This, together with the lack of physiological and psychological action of 3-O-methyl catechol amines observed by others with normetanephrine (*8*) and by us with metanephrine, points to catechol-O-methyl transferase as the principal enzyme for the inactivation of epinephrine.

Note added in proof: Since this communication was submitted for publication, a paper by Kirshner *et al.* (*9*) has appeared which reports that 47 percent of the radioactivity in the urine is "3-methyl-O-adrenaline" (metanephrine), free and conjugated, following the administration of *d,l*-adrenaline-2-C^{14} to man. This finding differs from that reported previously by these workers (*4*).

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16 July 1958

Evidence That the Mammalian Nephron Functions as a Countercurrent Multiplier System

Abstract. Fluid collected by micropuncture from the bend of the loop of Henle in the concentrating hamster kidney had the same osmotic pressure as fluid from a collecting duct at the same level, while that from the distal convolution was more dilute. This indicates that the tubular fluid is first concentrated, then diluted, before its final concentration.

Hargitay and Kuhn (*1*), in 1951, introduced a new and revolutionary concept for the mechanism of urine concentration in the mammalian kidney based on the premise that the loop of Henle acts as a countercurrent multiplier system. The loop of Henle mechanism was thought to make the interstitium of the medulla hyperosmotic, which in turn caused diffusion of water out of the collecting ducts and concentration of the urine. The great theoretical advantage of this mechanism is that at no level in the kidney need there be large osmotic gradients maintained by tubular structures only one cell layer thick.

The original experimental observations in support of this theory were those of Wirz, Hargitay, and Kuhn (*2*), who concluded from cryoscopic studies of slices from concentrating rat kidneys that the osmotic pressure was identical for all adjacent tubular structures at any level in the kidney, and that there was a steadily increasing osmotic gradient from the cortex, which was isosmotic with plasma, to the tip of the papilla. Recent analyses of distal tubular fluid by Wirz (*3*) and ourselves (*4*) demonstrate that fluid in all adjacent tubules does not have the same osmolality, invalidating this aspect of the original data which presumably was due to postmortem diffusion. This does not, however, invalidate the theory of increasing osmotic gradient from cortex to papilla. This report (*5*) presents the results of osmolality determinations on fluid collected directly from the loops of Henle of hamsters.

The papilla of the hamster's kidney, which extends into the upper portion of the ureter, was exposed in anesthetized animals. When observed microscopically, vasa recta and collecting ducts were readily apparent. Under proper illumination, segments of narrow tubular structures filled with clear fluid were sometimes visible. When punctured with a micropipette and filled with large amounts of dye, they were seen to form typical hairpin loops without anastomosis. On occasion it was subsequently possible to macerate the kidney and to follow the injected loop by microdissection to the proximal and distal convolutions of a juxtamedullary nephron, proving beyond doubt that the structure punctured in the papilla was a loop of Henle. In order to exclude the possibility that the sample was plasma from a vas rectum without red cells or anastomosis, it was sufficient to demonstrate that the sample contained little or no protein by qualitatively testing it with heat or trichloroacetic acid. Fluid was also collected from adjacent collecting ducts at the same level. Osmolality was determined by the microcryoscopic method of Ramsay and Brown (*6*).

The results of four typical analyses of fluid from the bends of the loops and collecting ducts are shown in Table 1. The osmolalities were the same or nearly so and were much higher than the osmolality of plasma from the inferior vena cava. Fluid from cortical segments of proximal tubules and late distal convolutions was isosmotic and from early distal convolutions, hypo-osmotic to plasma.

Table 1. Osmolality of fluid from the loops of Henle and collecting ducts and of plasma from the inferior vena cava.

Hamster No.	Osmolality (milliosmoles per kilogram of water)		
	Loop of Henle	Collecting duct	Plasma
1	1391	1402	308
2	725	720	336
3	1270	1206	325
4	453	453	

These results are highly consistent with the hypothesis of Hargitay and Kuhn (*1*) that the mammalian nephron functions as a countercurrent multiplier system to concentrate the urine. The details of the mechanism appear to be somewhat different from those first proposed (*7*).

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7. A detailed account of these and other studies is in preparation.

12 June 1958

A System of Names for Binary Numbers

Abstract. A nomenclature is proposed for the binary number system to permit expression of binary numbers in words and to encourage visualization of magnitudes expressed in binary notation without recourse to decimal translation.

Our everyday lives impinge increasingly on systems in which binary numerical notation is encountered—for example, computers, data-processing systems, accounting systems, counting devices, logical circuitry, communication, and instrument systems generally. Familiarity with binary notation and some ability to think in terms of binary arithmetic are necessary for all scientists and engineers and are desirable for any well-informed

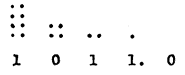
individual. It may well prove useful to arm every school child with skill in binary numbers.

The extreme simplicity of the binary system should make it a simple matter to achieve widespread acquaintance with its manipulation, provided that its use is not made to depend on a basic understanding of the mechanism of positional-notation number systems. More especially, its use should not depend implicitly or explicitly on conversion of binary numbers to or from decimal numbers. It is the purpose of this report to present a system of names that will permit expression of binary numbers without dependence on any other number system. To make this presentation self-sufficient for the benefit of those who have had no previous acquaintance with binary numbers, and to demonstrate the independent derivation of the binary number system, a brief description follows.

A binary number consists of a sequence of two alternative symbols, usually 0 and 1, as for example:

1 0 1 0 0 1 1 0 1 0

Each position in the sequence represents double the value of the position to its right and half the value of the position to its left. Assignment of unit value to a particular position fixes the values of all positions. The unity position is identified by placing a dot (.) called the binary point, to its right, thus: 10100.1010. If the point is omitted, the unity position is understood to be the ultimate position at the right end of the sequence. The value of a number is the sum of the position values specified by the symbol 1. The symbol 0 identifies the position values to be omitted from the sum. For example, the number

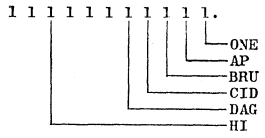


in which the value of each position is given by the number of dots in the array over the position, represents the number

The rules of binary arithmetic include only one that is unique to the binary system: 1 + 1 = 10. Thus:

$$0+0=0$$
$$1+0=1$$
$$1+1=10$$
$$1\times 1=1$$
$$1\times 0=0$$
$$1-1=0$$

The inability of the reader to express in words the rule 1 + 1 = 10 illustrates the lack of names for binary numbers. The names now proposed are as follows: The terms *one* (1) and *zero* (0) are retained for the symbols with the usual meanings of unity and nought. Position value names are



In assigning these names a mnemonic has been introduced that takes advantage of the widespread knowledge of Latin alphabetic order by making the initial letter of the name correspond to the binary order of magnitude.

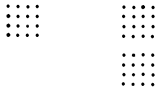
If the proposed nomenclature is to serve its purpose, these names must become mentally associated not with decimal equivalents but directly with magnitudes, as shown in Table 1. Note that the use of the comma to set off groups of positions (in groups of bru) also serves to reduce confusion with the decimal system (in which groups of ap one are used).

Numbers not specifically named are expressed as sums and products of the named values analogous to conventions used with the decimal system, thus:

1100 = 1000(CID) + 100(BRU) = CIDBRU

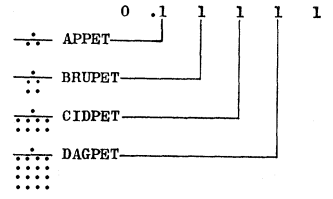
(the larger value "cid" being named first signifying *addition*) and,

10,0000 = 10(AP) x 1,0000(DAG) = APDAG



(the smaller value being named first signifying *multiplication*).

Fractional positions (to the right of the binary point) are to be named by adding the suffix *-pet* (a degradation of the word *part*) to the name of the reciprocal integral position, thus:



The number 0.11 is apone brupets

or the equivalent, bruap cidpets

It is interesting to compare the number of terms needed in the binary system and in the decimal system to express numbers up to the magnitudes included here. In the decimal-number nomenclature we have zero, one, two, three, four, five, six, seven, eight, nine, ten, hundred, and thousand—a total of thirteen terms. In the binary-number nomenclature we have zero, one, ap, bru, cid, dag, and hi —a total of bruapone (seven) of which bruone (five) are new.

Comparison of the number of syllables needed to express numbers in the two systems is unfavorable to the binary system, and long sequences become awkward at values much smaller than they do in the decimal system. It is not necessary, however, to go beyond the magnitudes named here (*1*) to achieve the primary purpose of this proposal, which is development of the ability to "think binary." Long sequences can be communicated by calling off the sequence of digits, just as is done, for example, in relaying telephone numbers.

A few additional examples of number names are shown in Table 2. Finally, the arithmetic rule 1 + 1 = 10, which we could not previously express, is now: One and one are ap.

Table 1. Names, symbols, and magnitudes of binary numbers.

NAME	SYMBOL	MAGNITUDE
ZERO	0	
ONE	1	·
AP	10	··
BRU	100	∴
CID	1000	∴·
DAG	10000	∴··
HI	1,0000,0000	∴∴ ∴∴ ∴∴ ∴∴ ∴∴ ∴∴ ∴∴ ∴∴ ∴∴ ∴∴ ∴∴ ∴∴ ∴∴ ∴∴ ∴∴ ∴∴

Table 2. Examples of number names.

Decimal	Binary
297	1,0010,1001
Two hundred ninety-seven	Hiapdagcidone
87	101,0111
Eighty-seven	Bruonedag bruapone
58.375	11,1010.011
Fifty-eight and three hundred seventy-five thousandths	Aponedagcidap and apone cidpets

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National Bureau of Standards, Washington, D.C.

Note

1. It has been suggested by G. W. Patterson of the Moore School of Electrical Engineering that the usefulness of the proposed system of names would be very much enhanced if the system were extended by adding means for expressing powers of hi. He suggests bihi, and so forth, for this purpose. While the author is largely in agreement with this point of view he has preferred to allow extension of the system to await demonstrated need. Appreciation is due Professor Patterson for critical review of the proposal and for a number of useful suggestions.

25 June 1958

Some Genetical Implications of Physical Studies of Human Haptoglobins

Genetical differences obtained with human and cattle serum proteins have been demonstrated by the technique of starch gel electrophoresis (*1, 2*). These proteins in man, which are known as haptoglobins, migrate with the α_2-globulins and have the specific property of binding hemoglobin (*1*). Family studies are usually compatible with the hypothesis that their synthesis is controlled by two autosomal genes with incomplete dominance (*3*). It has been proposed that the three genotypes should be designated Hp^1/Hp^1, Hp^2/Hp^1, and Hp^2/Hp^2 (*4*).

The electrophoretic differences which first enabled classification of human sera into the three groups are complex and are shown diagrammatically in Fig. 1, column 2. The serum corresponding to group 1–1 contains a protein with a mobility in the fast α_2 fraction which, when combined with hemoglobin, stains with benzidine, whereas that designated group 2–2 has three bands of slower mobility which also stain with benzidine when combined with hemoglobin. Although the heterozygote, group 2–1, also shows a weak band corresponding in position to the fast α_2-globulins, the three slower bands differ from those in the group 2–2 serum in position and relative intensity. An even greater degree of complexity is suggested by the frequent presence of additional hemoglobin binding proteins in trace amounts.

Electrophoretic separation of hemolyzed serum by conventional starch zone electrophoresis also enables a distinct differentiation of the three groups to be made. When this method is used, the red band of the haptoglobin-hemoglobin complex can be seen against the white starch background. The diagrams in Fig. 1, column 3, show that the most rapidly migrating red band is found in group 1–1, whereas the slowest corresponds to group 2–2. The heterozygote does not separate into two discrete colored zones, as might have been anticipated, but migrates as a single band of intermediate mobility. These observations are in striking contrast to many of the hemoglobinopathies in which the heterozygote usually reveals a mixture of the two components found in the homozygotes.

To investigate these proteins further, samples of the haptoglobin-hemoglobin complex of the three genetic groups were purified in the following manner. Fifteen to twenty milliliters of serum free from hemolysis were separated by starch-zone electrophoresis (barbital buffer, *p*H 8.6, $\Gamma/2$, 0.1). The α_2-globulin peak was eluted and concentrated, and hemoglobin C was added in sufficient quantity to ensure saturation of the hemoglobin-binding capacity of the haptoglobin. The mixture of α_2-globulin and hemoglobin C was separated on a second starch block (barbital buffer, *p*H 8.6, $\Gamma/2$, 0.05). The presence of hemoglobin C resulted in sufficient slowing of the haptoglobin-hemoglobin complex to allow it to be seen as a red band behind the other α_2-proteins and ahead of the excess free hemoglobin C. Hemoglobin A, which migrates more rapidly, causes less slowing of the haptoglobin complex and therefore results in poorer separation of the haptoglobins from the remainder of the α_2-globulins. Purified preparations of haptoglobin-hemoglobin complex from each of the three hemoglobin types were then studied in the ultracentrifuge (Fig. 1, column 4).

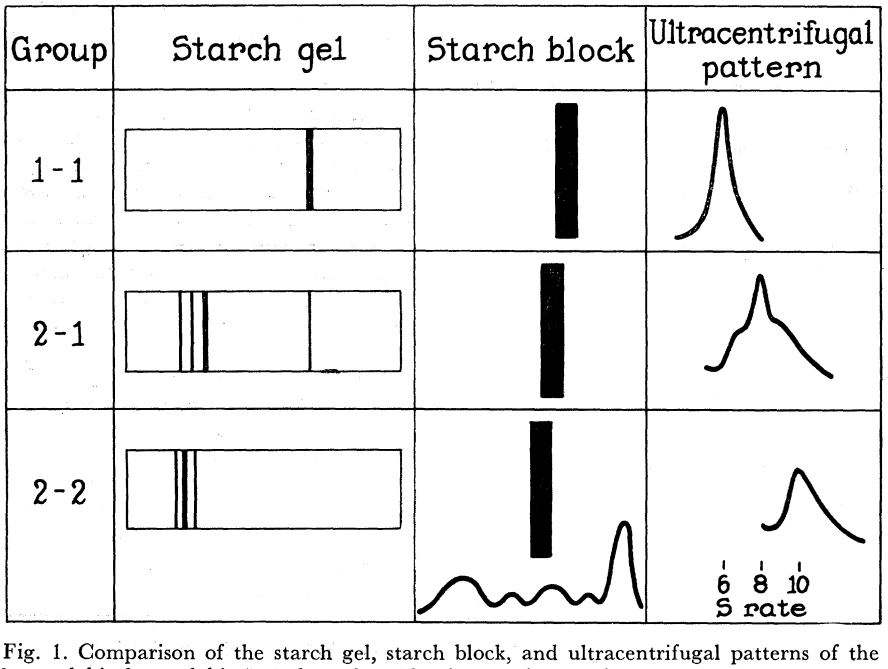

Fig. 1. Comparison of the starch gel, starch block, and ultracentrifugal patterns of the haptoglobin-hemoglobin complexes from the three main genetic groups.

Each of five specimens isolated from the sera of two individuals of group 1–1 had a single protein peak with an approximate sedimentation (s) rate of 6 *S* (5.4 to 6.3), whereas the predominant peak in six samples from three homozygotes corresponding to group 2–2 sedimented with an s rate of approximately 10 *S* (9.4 to 10.7). Because of dependence on concentration, these would correspond to $s^0_{20,w}$ values of approximately 6 and 11 *S* and are similar to the values reported by Jayle *et al.* (*5*) for two types of haptoglobin-hemoglobin complexes. In the heterozygote, however, each of eight fractions isolated from three individuals contained a major component with an s rate of about 8 *S* (7.6 to 8.8) and an approximate $s^0_{20,w}$ of 9 *S*. In addition, there were two minor components with s rates essentially similar to those present in the homozygotes. No material with an s rate of 8 *S* was detectable in either homozygote. Electrophoretically isolated α_2-globulins from two individuals of groups 1–1 and 2–2 were mixed in varying proportions, and hemoglobin C was added to saturate the haptoglobins present. The haptoglobin-hemoglobin complex of this "synthetic heterozygote" was then isolated and studied in the ultracentrifuge. Two distinct peaks with s rates of approximately 6 and 10 *S* were observed. No peak of intermediate sedimentation rate, such as was seen in the "true heterozygote," could be seen.

The presence of three different haptoglobin groups was also reflected by the distinct differences in the ultracentrifugal behavior of the whole α_2-globulin fractions, with and without added hemoglobin (*6*).

It is apparent that the two genes at the haptoglobin locus have given rise to three, and possibly more, closely related proteins some of which can be distinguished ultracentrifugally. One of these appears to be confined to the heterozygote. These findings in man bear some