CHAPTER V

CARDIAC ARRHYTHMIAS INDUCED BY HYPERCAPNIA
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The problem of cardiac arrhythmias is a great headache for the anesthetists and neuropsychiatrists, because during anesthesia or during carbon dioxide therapy, production of respiratory acidosis and a rapid withdrawal of this acidosis were frequently associated with various disturbances in cardiac rhythm often causing death of the subjects. The rapid correction of severe hypercapnic acidosis by hyperventilation with 100% oxygen is followed in experimental animals by ventricular fibrillation (25, 178). Inhalation of 30% carbon dioxide caused cardiac arrhythmias in conscious men where the electrocardiographic tracings showed auricular tachycardia and sometimes ventricular premature systoles (123). Auricular extrasystoles and tachycardia mainly occurred during recovery phase (150). Sudden ventricular arrhythmias were also observed during posthypercapnic period (123, 162).

The results of the previous chapter demonstrated the development of various types of arrhythmias produced during and after prolonged and repeated hypercapnia. These arrhythmias included from conduction block up to tachycardia and fibrillation, which were rarely noted in the short-term exposure of carbon dioxide but very often observed when the hypercapnic duration was prolonged or repeated in pentobarbital-anesthetised cats and rats. Though the susceptibility to various cardiac arrhythmias varied with the duration and dosage of carbon dioxide exposure and the anesthetic condition...
Materials and Methods

The procedure chapters were used slab of the carbon dioxide e toad heart perfusion an rats were used for anal induction and its withd hypercapnia and its wit movement pattern of iso

In order to e of rhythms, acute bilat in both the rats and th in a few experiments by blockade was considered vagi failed to cause ca

Results

Twenty rats a treatment for 15 minute same preparation. In e T waves followed by an to be due to vagal acti heart block, in three o sinus rhythm was restor the heart block reappea
Fig. 20. Some representative cardiac mechanograms of perfused toad hearts showing hypercapnic and posthypercapnic arrhythmias, when the induction of 30% CO₂ in oxygen is repeated several times.

[A] = CO₂ exposure second time.
[B] = Duration of CO₂ exposure is prolonged more than 15 minutes.
[C] = CO₂ exposure fourth time in each case. Duration is 5 minutes at an interval of 30 minutes.
damage. During with
In those cases the amplitude in mechan
occur, the P wave di
ventricular complexes complexes gradually seconds. Initial t was noted.
A variety including delayed on sinus tachycardia, tachycardia, bigemini cases where carbon a
In bilateral were delayed while dis disturbances in rhy failed to produced a

Discussion
Rhythmic e efficient pumping ou to all parts of the of excitation at the the atrial wall and Purkinji system at se sequence of events o events of conduct damage, there develop
Fig. 21. Varieties of electrocardiographic changes of perfused toad hearts after severe hypercapnia are illustrated in different panels.

Calibrations - T = Time in 2 secs and vertical bar represents 500 µV in the panel F, which follow in all the panels. In each panel, top ECG is the ventricular lead connected at the apex, and bottom ECG is from the auricular region of the same heart.

A: Control ECG before any treatment with CO₂; B: After the withdrawal of severe hypercapnia (30%) induced for 10 minutes showing paroxysmal tachycardia; C: ECG of another heart 5 minutes after withdrawal of hypercapnia (period of induction 10 minutes, repeated three times), showing ventricular premature contractions, the extrasystoles; D: ECG strip of another perfused heart, which has been treated with hypercapnia three times (20% CO₂ - duration of induction in each time 5 minutes) showing paroxysmal tachycardia along with bigeminal and trigeminal rhythms; E: ECG strip of perfused toad heart which has been pretreated with hypercapnia four times showing partial heart block along with delayed conduction and sinus arrhythmia; F: ECG strip of perfused toad heart pretreated with hypercapnia four times showing paroxysmal tachycardia.

ECG strips shown in the same figure under different panels are taken from different experiments in which the calibrations remain more or less same as shown in the panel F.
The mechanism involved in causation of the cardiac arrhythmias during and after prolonged hypercapnia includes disturbances in conduction pathways and excitability of the cardiac contractile elements. Substantial reports in the literature concerning the development of cardiac arrhythmias during hypercapnic acidosis are available. Inhalation of 30% carbon dioxide in male psychiatric patients has been reported to cause supraventricular arrhythmias, viz., auriicular tachycardia, and sometimes ventricular premature systoles (123). During cyclopropane anesthesia, when blood pCO₂ was increased deliberately, the cardiac rhythm of sinu3 nodal origin was observed which was associated with extrasystoles, bigeminal rhythm or multifocal ventricular tachycardia (162). Posthypercapnic ventricular fibrillation and death have been reported in dogs by Brown and Miller (25). Auricular extrasystoles and supraventricular tachycardia and sudden ventricular arrhythmias during recovery from carbon dioxide breathing have also been reported (123, 130, 161). The rate of carbon dioxide washout is directly related to the occurrence of these arrhythmias, the development of these disturbances of cardiac rhythm being dependent on the "suddenness" of the washout, as in the animals of Brown and Miller (25), in which elevated alveolar pCO₂ was slowly lowered and no fibrillation was observed.

Young et al (220) found that the duration of cardiac asystole caused by vagal stimulation was more during administration of carbon dioxide and it was suggested by them that effect of vagal stimulation in presence of acidosis or heightened vagal tone might be causal of these arrhythmias during hypercapnia. Evidence of enhanced vagal activity during and after withdrawal of hypercapnia in the present series of experiments perhaps is related to the above observation, but as arrhythmias were observed also in the vagotomized or atropinized animals, the exclusive role of vagus in production of arrhythmias can also be delineated.
Price and his co-workers (161, 162) have noted that most of the types of arrhythmias observed during carbon dioxide inhalation can be produced directly by stimulation of cardiac sympathetic nerves or administration of epinephrine and also that blockade of cardiac sympathetic nerve can elevate the threshold for ventricular arrhythmias to carbon dioxide levels higher than 120 mm Hg. They have concluded that the sympatho-adrenal response to carbon dioxide gas is concerned in the production of cardiac arrhythmias. Though the catecholamine content of blood or heart was not measured, no remarkable pressure responses were noted in cases of cats after prolonged hypercapnia (vide Chapter I) which could be related with enhanced sympatho-adrenal activity for causation of arrhythmias, but its role cannot be excluded also. Curiously enough, in the reserpine treated hearts, during withdrawal of hypercapnia, sudden aberrant rhythm with ventricular extrasystoles were frequently observed, and this perhaps is due to the hypersensitization of the sympathetic nerve endings within the cardiac muscle. The role of adrenalin in producing ventricular fibrillation has been a subject of much controversy though. Adrenalin injection during withdrawal phase after prolonged hypercapnia can produce or facilitate the development of ectopic ventricular beats. But from the results the onset of ventricular fibrillation during hypercapnia cannot be explained on the basis of greater output of catecholamines.

Hindrance of conduction of impulses within the dog heart during acidosis has been reported by Gertler et al (72). Distinct slowing of A-V-conduction up to complete heart block has also been reported by Mines (139) and Andrus and Carter (6) during acid infusion of the heart. Disturbances in the conduction during hypercapnia can be explained also on the basis of acidifying property of carbon dioxide or on the specific action of carbon dioxide or on the specific action of carbon dioxide on conduction velocity.

Onset of ventricular or atrial fibrillation is known to be accompanied
by a marked increase in an inward movement of sodium, potassium leaving
the tissue in exchange (16, 182), increased Ca\textsuperscript{45} influx (182) and altered
Ca/K ratio (34, 83). Hyperkalemia as reported by various authors, produced
during carbon dioxide induction (61, 107, 173, 216), is found to be associated
with ventricular arrhythmias which can be prevented by increasing the plasma
sodium and thereby compensating the fall in Na/K ratio, with infusion of sodium
chloride (146, 218). Although this does not provide an explanation of the
mechanism involved, it appears that the combination of elevated plasma potassium
concentration and a rapid fall in carbon dioxide tension and/or hydrogen ion
concentration perhaps work together to produce the cardiac arrhythmias.

Whatever might be the cause, there is a depression of excitability of
cardiac tissue during hypercapnia as manifested by prolonged conduction or
A-V block and a posthypercapnic augmentation phenomenon during carbon dioxide
washout. These are closely related with disturbances of the ionic milieu
of cardiac cells. Of course, the heterogeneity of the excitability of different
regions of cardiac tissue should also be considered. It is not possible to state
at this stage that the causal relationship of the sympathetic-parasympathetic
interaction, the pH shift, or the changes in sodium uptake and potassium
loss inside the cardiac muscle be responsible for the causation of cardiac
arrhythmias. Therefore, it would be of interest to study the role of electrolytes
on cardiac contractility and excitability during and after hypercapnia (which is
dealt with in the following chapter) as it is well known that the concentration
of potassium and calcium in extracellular fluid are of paramount importance for
maintenance of normal cardiac function.

Furthermore, it is the impression of the present author that the
cardiac arrhythmias produced by repeatedly prolonged hypercapnia could be
utilized experimentally to assess quantitatively the role of electrolytes,
catecholamines or other drugs and electrical stimulation which may influence the
existing hypersensitive foci of cardiac muscle responsible for the development
of such arrhythmias.