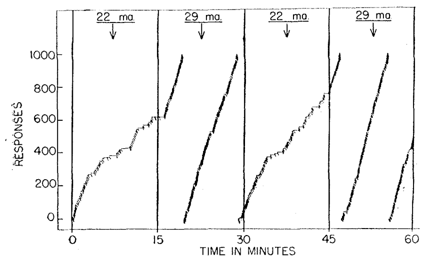

Fig. 2. A 60-minute session under fixed-ratio (8:1) during which the electric stimulus current was varied in alternate 15-minute periods (cat E-5, 7 Mar. 1955).

food and water deprivation, and conditioned "anxiety" states, on behavior controlled by brain stimulation. Reports of these investigations are now in preparation.

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21 June 1955

Proton Affinity of Phosphine in the Phosphonium Halides

It has been pointed out by Grimm (*1*) that it is possible to calculate the proton affinity of ammonia, P_{NH_3}, if the crystal energies of the ammonium halides and the electron affinities of the halogens are known. Using this method, Sherman (*2*) has calculated the proton affinity of ammonia in the ammonium halides and found it to be 221.0, 209.0, 208.6, and 202.7 kcal in NH_4F, NH_4Cl, NH_4Br, and NH_4I, respectively. An average value of 206.8 kcal was adopted. Similar calculations were made for the proton affinity of water, the calculated value being 182 kcal.

Experimental evidence indicates that phosphine is a weaker base than ammonia. The absence of a series of phosphonium salts comparable in stability to the ammonium salts is evidence for the decreased basicity. At room temperature PH_4I is a solid (sublimation point 62°C), while the bromide and chloride are dissociated gases. Since the proton affinity of a molecule is a measure of basicity, it was of interest to calculate this value for phosphine.

The proton affinity of phosphine, P_{PH_3}, is defined as the energy change for the reaction

$$PH_4^+ \rightarrow PH_3 + H^+$$

This energy change can be calculated indirectly by use of the familiar Born-Haber cycle. This cycle is represented as

$$\begin{tikzcd}
 & (PH_4X) \arrow[r, "U"] & PH_4^+ + X^- \arrow[d, "P_{PH_3}"] \\
\tfrac{1}{4}P_4 + 2H_2 + \tfrac{1}{2}X_2 \arrow[ur, "-Q_{PH_4X}"] & & PH_3 + H^+ + X^- \arrow[dl, "-I_H + E_X"] \\
 & PH_3 + H + X \arrow[ul, "Q_{PH_3}", "-D_H - D_X"'] &
\end{tikzcd}$$

The proton affinity at 0°K is given by the relation

$$P_{PH_3} = U + Q_{PH_4X} - Q_{PH_3} + D_H + I_H + D_X - E_X - 5/2RT,$$

where U is the lattice energy of the PH_4X (X representing chlorine, bromine, or iodine) Q_{PH_4X} is the heat of formation of PH_4X, Q_{PH_3} is the heat of formation of phosphine, D_H is the heat of dissociation of hydrogen, I_H is the ionization potential of hydrogen, D_X is the heat of dissociation of the halogen molecule, E_X is the electron affinity of the halogen, and RT is the gas constant, 1.987 cal deg^{-1} $mole^{-1}$, times the temperature, 298.1°K.

Table 1 gives the thermal data required to calculate the proton affinity of phosphine in PH_4I, PH_4Br, and PH_4Cl. Because of the unreliability of many of the data, the calculated proton affinities are accurate only to about ± 5 percent in PH_4I and about ± 10 percent in the other two halides. The error is of this magnitude because the crystal lattice of PH_4I is the only one known with accuracy (*3*). Similar structures have been assumed for the other two halides. Thus, the PH_4I value for the proton affinity would be the most reliable.

Recent electron affinity values for the halogens E_X (*4*) are lower by about 5 to 7 percent than the values used by Sherman (*2*). This would give a higher proton affinity for ammonia by about 2 to 5 percent. Thus, the new values would be in the range from 226 to 210 kcal. However, even with this revision, the

Table 1. Proton affinity of phosphine at 0°K

Quantity	PH_4I	PH_4Br	PH_4Cl
U*	131.5†	130.3	132.2
$-Q_{PH_4X}$ (*5*)	15.8	29.5	42.5‡
Q_{PH_3}	2.21	2.21	2.21
$-D_H$	52.1	52.1	52.1
$-I_H$	311.9	311.9	311.9
$-D_X$	25.5	26.7	28.9
E_X (*4*)	74.6 (*6*)	81.5	86.5
$5/2RT$	1.5	1.5	1.5
$-P_{PH_3}$	200 ± 10	209 ± 21	217 ± 22

* Assume a CsCl lattice, densities of PH_4Br and PH_4Cl estimated at 1.94 and 1.27 g/cm^3, respectively.
† All values in kilocalories.
‡ Estimated from the Q_{PH_4Cl} in the gas phase.

proton affinity of phosphine is of the same order of magnitude as that of ammonia.

The low value for the proton affinity of water would indicate that the H_3O^+ is less stable than the PH_4^+. The reverse seems to be true because the phosphonium halides, unlike the ammonium halides, are readily hydrolyzed by water according to the equation

$$PH_4X + H_2O \rightarrow PH_3 + H_3O^+ + X^-$$

Apparently other factors must enter in, because this result is not what would be predicted according to the calculated proton affinities of water and phosphine.

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15 March 1955

Ecology and the Population Problem

In commenting on the problem of providing space and food for the growing human population, A. M. Woodbury implies [*Science* **122**, 200 (1955)] that this problem is sufficiently critical in the United States to reduce such questions as those concerning the preservation of our national parks and monuments and recreation areas to the status of "minor matters." Woodbury is my former teacher and companion in fieldwork, and he is the man most directly responsible for my initial decision to become an ecologist; hence, there is no one to whom I would listen more intently and respectfully on the solution of an ecological problem. This time, however, I must take exception, for I feel that in much of the loud discussion of the "population problem," a clamor to which Woodbury has now added his voice, at least one-half of the fundamental ecological considerations are commonly ignored.

The reasoning behind proposals such as the one under discussion is, briefly, as follows. "The human population is growing. If we extrapolate this curve of growth into the future we find that it will not be long before present facilities will be inadequate to feed or otherwise provide for the population. Therefore, we must provide new facilities." The proposals for new facilities vary from writer to writer and include the restoration of damaged agricultural land, new methods of exploiting submarginal land, increasing the harvest from the oceans, fish farming, algae farming, and various schemes for utilizing atomic energy.

Woodbury leans toward engineering feats that will make it possible to utilize lands now nonproductive because of aridity. These are all technical proposals for increasing the "carrying capacity" of the earth for human populations. Of more fundamental ecological interest are these neglected questions: Is it legitimate to extrapolate the curve of population growth? How large a population is it desirable to have? Will an increase in carrying capacity solve the population problem? These questions, I believe, deserve serious consideration in the light of ecological knowledge.

The growth of any population, plant or animal, can be resolved at least qualitatively into two phenomena, the capacity of the organisms to increase in numbers and the capacity of the environment to support organisms of that type. All species are potentially capable of increase beyond the capacity of the environment. The earth, or for that matter, the universe, is not large enough to contain all the houseflies or mushrooms that would exist after a few generations if the potential rate of increase could be sustained. The same generalization applies to elephants, whales, men, and sequoia trees; they would simply take a little longer to fill the universe.

Now, nearly all our experience with a great variety of species indicates that a population tends to grow rapidly when it is well below the capacity of the environment. The growth rate decreases as environmental resources become limited, and a population that has saturated its environment cannot, by the definition of capacity, increase at all. If the capacity of the environment is increased, the result to be anticipated is a new cycle of population growth. For this reason one may question whether anything permanent is to be gained by increasing the carrying capacity of the environment, unless there are other very good reasons for regarding a larger population as desirable. In his recent textbook of ecology, Woodbury relates a report that in Shanghai, prior to World War II, 25,000 infants were annually discarded in the garbage. A population twice as large and living in the same manner would presumably discard 50,000 infants annually. Enlarging the effective environment would not of itself provide any permanent solution to what I visualize as the "population problem."

Extending this somewhat imaginative picture to the United States, we can visualize a temporary relief of population pressures while the now-arid Great Basin and Southwest are becoming as densely populated as, say, Manhattan Island and while our lakes are being transformed into algae "factories." At the end of the cycle of population growth we would not have our recreation areas but we would still have the population problem.

The life-history pattern of man is such that a human population with plenty of room for expansion is potentially capable of exponential growth at an "interest rate" of about 3 percent continuously compounded. The population of the United States was growing at about this rate in 1790. Our present-day reproductive performance is not consistent with this rate of growth; for the U.S. and for the earth the present rate of human population growth is apparently slightly more than 1 percent and less than 2 percent per year. However, it is a completely obvious but commonly overlooked fact that any positive rate of population growth must ultimately cease. The capacity of the environment will determine how many people will be present when the population ceases to grow, but even if we could expand to the point of "standing room only" there would still have to come a time when population growth would stop.

When the population ceases to grow we must have, on the average, one individual leaving the population for each one entering it. It is irrelevant for the present discussion whether the final population will fluctuate or will reach an equilibrium size or steady state. In either case the average death rate must be equal to the average birth rate; this is the only real solution on earth to the population problem. (I admit to being already too old and staid to regard interplanetary emigration as offering a promising solution to the problem.)

It is commonly regarded as desirable to have a low death rate, and the only permanent way of achieving this is to have a low birth rate. How low can this go and the population still be sustained? If, as seems imminent, we can attain a mean length of life of 75 years, the minimum birth rate for replacement will be 1/75 birth per person per year, or 13.3 per 1000 population per year. But this is higher than any crude annual death rate experienced in the United States since 1920. Even if it should become possible to extend the average length of life to 100 years this would require, in order to maintain a stationary population, a birth rate and a death rate of 10 per 1000 population per year, which is above the U.S. rate that has prevailed since 1948. These are simple arithmetic facts, and neither socialized medicine nor the Corps of Engineers will alter them.

Here, I believe, we see an aspect of the population problem that should be aired. Inevitably there must come a time when birth rates and death rates will be equalized through the cessation of population growth. It would, however, take a brave administrator, when he was faced with a climbing death rate, to oppose any measure whatsoever proposed to combat the trend. Hence, until the population problem is considered in its entirety, we can anticipate pressures for keeping the population growing no matter what sacrifices may be required.

I have no intention of making specific proposals for managing natural resources or population growth in the United States, and I do not pretend to know what population size would be optimum. Even if I did know this, I could not say whether population stability could best be obtained by birth control, by restrictions on marriage, or by the "natural" controls such as famine, epidemics, and fertility changes, which will inevitably take over unless man finds a rational solution. The problem, however, is essentially ecological, and it can be approached objectively. I hope that it will be before too much of our natural heritage is sacrificed in the vain hope that dam-building projects and the like will solve the population problem.

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8 August 1955

A. M. Woodbury's discussion of science, population, and arid lands [*Science* **122**, 200 (1955)] seems to use some premises whose validity he does not clearly establish. From them he appears to argue that a scientific approach to the question of whether "to develop the Upper Colorado River for use of part of its waters," in certain interior states, would necessarily result in an attitude favorable to the proposal. He evidently regards conservationists who oppose the plan as emotional and unscientific; employing "diversionary tactics," they worry about "whether we are setting a precedent of invading a national monument, and various other minor matters." Scientists, it seems, are immune to the influence of emotion in making value judgments.

The author's citation of Paul B. Sears' editorial [*Science* **121**, 5A (29 Apr. 1955)] does not appear to support his own viewpoint clearly. Pertinent references I find in the editorial are to the need, "in matters of public policy where *verifiable physical knowledge* is involved" (italics mine), of "impersonal, disinterested, and competent boards of scientists" and this reference to one such group: "The Engineers Joint Council has investigated and reported (unfavorably) upon the Upper Colorado project" (parentheses Sears').

Woodbury seems to imply that it is wicked to doom arid lands "to remain arid with sparse populations," but he does not show why disinterested scientists would surely find it less wicked to favor "such a proposal as turning water from Yellowstone Lake through the divide into Snake River. . . ." Nor does he show why, once all pertinent scientific data were supplied, the problem of whether to convert an arid area into an area teeming with people would be a question to be decided by scientists but not by nonscientists.

It is to be hoped that scientists will not too hastily assume that they have become the only ones competent to make a value judgment.

ALEXANDER LINCOLN, JR.
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8 August 1955

Of the two accompanying papers commenting on my article [*Science* **122**, 200 (1955)], the one by Lamont C. Cole is a very fair statement to which I do not object; the other by Alexander Lincoln, Jr., distorts some of my meanings and imputes to me assumptions that I do not accept. Nowhere did I assume that anything discussed was "wicked," or that scientists are the only ones capable of making "value judgments." His article is a good example of the semantics used by "emotional" conservationists to which I called attention in the article.

I wrote the original article because I saw so much partisanship displayed on both sides of the controversy, and I hoped to find solid groundwork between the two extremes upon which reasonable people could agree. In essence, my proposal was to have the Congress authorize development of the Great Basin in accordance with the Colorado River Compact and refer disputed problems to a body of scientists trained in the art of fact finding (borrowed from the Sears' editorial). Such problems as (i) whether reservations for reclamation purposes were made before Dinosaur National Monument was established, (ii) whether the building of Echo Park Dam would be an invasion of the national park system, (iii) whether Echo Park or some other site should be used, and (iv) other disputed points should be referred to this group for decision.

Can it be that the type of conservationist represented by Lincoln is afraid to submit these controversial questions to scientific dissection? He signs himself as the representative of the Nature Conservancy, of which I am a charter member and have devoted much effort to conservation support. I am much interested in the national forest, national park, wildlife refuge, reclamation of arid lands, flood control, and other conservation movements and will continue to devote what effort I can to maintain such movements.

Cole marshals a lot of ecological data, most of which we share in common (we worked together in the Colorado Basin) to assist in analyzing the problems of the desert. It is on the implications and inferences from such data that we appear to differ. I go a step further than he does. I thoroughly agree with his implied conclusion that available habitat has an important influence on population control of plants, animals, and man, but there is one important difference between man and the other biota that he has not emphasized.

This difference is the use of intelligence by which man is making more habitat available to himself by dispossessing competitive plants and animals and transforming the habitat to provide more of his needs. The desert is one of the best places for making such a transformation. By diverting streams, man dispossesses fish and other stream animals of available habitat and, by putting water on sagebrush land, he not only dispossesses the sagebrush but also sage hens, sage thrashers, Brewer's sparrow, and many other sagebrush animals.

In place thereof, he substitutes homes (trees, flowers, lawns), towns or cities, industries, mines and related operations, military posts for which much space is needed, irrigated agriculture (least important at the present time), and many other more or less important items. Thus man can increase his available habitat and allow population to expand and fill it before he becomes subjected to the drastic population restrictions to which Cole has referred.

There is, however, an additional aspect that will allow further expansion. This is efficiency in utilization of natural resources. It is a race between research and population increase. If the latter overtakes the former, the population will necessarily become static, and the drastic controls will be automatically applied. This efficiency in greater production of human needs in available habitat is being manifested on all sides: more application of physical energy (water power, carbon fuels, atomic energy, solar energy); better processes of mining; more products of industry (automation); more efficient agricultural production (fertilizers, improved strains of crop plants and livestock, hybrids such as corn and sheep); better homes (individual homes with yards, lawns, and so forth); better health (sanitation, nutrition, antibiotics, medical advice); and many others.

Developments such as these not only will allow population expansion for a long time in the future but will tend to raise the standard of living. This will mean more leisure time to be devoted to recreation, more means of travel, and more demand for recreational sites and facilities. The Colorado Basin is rich in such recreation sites. There are thousands of miles of canyons and side canyons now unutilized. Perhaps there should be a program of development in the basin for recreation, comparable to that for water. With all available water applied to the basin, only a very small percentage of the land could be improved. The basin could never be converted into an "area teeming with people" by comparison with densely populated areas (contrary to Lincoln's imputation to me).

There have already been too many misunderstandings and distortions in this controversy. Let us not add any more. I use the following assumptions. (i) From the tone of the International Arid Lands Conference in New Mexico, I interpreted it to be an accepted objective of the participants to find ways and means of making arid and desert lands more productive of human needs. (ii) The Colorado Compact was a compromise of interests that provided an approximately fair division of the water of the Colorado River. (iii) This compact should be implemented by development of the Upper Colorado River to finish the program initiated in the Lower Basin. (iv) Plans for this development were under way before Dinosaur National Monument was enlarged to include Echo Park. (v) The controversy about building the dam at Echo Park should be settled on a basis of open-minded study rather than political controversy.

Here are a few points that I think should be clearly stated. (i) The development of the Upper Colorado Basin should not be confused with the problem of Echo Park Dam. (ii) The Echo Park reservoir would not flood the dinosaur bones quarry. (iii) The assumption should not be made on the basis of available evidence that the cost of development of the Upper Colorado Basin would be excessive. (iv) Desert homes properly supplied with water are preferred by many people to homes in more humid areas. (v) It has not yet been clearly established whether the building of Echo Park Dam would be an "invasion" of the national park system, or whether the extension of Dinosaur National Monument to cover Echo Park was an "invasion" of the reclamation program. (vi) The Colorado Basin is so rich in undeveloped scenic resources that the Echo Park region must be regarded as a relatively small part of the total recreational capacity.

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12 September 1955

6-Aminonicotinamide—a Potent Nicotinamide Antagonist

During the course of investigations on the inhibition of sulfonamide acetylation, it was observed that 6-aminonicotinamide was extremely toxic to rabbits (*1*). The delayed effect of the compound, the first sign of which was loss of control of the hind legs (*2*), suggested that 6-aminonicotinamide might be an antimetabolite of nicotinamide. This was confirmed by experiments in rats. In fact, it appears to be the most potent known antagonist of nicotinamide.

The median lethal dose (LD_{50}) of 6-aminonicotinamide (*3, 4*) for mice, shown in Table 1, is 35 mg/kg of body weight, as compared with 305 mg/kg for 3-acetylpyridine (*5*). Table 1 also shows that the simultaneous administration of 50 mg/kg of nicotinamide brings about an eightfold increase in the LD_{50} of 6-aminonicotinamide. Nictotinic acid, also, gives significant protection in contrast to its ineffectiveness against 3-acetylpyridine, when administered simultaneously with the latter (*2, 5*). Tryptophan appears to give some protection. The administration of 50 mg/kg of 6-aminonicotinamide resulted in 100-percent mortality within a week. When tryptophan was given simultaneously (50 mg/kg orally) with 6-aminonicotinamide, there were no deaths the first week, and 30 percent of the animals were alive at the end of 30 days.

Table 1. Effect of nicotinamide and nicotinic acid on the median lethal dose (LD_{50}) of 6-aminonicotinamide in mice. Metabolite and 6-aminonicotinamide were administered simultaneously intraperitoneally. Mice: CF-70 strain, 18 to 22 g.

Metabolite	Dose (mg/kg)	6-Aminonicotinamide (LD_{50} mg/kg)	No. of mice	95-percent fiducial limits
None		35	30	33– 37
Nicotinamide	25	121	30	113–129
Nicotinamide	50	308	40	281–331
Nicotinic acid	25	75	70	64– 89

Table 2. Oxygen consumption of liver from 6-aminonicotinamide-treated mice

Substrate	Oxygen uptake (μlit)*			
	15-min incubation		30-min incubation	
	Control	6-aminonicotinamide treated	Control	6-aminonicotinamide treated
None	55	16.5	100	30
Lactate 0.015*M*	69	35	129	66
Lactate 0.015*M* + DPN 0.002*M*	105	116	206	183

* Average values of duplicate vessels. Each vessel contained homogenate equivalent to 100 mg of tissue (wet weight). Homogenates were prepared in 0.25*M* sucrose under closely identical conditions and were incubated at 37°C in modified Krebs-Ringer phosphate.

On the assumption that 6-aminonicotinamide may give rise to an inactive DPN analog, it was of interest to compare the rate of oxygen uptake of tissues from treated animals with that of normal controls. The results of one experiment are shown in Table 2. In the absence of added substrate the oxygen uptake of mouse liver homogenate prepared from the treated animals was only 30 percent of the normal. Apparently the treated mice were depleted of both oxidizable substrate and DPN, since the addition of these substances *in vitro* greatly increased the rate of oxidation, while the addition of both together restored it almost to normal. The treated mice had received an intraperitoneal injection of 100 mg/kg of 6-aminonicotinamide and 25 mg/kg of nicotinic acid 72 hours prior to the experiment. No appreciable effect on oxygen uptake was observed when 50 mg/kg of 6-aminonicotinamide was used, or upon the addition of 6-aminonicotinamide *in vitro* to liver homogenate prepared from normal mice.

In view of the recent findings of Kaplan *et al.* (*5*) the toxicity of 6-aminonicotinamide may be due to the formation of an inactive DPN analog, with consequent depletion in certain tissues of DPN. It is of some interest that one of the pathological changes observed after an animal had received a toxic dose was involution of the spleen, a fact that may be related to the high rate of analog formation in this organ (*5*). Frequently, animals survived until 20 to 30 days after the administration of 6-aminonicotinamide. This may indicate, as is suggested by Zatman *et al.* (*6*), irreversibility of analog formation, with consequent inability of the tissues to rid themselves of the antimetabolite. These matters are at present under investigation in this laboratory. 6-Aminonicotinamide and its congeners are also being tested for their effect on neoplastic growths.

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30 June 1955

The great desideratum for any science is its reduction to the smallest number of dominating principles.—J. CLERK MAXWELL, *Matter and Motion.*