

sired level (Fig. 2). Each separation will convey the impression that the material was cut at that point and thus will expose another top surface. A thorough understanding of the possibilities of the perspective chart will reveal that it is even possible to indicate separations which are perpendicular to the original sections.

The completion of the line drawing in perspective may well convey all the information desired. If, however, the demonstration of more detail is a factor, a more complete rendering will be necessary. The rendering method should be selected to suit the specific needs of the researcher. The uncomplicated neuromuscular relationship, which was purposely chosen because of its simplicity, was rendered with an airbrush (Fig. 2). Even though a reduction in air pressure produces a stipple effect, final delineation of the top surfaces had to be completed with pencil. This method has proved very satisfactory with other illustrations that portray more complex structures, especially where a transparent or translucent effect was required (Fig. 3).

Skillful control of any rendering device is of little value without an understanding of light and shade. This understanding is acquired through the observation of the action of a light source upon real objects and through practice in applying the resultant effects to an illustration. A hypothetical light source from above the illustrator's left shoulder, casting shadows down and to the right rear, is considered standard. Sometimes a different light source will do more to explain the surfaces and therefore it should be considered a tool and used to the best advantage. The degree of intensity of the imaginary light source is pertinent and easily controlled. Precise shadows cast from an intense light source are apt to destroy the legibility of the form and it may be advantageous to indicate a more diffused light.

A technically accurate perspective illustration can not only solve the known problems but can expose and solve some which were previously undetected. Painsstaking attention to detail can result in a very realistic representation of the ultrastructural interrelation of tissue components as they would appear in three dimensions.

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Lactic Acid Metabolism in Hypertensive Patients

Abstract. *In patients (93) with either essential or renal hypertension the concentration of lactic acid in both venous and arterial blood was significantly ($p < .001$) elevated, whereas there was no significant increase ($p < .127$) in the concentration of blood pyruvate. Neither renal insufficiency nor various modes of therapy could be correlated with this increase in lactic acid.*

A survey of patients in our clinic confirms recent reports (1) that suggest a rather striking incidence of hyperuricemia in patients with uncomplicated hypertension. The cause of hyperuricemia in hypertension is unknown. It is known, however, that the lactate ion interferes with the renal excretion of uric acid in man (2). Therefore, lactic acid concentrations in peripheral venous blood of patients with hypertension were determined and compared with those for a group of normotensive control subjects. Because higher-than-normal ratios of blood lactate to blood pyruvate may reflect a greater degree of anaerobic metabolism in tissues (3, 4), concentrations of pyruvic acid were also determined on the same samples. The results showed a significant and rather consistent abnormality of the ratio of lactate to pyruvate in the blood of patients with both primary and secondary (renal) hypertensive disease. This abnormality did not appear to be related to the presence or absence of hyperuricemia.

Ninety-three ambulatory hypertensive patients (blood pressures repeatedly higher than 140/90) and 47 normotensive control subjects were studied. Seventy-three patients had "essential" or "primary" hypertension and 20 had hypertension secondary to renal or reno-

vascular disease; none exhibited signs of congestive heart failure at the time of study. Fifty-six of these patients were treated with antihypertensive medications, including the thiazide diuretics. None were normotensive at the time of the study.

Venous blood was obtained from the forearms of all subjects by venipuncture without application of tourniquets; the hypertensive patients had rested for at least 30 minutes previously. The controls were healthy, normotensive hospital employees. Arterial blood was obtained by percutaneous puncture of the brachial artery in nine hypertensive subjects anesthetized with 1-percent xylocaine. Lactic acid and pyruvic acid were measured by enzymatic methods (5) that depend on the reduction or oxidation of diphosphopyridine nucleotide (DPN), reactions catalyzed by the enzyme lactic dehydrogenase; the equilibrium of the reaction favors the formation of lactate and DPN⁺. By employing excess DPN⁺, an alkaline medium, and by trapping pyruvate by addition of hydrazine, quantitative conversion of lactate to pyruvate can be achieved, accompanied by stoichiometrical increase in DPN-H formation. The DPN-H formed, measured photometrically, reflects the lactate concentration. Conversely, quantitation of pyruvate is accomplished by measuring the amount of DPN-H oxidized in the course of the quantitative conversion of pyruvate to lactate under acid conditions. Lactic acid was measured in serum obtained from blood that had been allowed to clot by standing for 45 minutes; the separated serum was treated with an equal volume of 6-percent perchloric acid. Pyruvic acid content was measured after mixing

Table 1. Venous (V) and arterial (A) concentrations of lactic and pyruvic acids (milligrams per 100 milliliters) in nine patients with hypertension.

Lactic acid in serum		Pyruvic acid in blood		Lactate: pyruvate ratio	
V	A	V	A	V	A
29.9	29.1	0.54	0.56	55.4	52.0
29.0	24.9	.66	.57	43.9	43.7
30.1	22.3	.64	.48	47.0	46.5
18.7	13.9	.62	.51	30.2	27.3
32.8	24.8	.55	.50	59.6	49.6
29.4	28.5	.51	.62	57.6	46.0
30.1	29.2	.64	.53	47.0	55.1
35.2	33.6	.69	.51	51.0	65.9
30.5	28.3	.65	.59	46.9	48.0

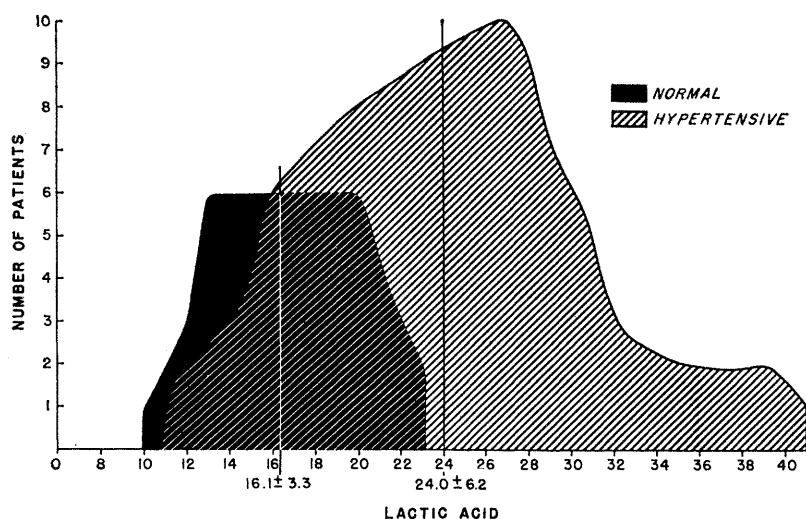


Fig. 1. Lactic acid in the serum (milligrams per 100 milliliters) of normal and hypertensive patients. Vertical lines indicate the means for the two groups.

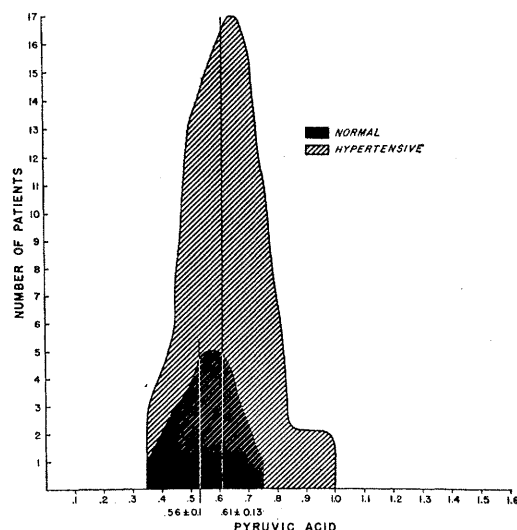


Fig. 2. Pyruvic acid in blood of normal and hypertensive patients. Vertical lines indicate the means for the two groups.

equal parts of 6-percent chilled perchloric acid and freshly collected whole blood.

In the hypertensive group, there was a statistically significant ($p < .001$) elevation in the lactate in the serum (Fig. 1), which was not accompanied by a statistically significant ($p < .127$) rise in the pyruvate level (Fig. 2). The ratio of serum lactate to blood pyruvate was 27:1 in the control group; in the hypertensive group, 38:1.

In all nine hypertensive patients whose arterial blood was sampled, the concentration of lactic acid in venous blood was higher than in arterial blood (Table 1); in eight of the nine the lactic acid concentration in arterial blood was also higher than the mean values for venous lactate for the normal controls, and in eight of the nine the ratio of lactate to pyruvate in both venous and arterial blood was greater than was found in the venous blood of the normal controls. In the patients with high concentrations of lactic acid in the venous serum there was no correlation between lactic acid concentration and height of blood pressure as measured with a sphygmomanometer, degree of impairment of renal functions as determined by the concentration of urea nitrogen in the blood, or the presence or absence of therapy for hypertension.

These results demonstrate that significant lacticacidemia and high ratio of lactate to pyruvate in the blood were present in a large percentage of ambulatory patients with arterial hypertension. The lactic acid content of

serum was not elevated in a comparable group of normotensive controls. Since this higher concentration occurred both in patients with primary hypertension and in those with renal hypertension, it seemed to be related more to the high blood pressure than to the etiology of the disease process. The increase in the concentration of lactic acid in serum was not sufficient to appreciably alter the acid-base balance in any hypertensive patient.

Three possible explanations for an increase in the ratio of blood lactate to pyruvate (6) are: (i) the peripheral vasoconstriction characteristic of hypertension may in some patients produce tissue anoxia in various areas and cause the cellular metabolism to become more anaerobic; (ii) the energy required by vascular smooth-muscle cells to sustain vascular constriction exceeds the supply of oxygen to the vessels and results in greater formation of lactate. Pertinent to greater formation of lactate is its occurrence in isolated peripheral arteries in vitro during administration of vasoconstrictor substances or when the vasoconstriction is induced by electrical stimulation (7); and (iii) lacticacidemia in patients with arterial hypertension may reflect the increase in the work of the heart characteristic of this condition (8).

The fact that concentrations of lactic acid in arterial blood were also elevated indicates that disturbance of metabolism was not confined to the arm. The lacticacidemia of hypertension is not likely to result from renal insufficiency because [as reported in (4)]

the lactate concentration in serum was not necessarily elevated in states of gross renal insufficiency. Urinary excretion of the lactate ion is negligible when compared with the extent of its production and removal by other tissues of the body. An increased renal excretion of excess lactate has in fact been reported in patients with hypertension (9). Since it is most probable that the concentration of lactate in arterial blood at any one time represents an equilibrium state at that moment for the entire body, these findings of high lactate:pyruvate ratios in arterial blood perhaps indicate a generalized metabolic derangement in hypertensive patients.

Virtually no biochemical abnormality has been identified hitherto for any large proportion of patients with arterial hypertension. Whether lacticacidemia is a metabolic reflection of the intensity of the hypertensive process itself or whether it is a consequence of abnormal blood flow and tissue perfusion in hypertensive disease awaits further study.

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Probability-Learning by the Turtle

Abstract. *Tested in a two-choice situation, the painted turtle, Chrysemys picta picta, shows random probability-matching in visual problems and in confounded visual-spatial problems, but only maximizing or nonrandom matching (reward-following) in spatial problems. The results are compared with those of analogous experiments on fish, bird, and mammal.*

Given a choice between two stimuli, one of which is rewarded, say, on a random 70 percent of trials and the other rewarded on the remaining trials (a so-called 70:30 problem), a rat or a monkey typically "maximizes" (1)—that is, it comes to choose the more-frequently rewarded stimulus on almost all trials. Occasionally, one of these animals "matches"—that is, its asymptotic choice-ratio approximates the reward-ratio; but the matching is nonrandom—that is, the patterns of choice give evidence of certain simple strategies that are reminiscent of the more complex strategies associated with probability-matching in man. In experiments with the rat (2), for example, matching has been traced to reward-following (a tendency on each trial to choose the alternative rewarded in the previous trial), while the opposite strategy (avoiding the previously rewarded alternative) has been found in experiments with the monkey (3). In experiments with the fish (4), by contrast, matching has appeared which may be characterized as random because the data show no sequential dependency. This difference in results for fish and mammal has led to the study of certain intermediate forms.

In our studies we used 22 experimentally naive, sexually mature painted turtles (width of carapace, about 10 cm) from the laboratory colony. After adaptation to individual 40-liter aquariums, the animals were trained in a black Plexiglas chamber containing about 1.5 cm of water (5). At one end of the chamber were two circular targets of translucent Plexiglas, which were illuminated with colored lamps at the start of each trial. The animal was trained to make a choice by pressing its nose or foot against one or the other of the targets. A correct choice turned off the target lights and caused a pellet of flounder to be rotated into the chamber on a tray at a point just above water and midway between the targets. At the same time, a white light above the point of delivery of the food was turned on for a few seconds to signal the presentation of food and to enable the animal to find it. The animal bit the food from the tray, lowered it into the water, and ate it. After an incorrect choice, the target lights were turned off for 6 seconds of darkness before the two targets were illuminated again. After a predetermined number of repetitive errors, the period of darkness was followed by illumination of the correct target alone (guidance), and the animal was rewarded for pressing it. All of the events of training were programmed automatically, and the responses were recorded on tape.

Each animal had six daily training sessions per week. There were ten trials per session for some animals and 20 trials per session for others, with an interval of 6 seconds (in darkness) between trials. In some instances, guidance followed three repetitive errors; in others, guidance followed the initial error (that is, there was no opportunity for repetitive error). Neither the number of trials per session nor the repetitive-error limit in use seemed to make a difference.

The performance of five turtles trained in 100:0, 70:30, and 50:50 visual problems is plotted in Fig. 1. In these problems, the two targets were illuminated with lamps of different colors on each trial (one red, the other green); the location of each color varied from trial to trial in quasi-random order (6). Three of the animals began with a 100:0 problem (in which choice of one of the colors was rewarded on all trials); they were then shifted to a 50:50 problem (in which

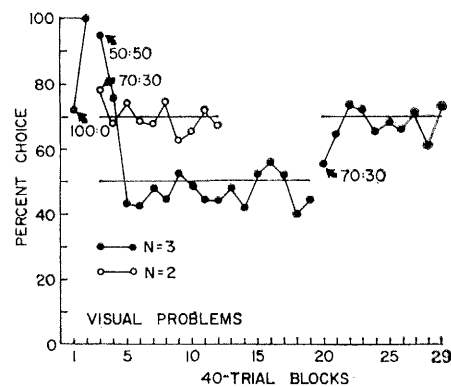


Fig. 1. Performances of five painted turtles in 100:0, 70:30, and 50:50 visual problems. *N*, number of turtles in each group; means of groups are plotted.

each color brought reward on a random half of the trials), and finally shifted to a 70:30 problem (in which the color rewarded on all trials in the first problem was rewarded on a random 70 percent of trials, and the alternative color was rewarded on the remaining trials).

The performance of these animals is plotted in terms of the mean percentage of trials on which the color rewarded 100 percent of the time in the first problem was chosen by the turtle in each stage of training. The other two animals were trained from the outset on the 70:30 problem; their performance is plotted in terms of the mean percentage of trials on which the color rewarded 70 percent of the time was chosen. The correspondence between choice-ratio and reward-ratio evident in the mean curves is characteristic of the individual performances—all the animals showed good matching. The matching, furthermore, appeared to be random. Tests of the

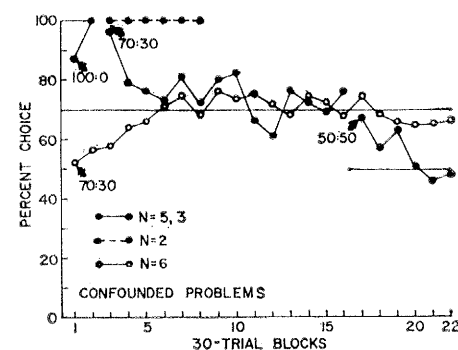


Fig. 2. Performances of 11 painted turtles in 100:0, 70:30, and 50:50 confounded (visual-spatial) problems. *N*, number of turtles in each group; means of groups are plotted.