C H A P T E R - I

R E V I E W O F L I T E R A T U R E

HEART IN HYPOTHERMIA

The term hypothermia is usually employed to mean a state in which the body temperature is lowered substantially below the normal, perhaps a minimum of 2^{o}- 3^{o}c below the lowest temperature generally encountered in a particular species (Cooper & Ross, 1960; Edholm, 1961). According to Starkov (1960) hypothermia is the end " result of excessive heat loss or of insufficient generation of heat where the temperature regulating mechanism is damaged ". The term " damaged " in the translation of Starkov's work probably implied dysfunction, whereas, Blair (1969) considers hypothermia, in a general sense, as a state of lowered temperature which may be modified by anaesthesia or as an anaesthetic effect which can be modified by reduced temperature . He has classified hypothermia under five different stages on the basis of progressive physiological changes.

The local numbing effect of cold was long time known, and for over a century experimental workers have studied the effects of cold upon the body . The idea that cold might be helpful under certain conditions was first suggested by Boyle in 1722. In 1797, James Currie investigated the effects of total body hypothermia in man in relation to survival after shipwreck in cold sea. The first use of hypothermia in surgery , however, was employed by Napolean's surgeon, Baron Larry, who amputed frozen limbs in the battle of Eylau in Poland, in 1807. In 1876, Claude Bernerd found that guinea pigs could be cooled to a body temperature of 18^{o} - 20^{o}C and subsequently rewarmed. In 1917 Norman Lake found a " state of suspended animation " by lowering the body temperature to -6^{o}C in which the tissue could be preserved intact and its potential vitality maintained at the normal standard for a prolonged period. Subsequently, the information on the subject was limited to the observations on accidental hypothermia in man (Reincke, 1875; Nicolayson, 1875) and infrequent studies on experimental hypothermia in animals (Walther, 1862 ; Britton, 1922; Hamilton, 1937; Pembrey and White, 1896; Simpson, 1902; Tait, 1922).

The modern investigation of hypothermia in man can be said to date from the work of Temple Fay and Smith carried

out in 1940 in order to slow the growth of inoperable carcinoma. The work of Fay stimulated further investigation on the physiology of hypothermia in man (Talbott, 1941; Dill & Forbes, 1941; Allen, 1941; Smith, 1956) and in animals (Barbour et al, 1943; Penrod & Hegnauer, 1948). Bigelow in 1950, first proposed the clinical use of hypothermia and till to date this has become an asset in performing intracardiac surgery (Borema et al, 1951; Delrome, 1952; Ross, 1954 a,b ; Brock & Ross, 1955; Drew et al, 1959) as well as in neurosurgery (Lougheed & Khan, 1955; Lougheed Sweet, et al, 1955; Botterell, 1956; Woodhaull & Reynold's, 1957; Hellings, 1958; Dundee and King, 1959). There is, however, a limit to such advantages gained by the technique. This limit is set forth almost invariably by the heart which fails to act as an effective pump beyond a critical temperature. The reason for the ineffectiveness of heart as a pump is still largely unknown. The material that follows is a review of the various changes that takes place in heart during hypothermia.

Cardiac metabolism in cold

The heart, owing to its unique structure and function have given rise to an extraordinarily complex metabolic system which is mainly aerobic. The most important metabolic substrate of heart is oxygen, of which the heart, at normal temperature, consumes 6.5-10 ml./100 gm. of tissue per minute at rest (Bing, R.J. 1954; Bing, R.J. 1961; Bing et al,1965; Bing, R.J. 1965; Lundsgaard - Hansen, P. 1966). In hypothermia the myocardial oxygen consumption is markedly decreased (Bing, 1965; Lundsgaard - Hansen, P. 1966; McKeever, et al, 1958; Monroe et al, 1960; Bernhard et al, 1961; Kohn, 1963; Klocke et al, 1965; Klocke et al, 1966; Graham et al, 1968; Greenberg et al, 1960; Lochner et al, 1968; Jude et al, 1957; Jordan et al, 1962; Klarween et al, 1962; Merguet et al, 1964; Russ et al, 1965). Gollan (1959) using controlled perfusion techniques have shown a direct relationship between temperature and myocardial oxygen consumption. Fuhrman et al (1950) working on rat heart slices at low temperature studied the metabolism and showed a decrease in oxygen consumption of the heart at low temperature. Heart-lung preparation experiments, applying a constant work load demonstrate an increase in myocardial efficiency and a fall in oxygen consumption as temperature falls (Evans, 1917; Badeer, 1956; Reissmann &

Van Citters, 1956). The above observations in intact dog, however, remained unsettled and controversy exists as to whether myocardial efficiency is increased (McMillan et al, 1957) or decreased (Edwards et al, 1954). Reissmann and Van Citters (1956) are of the opinion that the increase in efficiency is due to a lowering of oxygen requirement of heart in hypothermia. Penrod (1951) have shown that the coronary A-V oxygen difference remains constant as temperature falls to 20°C and there is no decrease in this difference even when ventilating with 100% oxygen. Jude et al (1957) demonstrated that the myocardial oxygen consumption as well as the cardiac output decreased in hypothermia and that the coronary blood flow was adequate to maintain the requisite supply of oxygen to the myocardium under the condition. Hegnauer and D'Amato (1954) also observed a decrease in the oxygen consumption rate and the minute volume of the heart in dogs subjected to immersion hypothermia and also pointed out that cardiac oxygenation under the condition is adequate at all temperatures even upto the point when heart goes to ventricular fibrillation.

Gerola et al (1959) using open chest dogs anaesthetized with pentobarbital studied the coronary flow and myocardial

oxygen extraction under hypothermia and found a decreased myocardial oxygen consumption. But when the aortic pressure was increased by aortic constriction a rise in heart oxygen uptake was observed in the cooled dog. They further observed that in the steady state phase of hypothermia, the coronary A-V oxygen difference remained fairly constant as the cardiac effort and myocardial oxygen varied. Russ et al (1965) are of opinion that the important factor in determining the metabolic response of the heart during hypothermia, is the ratio between the myocardial oxygen demand and its supply. They have observed that the oxygen demand of the heart following 12 hour of cooling was propertionately lower than the supply as shown by a decreased coefficient of oxygen extraction. This coefficient, however, increases after 24 hours indicating myocardial oxygen demand had become proportionately greater than supply, suggesting relative myocardial hypoxia. It has been further observed that the fall in the arterial oxygen content is not related to the increase in the coefficient of oxygen extraction as they bear an inverse relation. This was an observation made by Hackel et al (1954) in normothermic dogs. So this fall in arterial oxygen content does not appear to be the cause of myocardial hypoxia (Tsifutis et al , 1970).

Fuquay et al (1962), have shown that severe metabolic acidosis occur at 10°C suggesting the presence of significant anaerobic metabolism and oxygen debt. Zimny & Taylor (1965) observed in rats cooled to 11°- 19°C that the high energy phosphates and glycogen content of the heart muscle decrease, an observation also made by Szekers et al (1958) in the same animal and by Benson et al (1960) and Ellison et al (1960) in dogs. Zimny & Taylor (1965) also found a significant increase in the lactate content of the heart which they held to be due to tissue anoxia. Their work finds support in that by Lange et al (1949) in contrast to that observed by Hanson et al (1961) in guineapigs which were cooled only upto 30°C. They have further demonstrated that there is a reduction in the amount of TPND indicating a lack in the oxidative process. This is in agreement with the work of Siperstein et al (1958). These authors also showed an increase in succinic dehydrogenase activity in hypothermic rat heart muscle which is in agreement with other workers (Des Marais, 1955; Hannon, 1960; You et al (1951). This increase may be due to uncoupling of oxidative phosphorylation as a result of attempting to counteract the decreasing ATP.

Russ & Lee (1965) have further shown that myocardial glycolysis begins after 12 hour of cooling and at that time

pyruvate utilization is stopped. They have also observed that the heart utilizes nonesterified fatty acid (NEFA) during the late hours of cooling. The reason is not clear, but Bernhard et al (1957) also observed selective utilization of NEFA by the heart in dogs cooled to 10°C and subjected to cardiac arrest for 30 minutes. They opined that this utilization might be due to the oxygen debt and metabolic acidosis. Russ & Lee (1965) have shown an alteration in myocardial metabolism after 24 hours of cooling and found an increase in the coronary venous PGO-T activity. The reason for this increase is not known but many factors are linked with it such as relative myocardial hypoxia, prolonged pentobarbital anaesthesia (Russ & McCollester, 1959) nutritional state of the heart, or an increase in the permeability of cell membrane, either individually or in combination.

Electrolytes and Hypothermic Heart

Elliot & Crismon (1947) have reported that the hypothermic heart is more sensitive to a rise of serum potassium than the normothermic heart. Montogmary et al (1954) noted that the hypothermic heart gains potassium during respiratory

acidosis whereas during respiratory alkalosis it maintains potassium balance. Covino & Hegnauer (1955) observed in fibrillating hypothermic acidotic dogs that there was loss of potassium and hydrogen ions from cardiac muscle and a gain in calcium. But those animals which did not terminate by ventricular fibrillation the myocardium neither gained nor lost these ions. These workers explain the discrepant results of Montogomery et al (1954) on the basis that the latter workers used vagal stimulation in their experiments and the acetylcholine which is liberated caused the alteration in potassium balance of the heart. Smith [illegible] (1956) is also in agreement with Covino's work and they observed a loss of potassium ion from the heart muscle prior to ventricular fibrillation.

Information regarding the concentration of potassium in the cooled myocardium is scanty and also contradictory. Gollan et al (1957) utilizing radioactive potassium showed a decrease in potassium concentration in the auricle cooled to 23°C. Again, Swan in the same year reported a positive myocardial potassium balance in dogs cooled to 30°C. This difference might be due to a decrease in pH occuring in Swan's animals which were not ventilated (Beavers et al, 1959). Again, Young et al (1954) observed

an increase in hearts potassium concentration with hypercpnea, whereas, Klein & Holland (1958) showed a reduction in potassium loss from isolated rabbit auricle suspended in cooled Krebs solution. Beavers et al (1959) cooled dogs upto 20°C and analysed sodium, potassium, chloride and water content of cardiac muscle and observed an increase in cardiac muscle potassium and intracellular water content. After administering hypertonic glucose during cooling there was a further increase in cardiac muscle potassium but the calculated intracellular water of cardiac muscle was similar to normal values.

Blair (1969) reported that during hypothermia the sensitivity of potassium and calcium ions of the cell increases, and this is important with regard to the myocardium in that administration of potassium ion in the cold state accelerates the induction of ventricular stand-still, and administration of calcium enhances the possibility of ventricular fibrillation. Covino & Hegnauer (1955) reported that there was no gain or loss of myocardial sodium chloride and magnesium in hypothermic fibrillators and non fibrillators. Caldini et al (1958) working with isolated canine heart perfused with cooled blood from an intact donor animal showed that the magnesium artero-venous

difference in the coronary blood was negative, and on injecting small amounts of magnesium chloride directly into the heart resulted in ventricular fibrillation.

Morphological and Functional Changes in Heart in Hypothermia

Morphological Changes :

Informations in this direction are scanty. Knocker, Phyllis while studying the effects of experimental hypothermia on vital organs in 1955 have observed fatty infiltration, depletion of glycogen and vascuolization in cardiac cells.

Sarajas in 1956 observed small necrotic foci in the myocardium at low temperatures and these foci correspond grossly and histologically to the successive stages of myocardial infarction. The plausible cause of these microscopic myocardial infarcts is due to the cessation of blood flow in some capillaries. Lynch et al in 1957 while studying blood flow in small blood vessels during hypothermia did not reveal vasoconstriction, but total cessation of flow in majority of the blood vessels.

Excitability :

Low temperatures have a profound effect on the excitability of the heart. The activity of the pacemaker becomes progressively depressed during cooling leading to sinus bradyeardia. Conduction of the excitation wave is markedly slowed while both the atrioventricular as well as the intraventricular conductions are depressed as revealed by the electrocardiograph recording where there is a prolongation of the P-R and Q-S intervals (Caldini, 1959). Coraboeuf & Weidmann (1954) utilising intracellular technique on single Purkinje fibres observed no change in the magnitude of resting and spike potential between 25°to 40°C but the duration changes, when the temperature falls. This, in their opinion is due to a slowing of the speed of migration of ions during depolarization and repolarization of Purkinge tissue. Blair (1969) and Goldberg(1958) observed an increase in contractile force of the myocardium and a reduction in rates of contraction and relaxation during cooling with occasional myocardial depression. Bromberger, Barnea and Caldini (1958) recorded and measured the transmembrane potentials during hypothermia in humans and observed non-uniform depolarization and repolarization of the myocardium. Caldini (1959) opines that the heart recovers from the excitation in a less uniform manner during hypothermia than at normal temperature.

Hegnauer et al, 1956 also holds the same view and opines that there are no changes in the threshold of excitability of the dog ventricle during hypothermia.

Contractility :

Ventricular contraction and relaxation phases are markedly prolonged during hypothermia (Berne, 1954). These changes are associated with a lengthening of both the absolute and relative refractory periods of the ventricle (Brooks, 1955; Blair, 1969). Contractility of the myocardium increases at 25°C and then starts declining, but the work performance remains low.

Conductivity :

Prec et al (1949) observed prolongation of P-R interval, widening of QRS and elevation of S-T segment suggesting delay in the speed of conduction during hypothermia. But Moritzen & Murray (1966) showed that in experimental hypothermia there was progressive and proportionate increase in conduction time and in the refractory period down to 20°C. Blair(1969) have observed that the interval between the atrium and the bundle of His at 37°C is 49 msec which

increased to 277 msec. at 15°C , whereas the conduction velocity in the right bundle branch increases in duration from 22 msec. at 37°C to 57 msec. at 15°C.

Heart Rate :

Lowering of the temperature produces a profound effect on the heart rate. Several investigators have found that the heart rate diminishes as temperature is lowered (Hook & Stormont, 1941; Sabiston et al, 1955; Sellick, 1963; Dahlen, 1964; Evonuk, 1966; Blair, 1969). D'Amato (1960) further showed that the heart rate is halved at 25°C in the dog which he attributes as the cooling of the pacemaker leading to sinus bradycardia. According to Sellick (1963), administration of atropine is effective to overcome this bradycardia upto 30°C. Dahlen (1964) opines that the slowing of the heart rate is due mainly to an increase in Q-T interval of the cardiac cycle.

Prec et al (1949) made an observation similar to that by D'Amato (1960) and also reported that the prolonged cardiac cycle exhibits some interesting features different from that produced by vagal stimulation at normal body temperatures (Hegnauer et al, 1950). In the dog at a temperature of 37°C and with a heart rate of 170 beats per minute , systole occupies just over half the total cardiac

cycle. If the vagus is stimulated with the dog at the same body temperature, the heart slows to about 50 beats per minute and the duration of the cardiac cycle is increased threefold . The period occupied by systole is prolonged by only 50% and the duration of isometric relaxation is scarcely changed. Under these conditions, the time of total inactivity in each cycle is greatly increased. These findings contrast with the events which occur when the dog's heart is slowed to the same extent by cooling the animal down to about 23°C. Again the total cardiac cycle is prolonged to about three times the normal length. Now, however, the duration of systole and isometric relaxation are increased by 250% . The period of inactivity, or rest period, does not then undergo much relative increase in duration in the way that it does with vagal slowing at normal temperatures. These preceding observations are based on studies of the left intraventricular pressure curves.

Blood Pressure :

Hegnauer and Penrod (1950) observed a fall in the systemic arterial pressure with diminishing temperature and the rate of fall for each degree is accelerated below 24°C. Such fall in blood pressure during cold has also been reported by Mukherjee et al (1958). Sellick (1963) have observed an

increase in blood pressure in the initial stages of cooling which he attributes to an increase in the peripheral resistance but later on it fell when cold depresses cardiac activity . Dahlen (1964) have also observed a continuous decrease in the blood pressure in hypothermic cats.

Evonuk (1966) in studying the cardiovascular effects in normothermic dogs cross circulated with hypothermic dogs have observed that in four of the recipient animals the blood pressure decreased 7-10% during the first $2^{\circ}C$ drop in rectal temperature of the donor animal and levelled off during the remainder of the cooling period.

Cardiac Output :

Evonuk (1966) showed that there is a rapid decrease in the cardiac output from 100% to 40% during the first $2^{\circ}C$ drop in a cross perfusion experiment. This reduction in cardiac output is probably due for the most part to a reduced stroke volume of the heart with a probable shift in blood to the central circulation. Hegnauer & D'Amato (1954) have also shown that cardiac minute volume of the dog subjected to immersion hypothermia diminishes progressively with temperature. The work output is also reduced to 7-8% of normal at low temperature. Further, Brendel (1957) demonstrated in dogs

that the work output per minute of the dog's heart is reduced when the body is cooled. There is also a subsequent decrease in the cardiac output. This reduction in minute volume is related to the slowing of the heart.

Keatinge (1969) observed that there is an increase in cardiac output briefly at the start of cooling but when dogs were cooled to 25°- 26°C their cardiac output declined by 75% (Sabiston, et al. 1955)and when human patients were cooled to 30.5°- 32.5°C their output declined by 31% (Ross et al. 1957). In both cases the decline was due to slowing of the heart rate and not to a decline in stroke volume; the force of ventricular contraction in both dogs' and rabbits' hearts has in fact been shown to increase when they are cooled to such temperatures (Goldberg 1958; Covino & Beavers 1958). At these temperatures intact dogs maintain an adequate blood pressure but Hegnauer et al (1950) showed that below 25°C the slowing of the heart became extreme, the force of ventricular contraction declined, and cardiac output became insufficient to maintain an adequate arterial pressure. At a temperature of 18°C the mean arterial pressure fell to 55 mmHg with a heart rate of 20 beats/min. The fall in cardiac output at such temperatures causes increases in venous pressure of up to 20 cm H_2O in dogs (Bigelow et al. 1950).

Coronary Blood Flow :

Sabiston et al (1955) measured the blood flow in the dog's circumflex coronary artery during hypothermia induced by blood stream cooling, and they observed a fall as the temperature is lowered, but the percentage change in coronary flow was less than the percentage fall in cardiac output. Berne (1954) showed that the dog's coronary blood flow declined abruptly down to 33°C and thereafter the rate of fall of flow with temperature was more gradual. Gerola et al (1959) using open chest dogs anaesthetized with pentobarbitol studied the coronary flow and myocardial oxygen consumption. They kept the cardiac output constant with an input pump and by altering the peripheral resistance by partially occluding the thoracic aorta, they did not obtain a significant change in the absolute values of coronary flow during hypothermia , but there was a decreased myocardial oxygen consumption. Jude et al (1957) found that at 20°C the dog's coronary flow was reduced to a fifth of normal, myocardial oxygen uptake to a quarter, and the coronary vascular resistance was double.

The early reports of Anrep (1929) , Berne (1954) , Sabiston et al (1955) indicate an increase of coronary flow coinciding with a reduction of the perfusate temperature.

They believed this fall in resistance to be due to the relaxing effects of cold upon the coronary vessels. Subsequently, however, Gollan, Jude et al (1957) challenged their findings as they noted a definite increase in coronary resistance under similar experimental conditions. But more recently, Bernhard et al (1957) , Gerola et al (1959) have all noted a fall in resistance while Cross et al (1962) noted this to occur only when the arterial oxygen tension was permitted to fall, but not when pO_2 remained stable.

Electrocardiographic Changes during Hypothermia and Cardiac Arrhythmias.

Various changes occur in the elctrocardiogram at low body temperatures. The duration of QRS complex and the S-T interval increases whilst the P-R interval is prolonged (Dey, 1958). An increase in the duration in the T-P segment as compared with other components of the electrocardiogram indicates that there may be a direct influence of cold or other factors on the pacemaker of the heart in order to produce a slower heart rate. Badeer (1951) has demonstrated that the pacemaker of the dog's heart is susceptible to low temperature. Tomaszewki (1938) published electro-

cardiograph from an accidentally frozen patient which revealed an extra, slow inscribed deflection between QRS complex and the early part of the S-T segment. Later in 1943 Grosse Brockhof and Schoedel produced this same deflection experimentally in hypothermic dogs and since then it has been described by several workers in both human beings and animals.(Osborn,(1953) attributed this change as a current of injury caused by acidosis that develops in hypothermic animal. Burgen and Terroux (1953), Coraboeuf and Weidman (1954) opines that unbalanced electrical activity of the heart during cold causes the'J'deflection of the scaler electrocardiogram and this 'J' deflection may occur in adverse conditions, such as, myocardial injury, sudden change in excitability, acidosis etc.

Gray (1958) while studying electrocardiographs at low temperature found that cardiac systole taking up a greater fraction of the cardiac cycle than the normal and below 30°C the conduction changes are likely to be manifested by a prolonged P-R interval. Wynn (1954) observed the characteristic 'J' deflection with a defect in the A.V. conduction associated with bradycardia in their study on cats and dogs electrocardiogram cooled to 17°C. Emslie Smith et al (1959) also reported about the 'J' deflection in the electrocardiogram during hypothermia and are in the opinion that

this wave might represent an early repolarization of the cardiac muscle before depolarization is completed.

Blasius et al (1961) have reported the effects of hypothermia on the electrocardiograph of dogs and they obtained a linear increase of the P-Q interval and an exponential increase of the S-T interval which tally with the results of Dahlen (1964) in cats. Tofler (1962) have observed during induction of profound hypothermia a slowing of the normal sinus rhythm giving rise initially to atrial fibrillation which finally results in ventricular fibrillation. Dahlen (1964) chose cats as his experimental animal because of the shorter conduction pathway and smaller heart size observed no significant change in the amplitude of the depolarization wave but an appearance of a hypothermic wave with T inversion at 27.7°C. They are in the opinion that the cause of death in cats in hypothermia is not due to ventricular fibrillation as seen in larger animals (dogs etc.) but rather to asystole. Schwab et al (1964) have reported that eight out of ten patients having a normal sinus rhythm before cooling, developed atrial fibrillation before ventricular fibrillation at 27.2°C. He further observed that five out of eleven patients had marked alteration in the QRS configuration over a wide range of temperature change. Again nine out of eleven patients had

an increase in QRS intrinsicoid deflection of 24% just prior to the onset of ventricular fibrillation and ten out of ten patients had an increase in QRS duration. The increase in QRS intrinsicoid deflection had an important value as an indicator of incipient ventricular fibrillation. Schwab also observed the 'J' wave previously described by other workers in eleven out of twelve patients. The origin of this 'J' wave in his opinion is a matter of speculation. Whether it represents early repolarization or late depolarization is not known. But it has been suggested that this wave is due to a delay in conduction in a cold sensitive portion of the conducting system. There is also an evidence that the area is situated at the base of the intraventricular septum which is the last part to be depolarized, and in this study it was found that the 'J' wave occured at a temperature when there was a considerable widening of the QRS complex which does not exclude the previous finding. Measurement of the QRS intrinsicoid deflection revealed delay at temperatures considerably higher than those at which the 'J' wave appears. This fact indicates that if the 'J' wave is due to a delay in depolarization then there must be a considerable difference in sensitivity to cold in various areas of the myocardium.

Starkov (1960) while studying the elctrocardiogram in a heart lung preparation at low temperature found that the P wave was always positive, the P-Q interval usually showed

no change upto 30°C . The Q-S interval increased at 20°-23°C and there was a split in the R wave. The R-S line, however, undergoes more extensive changes becoming thickened initially and then showing considerable splitting and finally becomes arched . At this stage the ventricular systole is prolonged and the R-T interval very great. The duration of the ventricular complex was 0.25 sec. at 35°C increased to 0.40 sec. at 30°C to 0.7 sec. at 25°C and reached a duration of 1 sec. or more at temperatures 20°C and below. Starkov on analyzing the electrocardiogram found that functional changes taking place in the heart at low temperature are reversible. He attributes the disturbance in the cardiac rhythm at low temperature as due to excess flow of blood to the heart and was accompanied by symptoms of partial or complete A-V block. The latter was functional in nature and passed off when the blood temperature rose. The excessive changes which took place in the ventricular complex indicate drastic changes in the conduction of excitation through the conducting system of the heart and through the ventricular myocardium.

Hypothermia is capable of producing any type of cardiac arrhythmia (Jouvenelles et al, 1954, Drew, 1961) and it is thought that the possibility of fibrillation increases as hypothermia becomes more pronounced. Covino et al (1954)

noted that ventricular fibrillation occur less frequently in profound hypothermia in dogs under thiopental or ether than under pentobarbital, whereas in normothermic dogs arrhythmias are more frequent under pentothal anaesthesia. Riley and his co-workers similarly reported in 1956, that there is a lower incidence of ventricular fibrillation with thiopental anaesthesia compared to pentobarbital. But Bigelow, Lindsay & Greenwood (1950) did not observe any difference on the different types of anaesthesia used in hypothermia which failed to give the role of anaesthetic agent as a predisposing factor in development of ventricular fibrillation.

Cookson & Di-Palma (1955) found that a cardiac crisis occurs in dogs cooled to temperatures between 23°C and 15°C . This is manifested by the cessation of sinus rhythm , the onset of nodal rhythm, of intense bradycardia, ventricullar fibrillation or more rarely of heart block or sinus tachycardia. It appears that ventricular ectopics heralds the ventricular fibrillations and a shifting pace-maker the bradycardia. The bradycardia is not relieved by atropine or vagotomy (Cecil Gray 1958) . It is the danger of ventricular fibrillation which has prevented , so far , the use of this technique to its fullest exploitation.