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The True Nature of the Boiling of Body Fluids in Space

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HE boiling of body fluids at low barometric pressures and in free space has become a subject of such renewed interest that it is desirable to outline the fundamental factors delineating this problem. Misconceptions about this medical problem should not arise either among professional workers or in the mind of the general public. In popular periodicals and to some extent in the scientific literature, there has arisen the concept of the fixed altitude boundary at 63,000 feet for the boiling of body fluids. Certain instantaneous death was thought to lie just inches above this line for the unprotected flyer unfortunate enough to be decompressed there. It is the purpose of this report to point out the fluidity of such a boundary, the derivation of which arises from a number of highly inconstant variables.

HISTORICAL

The concept of achieving the boiling point of a liquid by either raising its temperature or by lowering the ambient pressure has been known since the time of Boyle's original studies and Dalton's subsequent investigations of vapor pressure. Felix Hoppe-Seyler¹² in 1857 made the first

systematic observations of the boiling of body fluids of frogs, birds and mammals under low ambient pressures. but many of his observations are confused because of the effect of hypoxia which was poorly understood at that time. From the standpoint of aviation medicine, the first description of such a phenomenon occurring in animal body fluids was made by Armstrong¹ in 1938. Blood from the jugular vein and carotid artery of intact animals was shunted into a small glass cell where observations of bubble formation and water vaporization were made. Armstrong also observed that between 40,000 and 70,000 feet there was a very rapid rate of water-loss from the body of the living animal. He believed that this phenomenon was probably due to the fact that the vaporization rate of body fluids at constant (body) temperature is proportional to the decrease of barometric Since 1938, a number of pressure. reports have been published concerning certain aspects of this phenomenon. 3,13,15,18 In a recent report Beischer³ studied dehydration of frogs, cockroaches and worms at 5 mm. Hg. pressure for periods of from one to six hours, following which the organisms were rehydrated and remained viable.

TERMINOLOGY

The use of the word *boil* in reference to this physiopathologic condition is unfortunate. Both the transitive

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and intransitive forms of the verb boil either directly indicate or imply the addition of heat to a liquid to bring it to the boiling point. The term space ebullism* is suggested to describe the phenomenon of vaporization of body fluids at body temperatures in space, because the word ebullism does not connote the addition of heat to produce vapor. The word ebullism is used in a medical syndrome sense to describe the clinical events which occur in living tissue. It is to be differentiated from the word ebullition which applies to this chemical-physical phenomenon occurring in inanimate objects. term ebullism covers all of the signs and symptoms observed as the result of boiling of body fluids at very high altitudes. Heat loss, down to the actual freezing point of body tissues, is the terminal phase of the ebullism syndrome. Ebullism may occur at an ambient pressure which equals the vapor pressure of the liquid without formation of bubbles, as pointed out by Hitchcock and Kemph.11 However, bubble formation is absent only during a slow rate of decrease in barometric pressure and in a liquid virtually free of dissolved gas bubbles. These circumstances will not exist in a decompression in space, because gas bubbles will be dissolved in all body fluids and the decompression will likely be most rapid or even explosive, if it occurs at all.

GENERAL BOILING PHENOMENON

Vaporization of a liquid occurs when the vapor pressure of that liquid at a specified absolute temperature equals the ambient pressure in contact with the liquid. Actually molecules of the liquid leave the liquid surface in a vapor state even at low temperatures and at high pressures with vapor-saturated air above the liquid but, because of the dynamic equilibrium present (i.e., the return to the liquid surface of equal numbers of molecules from the vapor state), the material remains as a liquid.

At equilibrium the number of molecules per unit volume of saturated vapor is less than in an equal volume of liquid. This difference, however, decreases as the critical temperature is approached. Before a molecule can attain the vapor state it must overcome the attraction exerted by the other molecules in the liquid phase, i.e., the forces of cohesion. Therefore. the average potential energy of the molecules in the vapor phase is greater than the mean potential energy of the molecules in liquid phase. Expressed mathematically:6

$$\frac{n_v}{n_r} = e^{-L_i/RT}$$

where $n_v =$ number of molecules per unit volume of vapor, $n_L =$ number of molecules per unit volume of liquid, $L_i =$ internal latent heat of vaporization per mole, R = gas law constant and T = absolute temperature. As the temperature is raised and the ratio n_v/n_L increases (n_L does not vary appreciably with temperature), the molecular concentration in the gas phase, and hence the vapor pressure, increases. Consideration must be given the factors which influence the vapor pressure of liquids and the natural laws which govern these factors, as

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^{*}From Latin ebullire, meaning "to bubble out, or to boil up."

well as the criteria influencing the way in which boiling may be manifested.

In the laboratory, the change in vapor pressure of a "pure" liquid is a function of the temperatures involved, the specific volumes of the molecules in both liquid and vapor states, and the heat of vaporization for that liquid at the particular temperature considered. Broadly speaking, the specific volume of the liquid or vapor is a general statement of the cohesiveness of the molecules at a particular temperature and pressure, whereas the heat of vaporization is an expression of the energy required to convert a given number of molecules of the liquid into vapor at a specified temperature and pressure. This relationship may be expressed mathematically by the Clapeyron equation.*

$$\frac{dp/dT}{T(V_2-V_1)}$$

where dp/dT is the rate of vapor pressure change with respect to temperature, L is the molar heat of vaporization, T = absolute temperature, V_2 = the volume of 1 mole in the vapor state, and V_1 = the volume of 1 mole in the liquid state. example, water at 37° C. has a heat of vaporization of 575.8 calories per

gram, and the volumes occupied by 1 gram of water and vapor are 1.007 ml and 22.780 ml, respectively. fore, at 37° C. the rate of change of vapor pressure of water is 2.553 mm. Hg per degree (1 calorie = 41.29 ml-atm.). At "body temperature," then, the rate of change of vapor pressure is quite small when compared to the value obtained for water at its ordinary boiling point of 100° C. Under the latter conditions, there is a 27.1 mm. Hg per degree centigrade rate of vapor pressure change, a tenfold increase.

In other words, whereas slight variation in temperature at relatively high "cooking" temperatures has a marked influence upon vapor pressure, at body temperatures the variation of vapor pressure with slight temperature changes is small, but still significant. Assuming a temperature gradient over the entire body including skin of, for example, 15° C. (37° C. to 22° C.), this would account for a difference in water vapor pressure of about 27 mm. Hg. between various areas on the basis of temperature alone. Neglecting for the moment all other (quite important) factors, such differences would be relatively rapidly stabilized, however, when one considers that for each gram of water vaporized, about 575 calories of heat would be lost. Such evaporation would tend to occur at a greater rate in the warmest portions of the body gradient since vapor pressure would be highest there, and the warmest areas would then be cooled progressively down to the level of the coolest portions of the body, at which point the vapor pressures would be the same for the entire body with no

Integration evolves the form $\label{eq:power} \ln\,p = \frac{^{-L}}{RT} + C,$

$$\ln p = \frac{-L}{RT} + C,$$

 RT^2

dT

where C = the integration constant, allowing reasonably accurate calculation of the absolute vapor pressure.

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^{*}A modification of this expression is the Clausius-Clapeyron equation, in which the specific volume of the liquid (V₁) is considered negligible compared to the specific volume of the vapor (V₂). And since by the basic gas laws PV = RT (R = gas law constant) then RT/P may be substituted and the equation becomes dp = Lp.

temperature gradient, and generalized vaporization at equal rates would proceed. If only 5 per cent of the body weight of an 80 kilogram man is lost through evaporation, more than 2,000 kilo calories of heat would be dissipated. If this heat loss occurred over a period of minutes or seconds. multiple areas of freezing would occur (normally 8-10,000 K cal/day are dissipated). Because human body tissue is a poor heat-conducting medium, such theoretical heat transfer would be limited in some measure. In space the vaporization and heat loss will continue until generalized freezing occurs, when the vapor pressure of the solid water will be the same as the liquid water. In time, the vapor pressure of the frozen liquids and tissue will continue to fall as more heat loss occurs by radiation.

Non-Volatile Solutes .- Another important influence upon vapor pressures of liquids is the presence of another substance within the liquid system. The nonvolatile solute affects the ability of the solution to vaporize, by decreasing the tendency of molecules to escape from solution into vapor form. The degree to which a nonvolatile dissolved substance will affect the vapor pressure of the solvent is more nearly a mole function rather than weight function of the solute and solvent. Raoult's law is the basic formula which correlates the concentration of the solute with the vapor pressure of the solvent and is expressed mathematically by

 $p = Np^{1}$ where p is the vapor pressure of the solution, i.e., the partial pressure of the solvent in the solution, p^{1} is the

vapor pressure of the pure solvent and N is the mole fraction of the solute. This formula is quite accurate for dilute solutions (below 1 molal). With rearrangement of terms

$$\frac{p^1-p}{p^1} \; = \; \frac{n^2}{n_1+n_2} = \; N_2$$

where $n_1 = no$, of moles of solvent, $n_2 = no$, of moles of solute and $N_2 = mole$ fraction of solute.

Although it is usually not convenient to determine molality of a solution directly, a close approximation is indirectly provided where the freezing point constant* (Molal depression constant) of the solvent and the freezing point of the solution are known. For example, the freezing point constant for water is 1.86° C, and the freezing point of serum is normally about -0.56° C. Then the molal concentration of human blood serum is about 0.56/1.86 = 0.3 molal. Therefore, on the basis of the nonvolatile solutes in serum alone we would theoretically expect that the vapor pressure would be slightly below (0.25 mm. Hg. depression) that of water at 37° C., or about 46.75 mm. Hg.

Mole for mole, protein polymers have much less effect than a dissociated salt upon vapor pressure depression of a solution. If a long molecule in solution moves in segments, its vapor pressure and osmotic pressure can be assumed to be affected by the effective mole fraction and not the actual mole fraction. Therefore the more molecules of the protein going to make

^{*}The freezing point constant is $K_t = RT^2M$

 $[\]frac{}{L_1 \times 1000}$: where R = 1.987, T = 273.1°, where M = molecular weight of fluid; L_1 = heat of fusion.

up the polymer chain, the less effect will be exerted upon vapor pressure depression.¹⁶ This may be expressed by

$$\frac{p^1-p}{p^1}=\,N'_2=\frac{n'_2}{n_1+n'_2}$$

where N'_2 = effective solute mole fraction, n_1 = no. of molecules of solvent, n'_2 = effective number of molecules of solute.

is VolatileSolutes.-Water the most important volatile liquid component of the body, constituting about 70 per cent of the total weight. However, certain other substances found within the body in relatively small quantities also may be volatilized, including certain organic acids and alcohols and, in larger amounts, hydrochloric acid in the stomach (about 0.4 per cent concentration as secreted). The behavior of such binary systems is complex in that they may exhibit socalled "maximum" or "minimum" boiling point curves.5 Because the slight importance of binary systems of solutions in the body does not warrant more discussion, suffice to state that with gastric contents under extremely low ambient pressures we would expect vaporization of the gastric juices to evolve virtually pure water until a specific high concentration of HCl is achieved. Such a highly concentrated acid residue is theoretically capable of producing gastric tissue injury. After achieving this "maximum," the evolved vapor would constantly contain the same concentration.

Colloids.—The most important stabilizing factors in a colloidal solution are the state of hydration and/or the zeta

potential, i.e., the electrical charge of the particles. Lyophobic colloid suspensions depend only upon the repelling charge for separation. However, lyophilic colloids maintain a film of adsorbed liquid on their surface (and sometimes also a zeta potential) to maintain dispersion in the colloidal state. When this film is lost, if no repelling charge exists, coagulation occurs. It has been noted in an interesting pilot study reported by Guest⁸ that there may be a basic change in the zeta potential on the red cells and plasma colloids following exposure of blood samples to 30.4 mm. Hg. ambient pressure. Although adsorptive pressures tending to maintain the solvent film may be tremendous, e.g., in the order of hundreds or thousands of atmospheres per square inch, evaporation can still occur quite readily, for these expressions of adsorptive pressure reflect only the extremely small size of the colloid particle (the hemoglobin molecules ranges between 10-4 and 10-7) and the consequent enormous surface area involved in a colloid solution. Because of some of the peculiar characteristics of water, hydration is one of degree, ranging from mechanical entanglement to the closely adhered water molecules of "saturated water" in an intense electrostatic field. The probable primary effect upon vapor pressure of proteins in colloidal suspension with a crystalloid is an alteration of the amount of water present to act as solvent for the crystalloid, acting to slightly depress the vapor pressure of the water solvent. This effect would in some measure balance the effective mole fraction effect of protein polymers, tending to make

Raoult's law more nearly correct for human serum.

It is well established that lyophilization followed by rehydration may substantially alter the biochemical and physiologic properties of certain body proteins. In an episode of space ebullism it would be expected that only certain body proteins would undergo this severe degree of dehydration before death of the organism would Specifically, only proteins found in the body integument would have the opportunity to be subjected to this rapid drying action prior to death. Therefore, one might postulate that if an episode of ebullism occurred in space and if rapid enough emergency measures were taken and the individual recovered, it is conceivable that some functions of skin proteins might be temporarily altered, e.g., vitamin D synthesis.

ANATOMICAL CONSIDERATIONS

Because of certain local factors, various regions of the body display a more marked effect upon the water vapor tension. In 1933 Christie and Loomis4 accurately measured the vapor pressure of the water in normal respiratory alveolar air and found that this value was about 2 mm. Hg. lower than the accepted value of 47 mm. Hg. This observation was partially explained by: (1) the lack of equilibrium between blood and alveolar air; (2) the difference in the osmotic pressure of the blood and water; and (3) a lung temperature 0.24° C. lower than the measured rectal temperature. It is also of interest that these authors found that the alveolar water vapor pressure inexplicably dropped as much as 9

mm. Hg. during a ten to fifteen-second period of hyperventilation.

Because vaporization is essentially a "surface" (gas-liquid interface) phenomenon, the greatest water loss will occur on integumental surfaces. At altitudes far below the 63,000 foot level, the presence of reduced barometric pressure increases both evaporative and perspiration rates at a given body temperature (mechanism unknown). At lower altitudes this produces a beneficial effect so that by augmenting the body heat loss, the thermal tolerance of man at altitude is increased. Although this surface type of water vaporization will be entirely devoid of visible vapor or bubble formation, it will probably account for the major fraction of vapor formation. Decompression to ambient pressures below the pressure of water vaporization will produce most active ebullism on moist integumental surfaces, particularly the mucous membranes of the mouth, anus, and ocular conjunctivae. Likewise the moist surfaces of the gastrointestinal tract will provide a copious source of water vapor, which, added to the relative gas expansion of trapped gases already within the bowel. may produce gastrointestinal injury.

Any area of the body which operates under a relative negative pressure differential with respect to ambient pressures may be expected to evolve water vapor almost immediately after extremely low pressure decompression. For example, vigorous inspiration movements with the glottis firmly closed may lower the intrapulmonic pressure 30 to 80 mm. Hg. below atmospheric pressure. During normal inspiration, there is about a 4 mm.

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Hg. pressure drop in intrathoracic pressure, below atmospheric pressure. It has been noted⁹ that intrathoracic water vapor begins to form at 51 mm.

spans from the left ventricle throughout the circulatory tree and continues in a decreasing slope until the right ventricle is reached, should be consid-

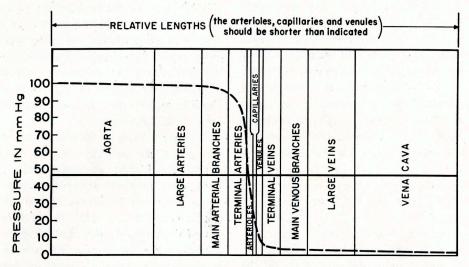


Fig. 1. Schematic diagram of mean blood pressure in different blood vessels during circulation with the superimposed water vapor pressure line (modified from Green⁷).

Hg. ambient pressure in the dog. Such a "vapothorax" may rapidly collapse the lungs and cause serious circulatory embarrassment.

Because of a relatively constant intraocular tension in man of from 20 to 25 mm. Hg., it may be expected that water vapor formation in the anterior and posterior ocular chambers will begin at about the same time as intravascular arteriolar and capillary vaporization. Sufficient vapor could form rapidly enough to seriously interfere with the ocular refractive system and cause severe visual impairment. This localization of ebullism could occur at altitudes above 84,000 feet.

Circulatory Pressures.—The systemic pressure gradient spectrum, which

ered from the standpoint of the initial impact of circulatory ebullism. In resting man, the pressures in the great veins at the entrance to the heart may range in the order of from 0 to 3 mm. Hg., and at the venous ends of the capillaries from 6 to 18 mm. Hg. pressures are encountered (Fig. 1). Of course this gradient may be increased by an increased rate of right heart output, by arteriolar dilatation accompanied by venoconstruction, and by increased negative intrathoracic pressure established by elastic recoil of the lungs. On the arterial side of the tree, a progressive gradient occurs with pressures below 40 mm. Hg. in the terminal arteries and arterioles up to a mean aortic pressure of about 100 mm. Hg. Therefore, we may assume that in the circulatory tree following decom-

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pression to ambient pressures well below 47 mm. Hg, vaporization of the blood will begin most vigorously at the entrance of the great veins to the heart and rapidly progress in a retrograde fashion down to tissue level, producing in effect an acute right heart failure. Because of the rapid dilatation of the peripheral arterioles which will occur as a compensatory mechanism for ischemia from generalized hypoxia and from the ischemia engendered by the right heart failure, arterial pressures will rapidly fall below the vapor pressure of water, allowing further retrograde vaporization up the arterial side of the vascular bed, and finally gas bubble formation within the left heart chambers. Such conjecture has been partially confirmed by Hitchcock and Kemph,11 who detected gas in the heart (cardiac vapor lock) in 50 per cent of dog subjects after explosive decompression to ambient pressures of 30 mm. Hg. Gas bubbles were noted to appear first in the right, then in the left ventricles. Cardiac vapor lock and circulatory arrest occured well within fifteen seconds following decompression in this series.

It has been shown that the assumption of a uniform, constant temperature of blood and tissues is false. Temperatures as low as 21.5° C. and 31.1° C. for the radial and brachial arteries, respectively, have been reported,² without the subject being unduly cold. A common central temperature within the main central vessels is found only when an individual has been maintained at rest for a considerable interval in a warm room and a steady state has been achieved. The temperature gradient within the blood vessels is quite variable, being depend-

ent upon the skin temperature distal to the vessel, the degree of peripheral vasoconstriction or vasodilatation, the efficiency of anastomoses, and other related factors. Because of the small rate of change of vapor pressure with respect to temperature, within the body temperature range, and counterbalancing hydrostatic pressures, the actual sequential progression of intravascular ebullism will not be essentially changed from that described.

Because confusion might arise on this point, for practical reasons it is desirable to indicate the actual ambient barometric pressure at which vaporization of a liquid will occur in a particular body area. For this purpose the use of the term effective ebullism pressure is suggested to take into consideration all factors which would tend to produce ebullism at a particular body site, and the corollary terminology, specific altitude of ebullism, indicating the actual altitude at which ebullism occurs for a stated anatomic location. As an example, the theoretical effective ebullism pressure and specific altitude of ebullism for blood in the median basilic vein are derived:

^{*}Temperatures of this magnitude encountered in median basilic vein with room temperature 21°C. dry bulb, 16°C wet bulb.

**Approximate values within range normally encountered.

Weightlessness. - Our present knowledge concerning the effects of the zero-gravity state upon circulation has been derived from brief periods of weightlessness in flight. However, from animal manned rocket studies by Henry and his associates,10 there is an indication that a fall in systolic and diastolic pressures may occur, possibly as a reaction of the cardiovascular system to short exposures to the gravity free state. Actually hydrostatic pressures per se will not exist since the fluids are weightless; cardiac circulatory pressures are basically tension pressures. The only effect of a constantly lower vascular pressure would be that intravascular vaporization will proceed much more violently and rapidly in free space than in a similar vacuum produced within an earthbound low pressure chamber. It is possible that on prolonged exposure to zerogravity, compensatory mechanisms of vascular-pressor receptors will maintain relatively normal vascular tensions.

Evolution of Dissolved Gases.—It is not within the realm of this paper to reconsider the evolution of carbon dioxide and oxygen from the blood and tissues under low barometric pressures except as this affects the release of water vapor. Clinical observation of animal subjects at low pressures has been confused by release of oxygen at about 60 mm. Hg. and carbon dioxide at about 40 mm. Hg. ambient pressures. Without gas analysis it is impossible to determine empirically the composition of the gases released at a particular altitude. Evolution of these gases is a function of their respective dissociation curves,

temperature, pH, elastic and hydrostatic pressures, as well as the ambient barometric pressures. These gases affect water vapor release in that they provide a nucleus for the formation of vapor, bubbles, presenting a gaseous-liquid interphase at which liquid vaporization can proceed. For this reason space ebullism, as an acute phenomenon, will manifest extensive tissue and vascular bubbling. The actual physics of physiologic bubble formation is quite complex and has been thoroughly studied by Harvey and his associates.⁹

Tissue Tensions.—One major factor limiting the degree of swelling and expansion of tissues is their elasticity and the rigidity of the enclosing structures. Vapor formation within the tissues of the cranial vault and within bone marrow is markedly limited. Similarly, in all enclosed body tissues, the degree of ebullism will be governed by the tissue elasticity. Kemph, Beman and Hitchcock¹⁴ measured the subcutaneous pressure in dogs sixty seconds after explosive decompression from 740 to 25 mm. Hg., and found a 34 mm. Hg. differential pressure (59 mm. Hg. absolute pressure). The differential pressure is greater than the fluid vapor pressure by the pressures exerted by the evolved nitrogen, carbon dioxide and oxygen. Therefore, we may expect vaporization to proceed until the tissue tensions equal the differential tissue pressure, or until tissue rupture occurs.

CLINICAL IMPLICATIONS

The space flight surgeon and space flyer must understand the process of space ebullism in order to prevent it from becoming something other than a theoretical medical curiosity.

The 63,000 feet altitude level should not be considered a "functional boundary" above which total space equivalence19 for this particular condition exists. In a sense, altitudes above 60,000 feet should be considered as variably but progressively space equivalent for ebullism because the severity and rate of progression of this pathologic process will be determined by the actual ambient pressure and the duration of exposure. As has been pointed out, vaporization of body fluids via the skin begins at ground level and the rate of water vaporization at a particular body temperature increases with decreasing ambient barometric pressures. At approximately 50 mm. Hg. (61,500 feet) intrathoracic water vapor may form. However, during a vigorous "negative" Valsalva maneuver it is theoretically possible for intrathoracic water vaporization to occur at altitudes as low as 43,500 feet although recondensation would immediately occur on relaxation. Most body fluids can be expected to begin vigorous vaporization from 63,000 to 63,500 feet (this small difference is accounted for by the effect of solutes in body fluids) up to 67,000 feet (this larger span is accounted for by body temperature gradients). Within this same altitude range, tissue and intravascular ebullism will begin in the venous circuit, producing acute right heart failure. Simultaneously mental disorientation and ocular involvement may occur. Death will supervene by circulatory or respiratory failure.

Explosive decompression above 150,000 feet may terminate in death

within a few seconds because of the extremely high rate of water vaporization. On the other hand, at lower altitudes the survival time will be considerably longer. Hornberger¹³ was explosively decompressed to 62,300 feet for ten seconds before unconsciousness from hypoxia ensued and no visible evidence of water vapor formation (particularly gas bubbles) was seen.

At present, there is only one conceivable way in which survival from this condition could occur at altitudes above 100,000 feet. If the automatic (C-1 assembly) triggering device of the Air Force partial pressure suit17 should fail following explosive decompression above 100,000 feet, the flyer would probably have less than seven seconds in which to manually activate his capstans and breathing pressure. At altitudes around 65,000 feet the time of useful consciousness will be primarily determined by the rapid onset of hypoxia in from ten to twelve seconds. Above this altitude, this vital time will be proportionately reduced by the ebullism phenomenon.

SUMMARY

Recent increasing aeromedical interest has been directed toward the physiologic problems encountered in space equivalent flight. In the literature, numerous references have been made to the fact that water maintained at 37°C will boil at 63,000 feet altitude and therefore body fluids also may be expected to boil at this level. There is no fixed altitude boundary for the boiling of body fluids; the exact altitude at which any particular fluid will boil is dependent upon a number of highly in-

constant variables. The term "ebullism" is introduced to describe the phenomenon of vaporization of body fluids at low atmospheric pressures and at body temperatures, thereby avoiding the use of the word "boiling" to describe a medical syndrome.

The general phenomenon of boiling liquids is discussed with particular emphasis on the factors influencing the vapor pressure of fluids, including the effects of temperature, volatile and nonvolatile solutes, and polymerized and colloidal suspensions as encountered in the body fluids. The relationships between hydrostatic and tension pressures, gravity free state, bubble formation, anatomic sites and the ebullism syndrome are discussed. Clinical implications derived from all theoretical considerations are discussed from the viewpoint of the space flyer and the space flight surgeon.

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