) The methods of chemosterilization can be extrapolated to field application: (i) free mestranol is rapidly broken down in the ecosystem, and coated grit particles pass through vertebrates lacking gizzards (*2, 5, 8*); (ii) population dynamics for pigeons may be predicted, based on models (*9*) and data (*6*).

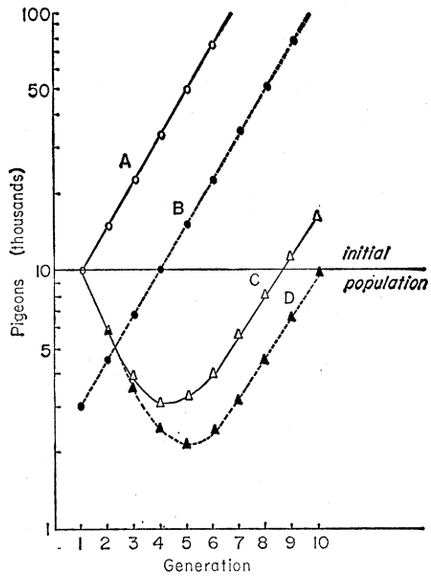

Fig. 1. Semilogarithmic representation of pigeon population dynamics. (*A*) No control technique applied to an original population of 10,000 pigeons. (*B*) A control of 70.0 percent kill of the adult pigeon population in generation 1. (*C*) Control technique of 70.0 percent sterility of the 10,000 adult pigeons in generation 1. (*D*) Seventy percent sterility of the original 10,000 adult pigeons in generation 1 with 50.0 percent permanent sterility of F_1 raised by the remaining 30.0 percent treated but not sterile adults.

Four situations predicted by the models are graphically presented in Fig. 1: (*A*) no treatment; (*B*) 70.0 percent kill of all parental birds in generation 1; (*C*) 70.0 percent sterility of the parental pigeons in generation 1; (*D*) 70.0 percent sterility of the parents with 50.0 percent stertility of F_1 raised by the 30.0 percent treated but not sterile parents. The initial population is 10,000 pigeons. Assumptions are: (i) each pair of pigeons will produce one viable clutch per year; (ii) 50.0 percent of the parents (including mature F_1 from the previous generation) will die from natural causes and therefore will be eliminated from the next breeding generation; (iii) courting and mating behavior is not changed by treatment; (iv) no debilitation occurs from treatment; (v) F_1 pigeons do not reproduce the year they are hatched. Two populations, one with no control and one with a 70.0 percent kill in the first generation will increase at a geometric rate; the population of 70.0 percent killed increases to its original number in three generations' time. A population with 70.0 percent sterility of the adult population in generation 1 slowly decreases and does not attain the original population number until the ninth generation, while a population of sterile adults and permanently sterile F_1 does not reach the original population size until the tenth generation. The figure depicts birds in a discrete population, and does not show the ingress or compensatory breeding which occurs when birds are killed or in other ways bodily removed from the population. Treated birds will remain in the population occupying space and competing for mates, thereby inhibiting any ingress due to space available, but the entire population will decrease with time. If adjacent areas were treated at the same time, the reduction in pigeons over the entire area would be evident at least 1 year after treatment, and probably before that, owing to natural mortality of the adults.

Mestranol influences fertility of males more readily than females, a fact thus adding to population control. Females will lay the eggs, then incubate for at least the normal period of 17 to 18 days, even if the eggs are not fertile. The male is not exclusively monogamous, and therefore will mate with more than one hen; if his fertility is reduced, he is taking the place of a fertile bird, and eggs laid by his second mate have a high chance of being sterile.

The advantages of the sterilization method for population control over killing or removal are: (i) birds are not killed but are completely viable; (ii) sterile birds will compete for space, food, and mates, as behavior is not changed; (iii) sterilized birds will, by movement, influence the reproduction of individuals in other neighboring areas and also alter the reproductive potential in subsequent generations; (iv) treated adult pigeons with depressed fertility have the potential of sterilizing their young that do hatch, through crop milk or passage of grit to the young; (v) the bonus effect—". . . sterilized organisms will be capable of adversely affecting the reproductive capacity of the remaining normal fertile organisms in a population to the same degree that the original population is affected by the sterilizing procedure" (*9*, p. 24)—is theoretically possible; and (vi) treatment can be manipulated to maintain the population at a level compatible with the environment.

The total population will not be sterilized; depending on the individual bird and its susceptibilty to sexual alteration, birds not affected by mestranol will be present and they will produce a normal number of progeny. Adults eating food with grit, will, if they are incubating eggs, add to the chemosterilization program by feeding their young crop milk in which the steroid level is increased, or by passing grit to them in crop food, thereby altering the fertility of the young.

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8. I have tested the effect of mestranol incorporated in grit on hybrid laboratory mice and *Drosophila melanogaster* (representing components of the pigeons' feeding area) in the same form as would be applied for pigeon bait; reproductive potential or productivity or both were not changed when these animals were allowed to feed on prepared bait containing grit with mestranol. Soil microorganisms are very active in degrading mestranol; gas-chromatographic analysis of soil washings after soil treatment with mestranol yielded no trace of the applied mestranol after 6 hours. As an added precaution, the grit particles in all experiments, including those with pigeons, were ultimately coated with a catalyzed resorcinol layer before being incorporated in the bait. Grit ingested by vertebrates lacking gizzard stones was excreted within a few hours.
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Water Transport in the Cloaca of Lizards: Active or Passive?

Abstract. *The withdrawal of water from the lizard cloaca can be a passive process resulting from the colloidal osmotic pressure of the plasma proteins. The forces necessary to withdraw water from lizard urine, the forces prevailing within the cloaca in vivo, and the counterbalancing of these forces by a protein solution placed in the cloaca all are in accord with this hypothesis.*

It is well known that water is withdrawn in the cloaca or lower intestine of birds and reptiles (*1*). Urine, as it leaves the kidney, is liquid (although it may contain crystalline uric acid); in the cloaca water may be withdrawn until the final urinary pellet (dropping) is firm and semisolid.

The mechanism for withdrawal of fluid from tissue spaces, from the intestine, and from the cloaca has been the subject of much discussion (*2*, *3*). The mechanisms commonly considered for water transport in biological systems are either primary active transport of a solute, followed by passive solute-linked water transport, or passive flow by simple physical means, such as flow of water along an osmotic gradient or flow due to hydrostatic pressure. An active transport of water as such (a "water pump") is not presently considered a plausible alternative for transport across animal membranes (with the possible exception of arthropods).

To examine whether water reabsorption in the cloaca can be explained without invoking processes of active transport we selected the desert iguana (*Dipsosaurus dorsalis*). This animal has several advantages; ectothermic animals lend themselves easily to experimental procedures, reptiles are unable to produce hypertonic urine (*4*), and the desert iguana normally lives in arid habitats and produces quite dry pellets of urine (*5*). As will be explained below, the plasma colloidal osmotic pressure could provide a force sufficient to cause withdrawal of water. We therefore wanted to (i) measure the force needed to withdraw fluid from lizard urine and compare this force with the plasma colloidal osmotic pressure; (ii) examine whether the forces prevailing within the cloaca in vivo are in accord with our hypothesis, and whether the intracloacal forces change with induced changes in plasma colloidal osmotic pressure; and (iii) see if the force causing withdrawal of water can be counterbalanced by the introduction into the cloaca of a protein solution of equal colloidal osmotic pressure.

If suction is applied to a liquid, the hydrostatic pressure, relative to atmospheric pressure, becomes negative; we will use the expression "negative pressure" (suction) to mean subatmospheric pressure.

If we attempt to withdraw water from a moistened mass of crystalline uric acid, the necessary negative force increases as the sample becomes drier. The water is held in the capillary spaces of the mass of crystals with increasing force, and progressively greater negative pressures must be applied to remove more fluid. To measure the negative pressures necessary for withdrawal of fluid from a paste of lizard urine, we used the wick method described by Scholander *et al.* (*6*). Clean pellets of lizard urine were dried at 70°C, and distilled water was added to make a suitable paste containing 55 percent water. The wick was suspended in the middle of this mixture, and the container with its contents was placed on a balance. This permitted us to follow the water content of the sample as it began to air-dry while simultaneously recording the negative pressures which developed. The water content of freshly voided urinary pellets, necessary for comparison with the results, was determined by weighing before and after drying at 70°C.

Table 1. Correlation between plasma colloidal osmotic pressure (corrected at 38°C) and cloacal hydrostatic pressure in normally hydrated and dehydrated desert iguanas. Means and S.E.; number of animals in parentheses; *r*, correlation coefficient as calculated with Pearson product-moment correlation.

Lizards	Plasma colloidal osmotic pressure ($mm\text{-}H_2O$)	Cloacal hydrostatic pressure ($mm\text{-}H_2O$)	*r*
Hydrated	215 ± 7.5 (9)	-207 ± 7.6 (9)	+0.96
Dehydrated	267 ± 9.5 (8)	-255 ± 9.6 (8)	+0.98
	$P < .01$	$P < .01$	