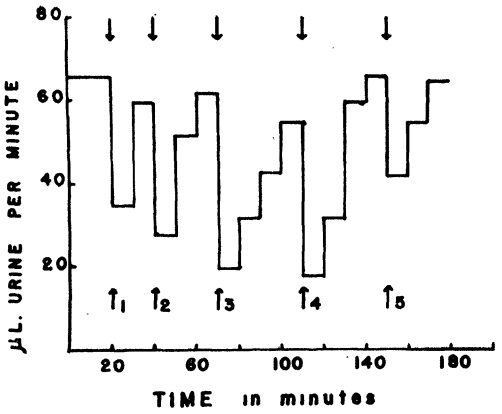

Fig. 1. Typical curve from assay procedure. Intravenous injections were made at the numbered arrows as follows: (1) 20 µU Pitressin; (2) 30 µU Pitressin; (3) 40 µU Pitressin; (4) 50 µU Pitressin; (5) 0.2 ml serum from rat exposed to ether for 5 min. The response indicates that the serum contained less than the equivalent of 0.1 mU Pitressin per milliliter.

ministration was not inhibited by a nondiuretic dose of epinephrine (20 µg/100 g). ADS release caused by a 5-min exposure to ether could not be blocked by the previous administration of medullary hormones in the doses used here.

Figure 1 illustrates the manner in which the values shown in Table 1 were estimated. At this time only relative values of ADS in blood serums may be assigned to these results. Although the method now employed is only semiquantitative, we regard it as an accurate index for the detection of ADS in blood serums. We interpret these data as indicating that (i) 5-min exposure to ether is a stronger stimulus in causing release of ADH than is the injection of 1 mg/kg morphine sulfate; and (ii) the diuretic action of the adrenal medullary hormones in the rat may, in part, be due to their blocking of the release of posterior pituitary antidiuretic hormone.

Table 1. Effects of medullary hormones on ADS in blood serum of rats.

Treatment	Cases	No. showing ADS	Estimated ADS (mU Pitressin/ml serum)
Decapitation	8	0	0.00
Morphine, 1 mg/kg Decapitation	8	8	.11
Epi., 20 µg/100 g Morphine 1 mg/kg Decapitation	5	4	.10
Epi., 100 µg/100 g Morphine 1 mg/kg Decapitation	9	0	.00
Nor-epi., 20 µg/100 g Morphine 1 mg/kg Decapitation	7	0	.00
Ether anesthesia Heart puncture	13	11	.18
Epi. 100 µg/100 g Ether anesthesia Heart puncture	15	11	.10
Nor-epi., 20 µg/100 g Ether anesthesia Heart puncture	6	6	.13

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3. Acknowledgment is made to M. L. Tainter of the Sterling-Winthrop Research Institute, for the pure forms of the adrenal medullary hormones, and to D. A. McGinty of Parke Davis Co., for the standard Pitressin. An explanation of some terms used in this paper follows: epinephrine, pure l-epinephrine bitartrate; nor-epinephrine, pure l-arterenol bitartrate monohydrate.
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A Single Diet for All Living Organisms

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Certain aspects of nutrition as a common denominator of biology are presented to indicate that diet can be considered as a single unit in the variables of biological research. A broad concept of comparative nutrition could be considered if different species could be reared on the same diet. Such a possibility may be induced from two considerations, the first being the great extent to which nutritional principles may be translated from one species to another. This is well illustrated by the fact that some of the individual B-vitamins, essential to the life of animals, were first discovered as microbial growth factors. Literature shows a striking similarity in the semisynthetic diets fed to monkeys, rats, mice, dogs, and chicks. Second, the qualitative nutritional requirements of most animals, plants, and microbial forms studied can be expressed in common terms as 15 to 50 nutritional elements (minerals, amino acids, vitamins, and a few unidentified factors). The suspected role of intestinal microorganisms in the production of vital unidentified factors for the host has been contraindicated by maintaining germfree chicks and rats (*1*) through one and six generations, respectively. This gives some assur-

ance that the major nutritional factors are present in experimental diets commonly used today.

Both considerations were expressed by Maynard (*2*):

> Superficially, the rations of man and animals have little in common since the kinds of food eaten are so different. Yet the essential constituents of these rations, that is, the elements required for adequate nutrition, are largely the same whatever the species. The general principles of nutrition are identical.

After surveying the nutritional requirements of invertebrate animals, Kidder concludes (*3*)

> . . . it is impressive that their nutritional patterns should so closely correspond with each other and to those of birds and mammals.

Thus, in theory, it may be possible to nurture all species with one diet. Ideally, this universal diet should contain all nutrients in an available state, with each nutrient in such quantity that it will satisfy the minimum dietary requirement for satisfactory growth, reproduction, and maintenance of all species without eliciting serious toxic reaction in any species. Such a diet would necessarily contain innocuous excess of some nutrients for many species—particularly autotrophs. The functional basis of the diet would not rest upon the nutritional requirements for maximal growth rate in any species; it would be a balance of nutrients with each in proper proportion to the whole to provide adequate nutrition to rear all species.

A diet with the proper formulation of all nutrients required to rear *all* species may never be known. In our present state of biological understanding, we would not expect to rear most parasites, viruses, fastidious microorganisms, or mammalian tissues with a semisynthetic diet; their complete nutritional requirements are not yet known. A finite end-point that may be anticipated is a diet that includes essential metabolites as nutrients for these parasitic forms. The experimental universal diet approaches the ideal in its ability to nurture selected representatives of the taxonomic classes (or orders) of living organisms. (The use of mere numbers of species without some system of representation would place undue emphasis on those classes with the largest number of species.) Natural universal diets, such as milk (fortified), whole cells (as yeast), or whole animals, would seem to be less useful in an academic study than a synthetic-type diet. Economic aspects could be considered to formulate practical universal diets.

Once written, the hypothesis fired the imagination. A semisynthetic "universal diet" was formulated in September 1952, and mice and guinea pigs were started the following month. Large amounts of vitamins were incorporated in the diet in order to satisfy any extraordinarily high requirement that might be encountered. The diet was made with special considerations for the salt requirements of chicks and guinea pigs, the fiber requirements of rabbits, the high protein requirement of chicks, and the fat requirement of dogs. Sugar was added to give good acceptability of the diet. The composition of Universal Diet No. 1 is given in grams of ingredient per kilogram of diet: purified casein, 300; corn oil, 80; cornstarch, 300; cellulose (alpha cell), 120; sucrose, 120; total salts, 80 (K acetate, 20.0; $CaCO_3$, 18.0; $CaHPO_4$, 13.5; Na_2HPO_4, 12.0; NaCl, 3.0; KI, 0.045; $MgSO_4 \cdot 7H_2O$, 4.5; MgO, 4.0; $MnSO_4 \cdot 4H_2O$, 0.75; $Fe(C_6H_5O_7)_2$, 4.5; $CuSO_4 \cdot 5H_2O$, 0.23; $CoCl \cdot 6H_2O$, 0.03; $ZnSO_4 \cdot 7H_2O$, 0.06; $Na_2B_4O_7 \cdot 10H_2O$, 0.03; $AlK(SO_4)_2 \cdot 10H_2O$, 0.045); vitamin A, 10,000 IU; vitamin D_3, 2000 IU; ascorbic acid, 10.0; α-tocopherol, 0.1; vitamin K (menadione), 0.01; thiamine Cl, 0.02; riboflavin, 0.02; nicotinamide, 0.1; Ca pantothenate, 0.05; inositol, 2.0; choline Cl, 2.0; pyridoxine Cl, 0.02; biotin, 0.001; folic acid, 0.02; and vitamin B_{12}, 0.0005.

Limitations of Universal Diet No. 1 are obvious. Small amounts of unknown nutrients may be present in the casein, corn oil, or cornstarch. Some of the known or suspected nutritional factors of today (such as thioctic acid, hematin, cholesterol, purines, pyrimidines, or molybdenum) were not intentionally added; such general application of this diet was not anticipated when it was formulated. Such omissions will be corrected when subsequent universal diets are made.

Preliminary experiments were intended to test one representative species in each taxonomic class of living organisms and one example from most orders of the class Mammalia. It might prove to be very interesting if other classes could be examined in more detail; however a major problem in such work is the provision of a suitable environment for the different species studied. Although no changes in composition have been made to date, the physical character of the diet was changed to suit the conditions of the experiment or the appeal of the animal being fed. Detailed results will be presented elsewhere.

Chlorella sp., Escherichia coli, Lactobacillus arabinosis, Penicillium expansum, Saccharomyces cerevisiae, and *Tetrahymena gelleii* were maintained in pure culture through ten transfers in sterile mixtures of the diet in water. Satisfactory growth rates were obtained when the diet was fed to monkeys, pigs, cats, dogs, rats, mice, rabbits, guinea pigs, an opossum, chicks, goldfishes, cockroaches, snails, and tomato plants. The guinea pigs and snails were carried through reproduction, and four consecutive generations of mice and cockroaches were fed the diet. The success of the diet in such general application gives nutritional evidence for a fundamental unity throughout these forms of life and indicates the validity of the concept of the universal diet. The experience should be helpful in formulating another universal diet for a more critical experimental examination of the thesis.

Acceptance of the concept and the eventual use of a universal diet would be of value in many ways. Diet could be considered as a unit variable instead of as a complex variable in biological research. Interspecies comparisons of LD_{50}, nutritional requirements, metabolic products, physiological tests, and so forth, and interlaboratory comparisons might be more valid if

a standard diet were used. The acceptance of one diet for many species could greatly simplify feeding problems for the biologist who uses a great variety of biological species and might make the work more acceptable from the viewpoint of insuring a well-fed subject. It would also facilitate the introduction of new species into the laboratory. Such a diet could be useful in a search for unknown nutritional factors; a species that fails to perform properly when fed this diet may be presumed to require an unidentified factor. This diet could appropriately be used to learn how far principles of nutrition may be applied in the complete range of biological material. Nutritional adaptations could then be better understood and eventually predicted. Nutritional similarities and differences between species, as expressed in terms of a common diet, might indicate the path of nutritional evolution and complement the work being done in comparative biochemistry and morphology. The concept of the universal diet should give proper perspective to the place of nutrition as a common denominator of biology (*4*).

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4. Acknowledgment is made of the helpful criticism offered in the preparation of this manuscript by G. M. Briggs, C. A. Elvehjem, R. Lawrence, C. G. King, A. G. Hogan, T. H. Jukes, T. Just, L. A. Maynard, H. H. Mitchell, and J. R. Reyniers. Experimental examination of this thesis was begun while I was a member of the faculty of the University of Notre Dame.

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Communications

An Instrument to Simplify Bone Drilling and Injection

There has been a need for an easier and quicker method for penetrating bone structures when intracerebral inoculations are made into animals. The present methods of trephining or cutting the skin and drilling are tedious and time consuming.

During the course of work involving a large number of monkeys, an instrument has been devised for simplifying the technique of making intracerebral injections. The instrument is shown in Fig. 1. It is a stainless steel cup *C* with a hole *B* through the bottom and with two needle-sharp stainless-steel pins *A* attached to the bottom, one on each side of the hole. The size of the hole is determined by the size of the drill bit that is needed for penetrating the bony structure. In our laboratory we use a No. 60 bit in a portable electric dental drill. The size of the steel cup is determined by the size of the drill chuck and of the syringe. For work with monkeys, the internal dimensions of the cup C are ¾ in. in diameter and ¾ in. deep, and each pin is placed 5/32 in. from the center of the hole with the point protruding 3/32 in. from the base of the cup.

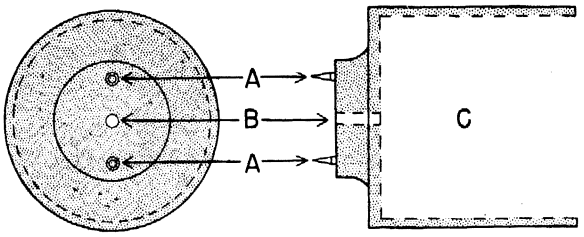

Fig. 1. Bone drilling and injection device.

Before use, both the instrument and the drill bit are sterilized. For making intracerebral inoculations into monkeys, the hair on the head is cut as short as possible with an electric clipper. The skin is then sterilized with iodine solution followed by a 70 percent alcohol rinse, and the instrument is placed firmly against the head of the animal so that the pins penetrate the skin and rest on the skull bone, thus securing the instrument and the skin so that both are immobilized. The bit of the electric drill is then inserted through the hole of the instrument, and a hole is drilled through the skull bone. After the drill bit is removed, inoculation into the brain is made through the same hole.

This instrument has been used on approximately 500 monkeys in which two intracerebral injections of 0.5 ml each were made—one injection into each hemisphere of the brain. By using two operators, one handling the drill and the other the syringe, the time required for drilling the two holes and making the injections average about 1 min for each monkey. Occasionally, some difficulty was encountered in inserting the needle through the hole in the bone. However, a second application of the drill was adequate for obtaining free access for the needle to the soft tissue under the bone. This instrument may be adapted with only slight modification of cup size to fit any hand or electric drill. It should be extremely useful to anyone interested in bone-drilling operations where fixing the location of the drill hole is important for subsequent operation. It can be adapted for use with any species of animal.

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