

THE PHYSICAL BASIS OF VITALITY

or

Mechanics of Circulatory Momentum, Lactate Tolerance, and Renal Excretion

PREFACE

While the function of the physician is to preserve life and quality of life in individual patients, the approach of organised medicine has largely been a negative one, concentrating rather on pathological processes and the contribution they make towards extinguishing life, rather than the more positive approach of enquiring why life persists, and the steps one might take to encourage that persistence. Hygienic and nutritional measures concentrate in the main on attempting to prevent the onset of pathology or disease processes, but the systematic investigation of the life process, its origin and maintenance, have not perhaps received the same emphasis to date.

The study of genetics and Mendelian inheritance, while it has produced exciting discoveries relating to inherited form and function in individuals, is still concentrated on inherited disabilities, and has produced little positive information concerning the origin and persistence of life forms. Indeed it is apparent that the genetic code is rather a 'blue print' for the development of the future individual that cannot proceed any further without the provision of life giving energy from another source.

The functional activity of individual tissues and organs, and the cells of which they are composed, is the province of physiology, and much information has accumulated regarding individual tissue function, together with the coordinating activity of nerves and humoral factors in producing a functional whole. The life process however, which distinguishes living tissues from dead ones, remains somewhat clouded. This does not mean that the individual mechanisms necessary for continued living are not understood, it simply indicates that the coordinating mechanisms to produce a functioning whole are still elusive.

Over recorded history it has been recognised that the life of an individual is closely associated with the persistence of readily recognised bodily functions. Unless it can be restarted immediately, life ceases when the heart stops beating; while continued loss of blood similarly leads to death unless the loss is rapidly controlled or the blood replaced; cessation of respiratory movements and exchange of respiratory gases will extinguish the life process, as will excessive temperature change whether by heat or cold, while deprivation of food and water lead to death after a slightly longer time interval.

The supply of a combination of fluid volume and energy in regulated amounts which maintains life, is related to each of these and the factors they have in common, that involve movement of a sufficient volume of body fluid with adequate kinetic energy of flow and concentration of respiratory gases, to maintain both metabolism and temperature control; i.e., sufficient momentum of blood containing an adequate level of respiratory gases, and sufficient metabolism to maintain body temperature. The purpose of the present account is to show a relationship between momentum, gas concentration, and body temperature, with the kinetic energy maintained in body fluid, as representing the physical aspect of the 'life force' or vitality, required to be maintained during the life time of the individual.

There can be little doubt about the need for an adequate but controlled supply of oxygen to maintain the living state in mammals, nor for the requirement of nutrient material derived from other life forms, which produce carbon compounds containing oxygen and hydrogen, to produce a continually controlled level of energy for maintenance of the life process. This implies the continuous production and maintenance of carbon dioxide concentration, and water from the combination with oxygen. Unless water, oxygen, and carbon dioxide are available in adequate amounts, the life process cannot persist. The process takes place in a water based fluid medium, where oxygen is obtained from the atmosphere, but carbon dioxide is produced as a result of the life process itself, and becomes an essential part of the continuing functioning life form, equally important with

oxygen and water for life to persist. There are of course many other essential ingredients for life in mammals, but the latter is quite impossible without water, oxygen and carbon dioxide being available in sufficient but controlled amounts, and of these, only carbon dioxide itself is largely produced as a result of the living state, and alone indicative of its persistence.

Tolerance to lactate concentration is an essential part of the metabolic processes involved in partition of energy between the cells, and the amount of fluid perfusing the tissue in which the cells are immersed. Excretion of fluid and waste products from metabolism are an equally essential part of the energy balance between cells and circulation that the 'life force' must accomplish, through altered mechanics of fluid flow in the blood vessels and in the tubules of the kidney.

The life of each individual mammal originates when male and female gametes fuse to produce a zygote in the process of fertilisation. Growth and division of cells then occurs with differentiation and maturation to eventually produce a mature organism.

But this development will not proceed satisfactorily without the provision of nutrient fluid of suitable constitution associated with energy at a sufficient level.

The volume of fluid provided requires energy of fluid motion (present as linear velocity of flow) as well as sufficient heat (or free energy) to maintain a suitable temperature within the system. It is the association of fluid with particular volume and constitution, heat energy (or random movement of fluid particles), and flow energy (or organised movement of fluid volume) which provide the conditions for continued growth and development of the embryo. These conditions must eventually be developed independently by the foetus, before it is able to assume an independent existence at birth, and is necessary to maintain that existence for the lifetime of the individual. Cessation of fluid movement extinguishes the life process, leading eventually to death of individual body cells. Movement of fluid of required composition, volume, and linear velocity of flow can be regarded as the 'life force' of that individual. It has chemical aspects involving the composition of the fluid, and also physical elements representing fluid momentum.

Although the life process originates with fertilisation, it may be arrested at certain stages for a varying period of time. The germ cells and gametes themselves have the potential to produce life, but this is potential life only, and unless fertilisation occurs there is no further development. Individual cells may however be preserved for relatively long periods by controlling energy exchange with the environment, for example by lowering the temperature, and they resume full vigour when the temperature is again raised. Preservation of early embryos may also be achieved by lowering the temperature.

Once fluid and energy exchange with the cells has been initiated and maintained on a regular basis, the life process is disrupted permanently unless fluid and energy exchange is continued without interruption for the remainder of that individual's lifetime. Maintenance of both chemical composition and physical volume and energy content of fluid require quite sophisticated mechanisms which involve embedding of the embryo in maternal tissue, where the 'life force' of the mother also provides the life force of the embryo, until such time as the latter becomes a foetus with its own circulation providing fluid momentum, but still needing assistance from the circulation of fluid and blood in the maternal tissues, to maintain the composition of its own circulating blood. Over the gestation period the foetus gradually loses its dependence on the maternal circulation and metabolism. Parturition occurs when the mature foetus is able at last to maintain its own internal environment, though still requiring nutrition from the mother, until its organs are sufficiently mature to obtain nutriment directly from its surroundings. There is a relatively prolonged period of gestation, followed by a more prolonged period of neo-natal development, before complete independence is achieved. Throughout all, maintenance of circulatory momentum is the over-riding necessity, and it is through the preservation of fluid momentum at an optimal level that all other bodily functions are developed, and maintained for the life span of the individual.

Though the concept is relatively simple, the mechanisms involved in maintaining circulatory momentum and the functions of the blood circulation that flow from it, become extremely complicated, and regulation of fluid and energy exchange comes to involve all of the cell and organ systems of the body in some degree.

An adequate account of circulatory momentum and its functional effects is really an account of the whole of mammalian physiology, and would be too comprehensive for the present purpose. For this reason it has been restricted to three elements or aspects that illustrate some of the more essential features. Circulatory momentum occupies a large section, commencing with the direct transfer from one generation to the next without interruption for the duration of the existence of the particular species. The gap between generations is bridged by the overlap between the maternal circulation, and the development of the circulation in the offspring, with both

contributing to the life of the foetus until the circulation of the latter becomes sufficiently mature to maintain the newborn as a relatively independent individual. Transmission through the female line remains continuous between generations, so that the inheritance of 'vitality' represents part of the 'race memory' transmitted directly as a physical entity rather than by way of the genetic code though there is a link between the two requiring the embryo to follow the phylogenetic pathway to development of its own circulation, and later transmission to its offspring in turn.

The mechanics of circulatory momentum occupies a large section of the current account. This subject has rarely been seriously considered by authors describing the cardiovascular system and fluid motion since the original account by Harvey, but it has important ramifications which need to be outlined.

The effect of the tissue concentration of lactate on the function of the cardiovascular system and cells of the effector organs, presents as a subject requiring elucidation through description of the regulation of tissue perfusion with respect to cell work performance, which appears as a prime function of this metabolite, where loss of this function leads to great disability.

Physical forces involved in fluid momentum affect renal function so profoundly that the effects on renal excretion cannot be ignored. Excretion by the kidney is greatly influenced by volume and velocity of flow in the blood vessels and tubules of the organ, and the effects that are produced on the metabolism of the renal tubule cells. These features have significance for renal cell metabolism, which are similar to the effects of mechanical forces on cells elsewhere, but are more readily observed in the kidney tubules.

In short, circulatory momentum may be modified by the concentration of lactate, and the partition of fluid between the volume exchanged with the tissue fluid, and that retained within the cells to augment their own volume. In a similar way, renal excretion depends upon the regulation of the level of momentum available in the blood when it is presented to the kidney.

Maintenance of momentum in the fluid environment of the tissue cells is seen as an essential feature of the life process. The physical forces which must be generated for this purpose in the mature individual are those necessary to sustain vitality, and need to be present at a very early stage in development of the embryo, even before it is able to produce the necessary mechanisms for a sustainable circulation of fluid, or suitable environment for its own survival. In order to produce a living offspring, the potential life form represented by the fertilised ovum or embryo, must also inherit an environment of fluid with a closely regulated constitution, and energy level provided by kinetic energy of the correct amount, which has to be maintained continuously for the duration of the individual's lifetime. The physical and chemical characteristics of this environment constitute the 'life force' or vitality which must be inherited as well as the genetic makeup, and which is necessary for life to develop and continue.

A suitable environment complete with fluid volume of the required constitution, and possessing the energy to initiate and sustain the existence and development of the embryo has to be supplied from an external source, usually the circulatory activity of the mother, and must be sustained until a suitable replica has been produced from the circulation of the developing foetus. There results a considerable hiatus, during which time the embryo is dependent for the initiation and maintenance of the necessary life force by the life force of the mother, until such time as it can develop its own internal environment according to its genetic inheritance. Its further development depends not only on its genetic constitution, but also on that of the mother, and the preceding generations which have developed the suitable internal constitution of fluid and energy to maintain life and development, and the capacity to transmit that capacity to succeeding generations independently of the genetic constitution of the new individual, until the latter can develop this function. In this sense the constitution of the internal environment represents a form of 'race memory' without which no succeeding generation would be able to survive, and the life force that sustains individual vitality, and the continuation of the species would be extinguished. The mechanism which bridges the gap between generations to sustain the vitality of the embryo must also be important in the development of the foetal circulation, and the manner in which it later assumes control of circulatory momentum in the mature individual. 'Life force' extends in a continuous chain from the ultimate ancestor, though renewed for each individual, with a bridging gap provided by the circulation of the mother, providing an essential stage in the life and development of the embryo.

Among problems the embryo has to surmount is the relative toxicity of high oxygen concentration for respiratory enzymes, and the requirement for relatively high carbon dioxide concentration needed to maintain tissue perfusion. These difficulties are solved in the maternal tissue fluid, where the concentrations are greatly modified compared with those in the atmosphere. When oxygen concentration in tissue fluid is increased, the local blood vessels are constricted (and linear velocity of blood is increased), while if blood viscosity is

increased (as carbon dioxide content rises) the increased velocity necessary to maintain motion requires the product of $[O_2][CO_2]$ to be proportional to circulatory length for a given force of ventricular contraction.

The composition of the moving fluid itself is rather complex, and further constituents are continually being discovered, often in minute amounts or traces which are still of great significance for function of the tissue cells. The volume and energy of the moving fluid should be more capable of ready definition, and it is this aspect which constitutes the physical basis of vitality which is pursued in further text

Involvement of the concentrations of the respiratory gases maintained in the tissues with the dimensions (and so volume) of the vascular system at any time, stem from the following considerations. The volume of blood in each blood vessel or series of blood vessels, is proportional to the length times the cross sectional area, which is an inverse function of oxygen concentration present in the tissue fluid. But the volume of each distensible vessel is also proportional to the viscosity of blood which impedes linear velocity of flow, and increases the cross sectional area as blood velocity slows and lateral pressure on the vessel walls increases to increase vascular filling, i.e., 'length / $[O_2] \propto$ volume', 'while volume $\propto \eta$ ', so that ' $l / [O_2] \propto \eta$ '. But viscosity is related to the gas concentrations and saturation of haemoglobin with oxygen, or ' $\eta \propto 1 /$ oxygen saturation of haemoglobin', and $\propto [CO_2]$, so that the product $[CO_2] \cdot [O_2] \propto l$, as previously indicated. The length of the blood vessels becomes a function of the gas concentrations in the tissues, and this relationship governs development and function which only proceeds satisfactorily while the gas concentrations are maintained within limits which are considerably different from the concentrations of atmospheric gases, maintained by the physical forces which are present in circulating fluid on a continuing basis.

This relationship allows a mathematical model to represent circulatory activity, and provides the physical basis for 'vitality' and the amount of 'life force' which has to be continued during the lifetime of the new individual, and transmitted in turn to the following generation directly from the mother's circulation, until the foetus develops its own circulation, firstly to maintain the gas supplies to the tissues at the correct concentrations, and the circulatory momentum to produce fluid exchange with the cells, and over the longer term to produce sufficient oxidative metabolism to maintain body temperature, and finally the ability to metabolise fat present in the mother's milk, which is essential to maintain body temperature in the maturing infant.

The basic relationship governing circulatory activity is that between the tissue gas concentrations, and the length of the blood vessels. All other parameters encountered in circulatory assessment are functions of $[CO_2][O_2]$, and the capacity to regulate the gas concentrations are functions the embryo must acquire at a very early stage associated with growth and development. Metabolism in turn is only possible if glycogen and glucose are available from the mother in controlled amounts, associated with the circulatory momentum available in her circulation. The latter supplies the embryo and foetus with controlled amounts of carbohydrate and blood gases, and disposes of any excess metabolites (e.g., *[lactate]*) through maternal metabolism, at the same time as it contributes as necessary to avoid any deficiencies the developing foetus may encounter.

The relationship between respiratory gas concentrations and circulatory length is the assumption which underlies the maintenance of circulatory momentum and state of 'living', which only persists while circulatory momentum and kinetic energy is maintained at an adequate level.

The implication is that while the embryo has the genetic pattern for a new individual, its survival, growth, and development, depend upon material and energy input from an existing individual (whether natural mother or surrogate) to provide the fluid, nutrients, and energy which together transmit 'life force' to allow the birth of an independent living individual able to maintain the state of living for the duration of its independent existence.

Linear velocity of flow and the kinetic energy in tissue fluid is transmitted directly through 'race memory' involving phylogenetic development of the embryo until it becomes a foetus, and able to develop its own internal environment with respect to both physical composition and energy content. By the time the foetus assumes an independent existence following parturition, it has developed its own mechanisms for maintaining energy development and transfer, but still preserving the linear velocity of flow of tissue fluid within limits set by the ancestral level.

At this stage there are two contributions to production of kinetic energy, that persisting from its own metabolism, and that persisting from its ancestral inheritance, and remaining essential for preservation of life, and equivalent to the level of

momentum present in tissue fluid ($V_x \cdot vx$), and equivalent to ' $l \cdot PR^2$ ' (or circulatory length times the square of the pulse rate). If it is granted that linear velocity of tissue fluid, or ' vx ', persists from one generation to the next sustained by metabolic energy which is essential for its persistence, how is the correct amount of energy generated by the new individual and translated into energy of motion?

Body tissues are water based and exist in a watery solution both inside and outside the cells. If in any body of fluid, energy is introduced into its volume, motion of its particles increases and the temperature rises as the resulting 'free energy' accumulates with the uncoordinated or random motion of its particles. But if the movement of particles is coordinated and organised in a particular fashion so that the motion of each particle complements that of the others, translation of the body of fluid to another location will follow with the development of momentum. Organisation of the motion of cell fluid can occur when a semi-permeable membrane allows movement in one direction only, so that fluid may leave the cell but not re-enter it unless circumstances are changed. The expelled fluid then contributes to motion in the extra-cellular fluid with linear velocity $\propto vx$, to augment the linear velocity already present.

If there is sufficient transfer of cell energy, equilibrium with blood in the venules is distorted, and fluid passes into the blood stream, to augment the venous return, and leave the linear velocity ' vx ' to assume its original value, while venous blood moves towards the heart with increased linear velocity of flow to overcome blood viscosity.

Linear velocity of the extra-vascular fluid is maintained by this transfer of energy, but its final value may not be altered. Energy may be transferred across the extra-vascular fluid, but with little or no change in the overall value of the contained energy. Metabolic energy maintains ' vx ' in this way, but the energy is used in overcoming blood viscosity and resistance, to maintain venous return, rather than altering ' vx ', which represents the ratio between carbon dioxide and oxygen concentrations maintained by oxidative metabolism, and originally determined by the inherited 'race memory'.

Energy given to extra-vascular fluid comes from two sources, the 'free energy' of the 'effector cells', and the force of contraction of the myocardium, each of which produces energy proportional to ' $l \cdot PR$ ', to produce power $\propto l^2 \cdot PR^2$.

Energy present in the system at systole is proportional to $APs^2 \cdot vx$, of which a factor APs is each contributed by effector cells and the myocardium, while ' vx ' is already present in the tissue fluid as the 'life force' which must be maintained. At diastole, energy is reduced to ' $v \cdot R \cdot vx \cdot \eta$ ' or peripheral resistance ' $v \cdot R \cdot \eta$ ', times ' vx '. The factor ' vx ' is always present while the individual is living, directly inherited from the mother. If ' vx ' should be extinguished, the circulation can only be restarted by a contribution from the environment; e.g., by cardiac massage to re-establish momentum in body fluid.

The pulse rate represents the timing of fluid exchange with the effector cells that becomes necessary in order to maintain adequate momentum in extra-cellular fluid. It depends on the rate at which fluid leaves the cell, which is proportional to ' vx ', or systemic blood volume / cell volume at diastole, and also on the level of accumulated cell energy $\propto l$, or amount of creatine phosphate present. Combined, they become proportional to 'stroke volume / diastolic cell volume', $\propto l \cdot \eta / [O_2]$, or 'internal resistance to blood flow / diastolic cell volume'. Pulse rate may be increased to maintain these ratios; so that if ' vx ' falls, ' l ' needs to increase for the pulse rate to remain constant, while if ' vx ' is increased ' l ' would need to be reduced, but if the product of the two is increased, pulse rate would also be increased.

Momentum in tissue fluid at diastole becomes proportional to the product of pulse rate (from the rate fluid is exchanged with the cells, and energy available to effect the exchange) times a further value of pulse rate (from the rate ventricular stroke volume is expelled from the ventricle), or PR^2 . The value of ' PR (heart)' is kept equivalent to ' PR (cells)' by altering the value of ' l ', or fibre length of cardiac muscle, with respect to ' l ', (or 'effector cell length' \propto length of circulation), through variation of ventricular shape at diastole; i.e. ventricular septal length / ventricular septal width at diastole, $\propto PR/Q$. The change in ventricular shape is accomplished by variation in circulatory momentum in venous blood presented to the heart (see Chapter 5).

This may all be modified by respiration and the negative pressure maintained in the chest cavity to accomplish ventricular filling ($Q \cdot R$, a function of ventricular diameter with respect to septal length, or PR), so that $Q \cdot R$ changes rather than PR . l represents a change in venous volume flow rather than alteration of linear velocity of flow which is necessary to vary pulse rate.

The relative rates at which fluid enters the cell from tissue fluid, and then leaves the cell again at diastole can be demonstrated by use of the finger plethysmograph to illustrate volume flow per beat at the periphery. The slope of the anacrotic limb depends on the ratio of stroke volume / systemic blood volume, and is proportional to l , representing the increase in linear velocity of flow given to circulating blood per beat, while the slope of the dicrotic limb also depends on l , but now representing the accumulated A.T.P. in the cell, and vx , which together are proportional to pulse rate, or $Q / [O_2]$, where Q is the product of the amount of A.T.P. in the cell with the concentration of creatine phosphate. The energy represented by both limbs of the volume pulse wave combined is $l \cdot PR$, or the force of ventricular contraction. The slope of the dicrotic limb compared with that of the anacrotic limb is represented by vx , or the linear velocity of tissue fluid, so that as the ratio vx approaches the value of unity, the slope becomes more acute, while as the value diminishes from the value of unity, the slope becomes less acute.

The value of pulse rate is then a function of $[CO_2]$. In the cells, the concentration of carbon dioxide is usually comparatively less than that of oxygen, and cell volume is consequently greater than systemic blood volume, but as cell volume is diminished and blood volume becomes relatively larger, pulse rate is increased and circulatory length is diminished with rising cell temperature which is then transmitted to tissue fluid.

(At the cell surface at systole, momentum in the extra-cellular fluid is equivalent to $l \cdot PR^2$, and energy represented by the lactate concentration $\propto R/Vs$, while inside the cell, free energy is $\propto l \cdot PR$, and lactate concentration times oxygen concentration indicates energy $\propto R/vx$. Energy to be overcome before energy can enter the cell is $l \cdot PR$, while lactate concentration is common to both sides when vx in tissue fluid is elevated to Vs inside the cell by passive permeability proportional to $[O_2]$, so energy introducing fluid into the cell is $v / l \cdot PR$, and equivalent to the increase in linear velocity per beat, or l , which regulates the anacrotic limb of the volume curve.)

Energy made available to expel fluid is PR , or $l \cdot vx$, regulating the slope of the dicrotic limb, which becomes less steep as vx is reduced, or $[CO_2]$ falls compared with $[O_2]$. Under these circumstances glycolysis and lactate concentration increase, and the increase facilitates oxidation via the 'Kreb's cycle'. These relationships determine $[lactate]$ and $[CO_2]$ compared with $[O_2]$. Any increase in pulse rate increases the slope of the dicrotic limb of the volume flow curve as a result of the alteration in vx , or ratio of the gas concentrations. The slope of the dicrotic limb becomes steeper as pulse rate increases, and somewhat flatter as oxygen concentration is increased, and carbon dioxide diminishes. Each of these facilitate an increase in lactate concentration which may then produce the opposite effect, lowering oxygen and increasing carbon dioxide in the short term. An increase in oxygen concentration retains energy within the effector cell, leading to increased energy storage and external work capacity, while an increase in carbon dioxide concentration assists the expulsion of energy and fluid from the cells and produces increased tissue perfusion as pulse rate also increases.

There is some variation in the amount of energy retained between cells subjected to volume change with pulse rate, and those which are depolarised to produce activity (contraction) and work performance. When the cell is depolarised the energy retained in the depolarised cell is proportional to R / Vs , but when cell energy and volume alter with the passage of the pulse wave, the energy retained at diastole is greater by a factor proportional to oxygen concentration, and remains proportional to $R \cdot [O_2] / Vs$ or lactate concentration

$[O_2]$. Depolarisation allows rather more energy to leave the cell, and more expenditure of stored energy, than that available without depolarisation, by a factor equivalent to the energy represented by cell oxygen concentration.

Lactate concentration elevated by oxygen concentration favours oxidative phosphorylation and an increase in the amount of A.T.P., while lactate concentration itself, facilitates oxidation via the Krebs's cycle, and elevation of carbon dioxide and tissue perfusion. The ratio of $[lactate] \cdot [O_2] / l \cdot \eta \propto [O_2]^2 / \eta$, or $[O_2] / vx \propto cell\ volume / vx$. Lactate concentration indicates the level of oxygen toxicity present in effector cells, unless glyconeogenesis reduces lactate to a level where oxidation is severely reduced if not impossible.

If ' $l \propto [O_2] \cdot [CO_2]$ ' is the basic relationship associating the respiratory gases with dimensions of the circulation, it suggests that oxidation needs to occur at the least value of oxygen concentration consistent with optimal oxidation so that 'vx' remains optimal for the least energy requirement from the circulating fluid, and from both cells and myocardium. If oxygen concentration is reduced, cell and arterial volume are reduced, and this requires reduced stroke volume, blood volume, energy exchange and metabolism, with pulse rate and arterial pressure all reduced, for the individual in a basal state.

The suggested relationships that outline the regulation of circulatory momentum are those which involve the concentrations of the respiratory gases, carbon dioxide and oxygen. In much earlier times the atmospheric concentrations of these gases were different from those at the present day, and it would seem probable that original life forms were adapted for the earlier composition of the atmosphere. The gas concentrations transmitted from one generation to succeeding ones may have been adapted to greater levels of carbon dioxide, and lower levels of oxygen resembling more closely those concentrations present in living tissues at the present day, and which body function seeks to maintain, to be consistent with the levels in the ultimate ancestors, and inherited as part of the 'race memory', essential to each new individual. By maintaining the original gas levels, the species can maintain the relationship ' $l \propto [CO_2] \cdot [O_2]$ ', representing the dimensions of individual cells as well as those of the vascular system without much variation from one generation to the next. In the same way 'passive permeability' of the effector cells (muscle, nerve etc.) remains proportional to the original level of oxygen concentration in the parent race, and to remain proportional to the cell volume at diastole, while 'active permeability' of the cells is related to a level of carbon dioxide which reflects a more primitive origin, but maintains perfusion of tissues and systemic blood volume suitable to the growth and development of the embryo in earlier times, and consistent with its genetic inheritance. It ensures consistency in the relationships which regulate the fluid volumes necessary to maintain circulatory momentum;

e.g., ' $Q / [O_2] \propto cell\ fluid\ exchange / cell\ volume \propto pulse\ rate$ which regulates pulse rate from the periphery by controlling the ejection of fluid from the cell;

$'Q / Vs' \propto stroke\ volume / systemic\ blood\ volume \propto 'l'$, circulatory (and cell) length;

$'v / Q' \propto volume\ of\ tissue\ fluid\ at\ systole / stroke\ volume\ (or\ volume\ of\ venous\ return) \propto 'Q'$, which can represent both venous volume and the volume of the circulation to the effector organs.

$'l \cdot PR / Q' \propto volume\ of\ tissue\ fluid\ at\ diastole / stroke\ volume \propto 'Vs'$ (systemic blood volume).

These relationships are further pursued in later chapters.

To these may be added the significance of the concentration of lactate in effector cells

The addition of lactate to the blood increases the force of ventricular contraction for a given value of 'vx'. The effect occurs because lactate assists oxidative phosphorylation by acting as a hydrogen donor, and this also increases oxidation by way of the Krebs's cycle by increasing pyruvate, to produce increases in both 'l' (A.T.P.) and $[CO_2]$ ([creatine phosphate]) or both

stored and accumulated energy, to increase stroke volume. The amount of lactate available in the cell, limits the amount of energy passing to the extra-cellular fluid; i.e., it increases the amount of energy remaining in the cell at diastole because $[lactate] / vx$ in the cell balances $[lactate]$ in tissue fluid which is $\propto R / Vs$ when permeability proportional to oxygen concentration is taken into account. While linear velocity of fluid is available in the extra-cellular fluid, energy equivalent to $[lactate]$ becomes ' R/Vs ' which is then equivalent to R / vx in the cell, and this allows energy equivalent to R / vx to remain in the cell at diastole, and maintains a minimum level of energy between beats. If there is depolarisation of the cell membrane, cell diastolic energy is $\propto R / Vs$ which may be elevated to be equivalent to ' R ' following repolarisation of the cell membrane by 'cell strength' (equivalent to concentration of A.T.P.) or $\propto l / [O_2]$, or ' η '.

If the cell membrane is not depolarised, cell energy level at diastole is proportional to $R \cdot [O_2] / Vs$, or R / vx , which is the lactate concentration times oxygen concentration in the cell.

Renal excretion and urine production have long been considered to require a physical basis in order to produce glomerular filtrate, which is later modified by the renal tubular cells to produce urine. Glomerular filtration is a function of both the pressure and flow rate of blood presented to the kidney. These physical forces are then applied to renal tubule cells through the energy remaining as kinetic energy in tubular fluid which influences the activity of renal cells directly, and alters their reabsorptive capacity and metabolism accordingly, (see chapter 17 to 24).

Renal excretion becomes a function of circulatory momentum, and the division between stored energy in the cells, and the kinetic energy of flow, which are both essential to the process of living. The appropriate separation between these two essential energy requirements is in turn regulated by $[lactate]$ in the effector cells, and regulates the tolerance exhibited by the individual to introduced lactate in the 'Lactate Tolerance Test'. The ability to metabolise or otherwise dispose of excess lactate is a part of the capacity to maintain vitality, just as the ability to excrete nitrogenous and other waste by renal function, and to maintain circulatory momentum by metabolic processes are all essential to the life process, which finally depends on regulation of gas concentrations in effector cells.

The current account deals initially with the mechanics of circulatory momentum in the systemic circulation and the effects it produces in the extra-cellular and intra-cellular compartments through exchange of fluid volume and the energy of fluid movement between them and the systemic circulation, to produce circulatory activity. A close association seems to exist between circulatory dimensions and those of the effector cells, which reflect the relationships between the concentrations of the respiratory gases and the dimensions of both cells and circulatory system. The ultimate size of each of these depends on their level of activity, indicated by the concentrations of oxygen and carbon dioxide maintained in the cells and tissues, and regulated by the level of metabolites which persist there, of which the most active appears to be the concentration of lactate. Variations of respiratory gas concentrations regulate cell and circulatory dimensions, but these variations are associated with the lactate concentration maintained in the active tissues that depend on polarisation of cell membranes to control their activities. The tolerance exhibited towards the concentration of lactate becomes equally important with the gas concentrations in maintaining adequate fluid exchange and movement throughout the body, and it is accordingly given considerable prominence in a section of the book following the initial outline of circulatory momentum, and the movement of fluid and energy associated with it. Large variations of lactate concentration become associated with significant disturbances of circulatory function, and it is important to understand how these disturbances arise, and if possible how to avoid them.

A final section is concerned with the mechanics of renal function, and the excretion of inorganic and nitrogenous waste. Inorganic ions accumulate mainly from inappropriate ingestion with respect to bodily function at that particular time, but also because body requirements vary with respect to availability, and the requirement to alter fluid volumes and electrolytes to maintain osmotic balance and pH between different regions with altered function from time to time, with changing work levels and external temperature in the environment. The ingestion of available protein often includes amino-acids in concentrations which are not appropriate for anabolic purposes, but can be utilised for energy generation and conversion to carbohydrate, after removal of amino groups which are converted to urea and need to be excreted. Both inorganic radicles and nitrogenous compounds are appropriately removed in aqueous solution in urine, and circulatory energy is involved in their selection and removal from circulating plasma. This is largely a physical process of some

complexity that is not completely understood, and is now re-examined with respect to the physical forces involved. These forces are essentially those that produce circulatory momentum, and which affect the cells of the renal tubules with respect to their function in a somewhat similar fashion to that produced in the cells of effector organs, and are set out with some experimental findings which appear to indicate the effects of physical forces on the function of the renal cells to produce urine, by altering their metabolic activity.

The conclusion which has been reached, is that the activity of effector cells (including myocardial cells) in energy development and application is a function of their physical shape and dimensions, which in turn bear a close relationship with the shape, size, and dimensions of the blood vascular system, and the parameters which are involved in the circulation of blood and tissue fluid to maintain the living state. Furthermore, it is the movement of fluid and its contained energy which results in all bodily activity, and which in turn may be represented by variation in the concentrations of the respiratory gases which are present in cells and tissues during these episodes of function to produce mechanical pressure, force, and movement. The parameters that prescribe mechanical activity all have the base formula of the product of different multiples of oxygen and carbon dioxide concentration for each parameter, and so are all closely related, the only difference between them being the number of multiples of each respiratory gas concentration represented, variation in the value of each parameter from the others being the alterations in gas concentrations with activity.