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Cardiovascular Defense against Asphyxia

Studies of circulatory responses to diving in aquatic and land animals clarify some reactions to asphyxia.

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The comparative physiologist chooses from the broad spectrum of animal species those which best demonstrate the phenomenon he wishes to study. Accordingly, investigations into the physiology of asphyxia might logically start with those animals which have a special adaptation to breath-holding during prolonged underwater dives. In this article we shall consider some inferences from the comparative physiology of diving by examining the cardiovascular responses to immersion of some aquatic species and comparing them with responses of some terrestrial animals, including man. Apnea, simple cessation of breathing during immersion, is characteristic of diving. It leads to progressively increasing tissue anoxia and hypercapnia, and eventually to asphyxial death. It will be seen that the associated circulatory and cardiac adjustments are so profound as to considerably extend the normal range of physiological responses.

Historical Review

Nearly one hundred years ago the French physiologist Paul Bert made the initial observation of cardiovascular events associated with diving. He discovered that the duck when diving underwater experienced slowing of the heart rate from 100 to 14 beats per minute during a 7-minute dive (*1*). A few years later another French physiologist, Charles Richet, demonstrated that the bradycardia of diving could be eliminated by cutting the vagus nerves or by administering atropine (*2*). The physiological advantages of bradycardia during diving asphyxia evaded clarification until many years after its original discovery.

It is a common observation that some parts of an animal, the limbs for instance, can be deprived of oxygen, as by a tourniquet, for as much as 1 hour without permanent damage. The dependence of vital organs upon an almost constant oxygen supply is readily apparent, however, when the circulation of blood to the brain is interrupted for more than a few seconds. In 1934, Irving postulated a differential distribution of circulation during asphyxia such that oxygen available in the lungs and circulating blood was selectively distributed to brain and heart muscle, the two tissues known to be damaged by brief periods of anoxia (*3*). This hypothesis was tested in a variety of animals, including beaver, muskrat, cat, dog, and rabbit, with the use of a hot wire flowmeter to indicate changes in blood flow. Irving observed that asphyxia, induced by tracheal clamping or lung inflation, produced in these species a decrease in muscle flow and maintained or increased blood flow in the brain (*4*).

Working in Oslo about the same time, Scholander studied the physiology of diving seals by measuring the lactic acid concentration in arterial blood during diving and noted that it increased only slightly, if at all, during the dive, but that lactic acid appeared in great quantity immediately after surfacing. He interpreted this to mean that the lactate was sequestered in muscle cells and that these were not in communication with the circulating blood until the animal took its first breath after the dive (*5*).

Scholander joined Irving at Swarthmore College in 1940, and their collaborative efforts produced a considerable advance in our understanding of the physiological response to asphyxia. Among the pertinent observations were the following: despite the often profound bradycardia in the seal (sometimes the heart slowed from 100 to 8 beats per minute), central arterial blood pressure remained constant, while pressure in a small flipper artery fell during the dive. This demonstrated massive peripheral vasoconstriction even proximal to the usual site of control in the arterioles (*6*). During the dive the oxygen in myoglobin-rich muscle in a seal was depleted more rapidly than oxygen in the circulating arterial blood, arguing further for the lack of communication between circulating blood and muscle tissue during the dive (*7*). Perhaps most striking of all was the direct observation of intense vasoconstriction in the exposed mesentery of a seal during immersion (*6*).

A cessation of renal function was

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later shown to occur in a diving harbor seal as a consequence, presumably, of decreased kidney blood flow (*8*). More recently, decreased limb blood flow in submerged ducks was demonstrated (*9*). Other studies in a variety of diving animals and birds and in fish taken out of water have been reviewed by Scholander *et al.* (*10*).

On the strength of these lines of evidence, therefore, it seemed clear that a widespread and selective vasoconstriction occurred during diving and that this provided for continued oxygenation of vital organs, such as brain, at the expense of organs of greater anaerobic capacity, such as muscle and intestine. Just how profound these changes were remained to be seen. We hoped to explore this by the use of modern cardiovascular instrumentation. We have studied diving animals, such as elephant seals, harbor seals, and sea lions, and compared their reactions with terrestrial species, dogs and man.

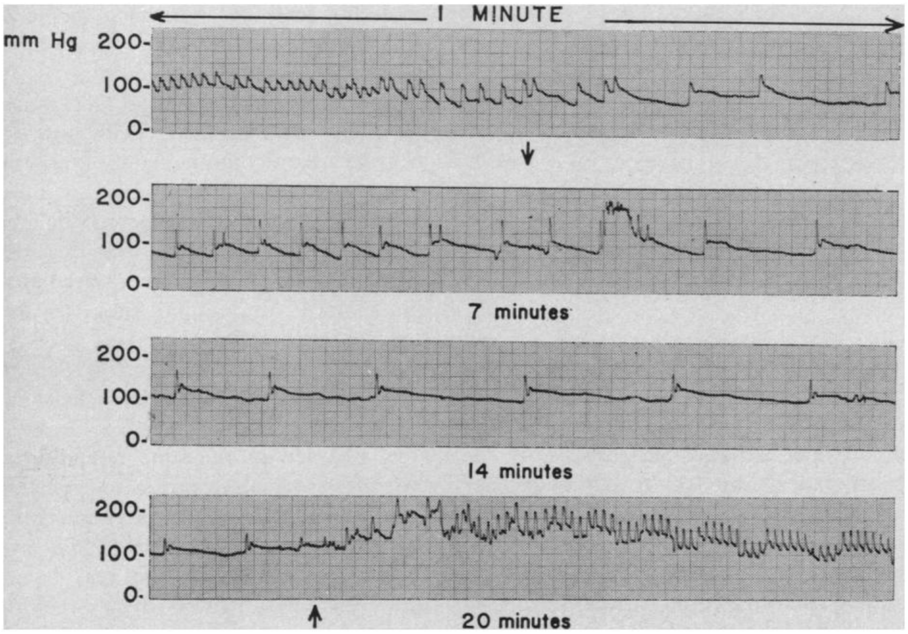

Fig. 1. Blood pressure in the abdominal aorta of a northern elephant seal *Mirounga angustirostris* at intervals during a 20-minute dive.

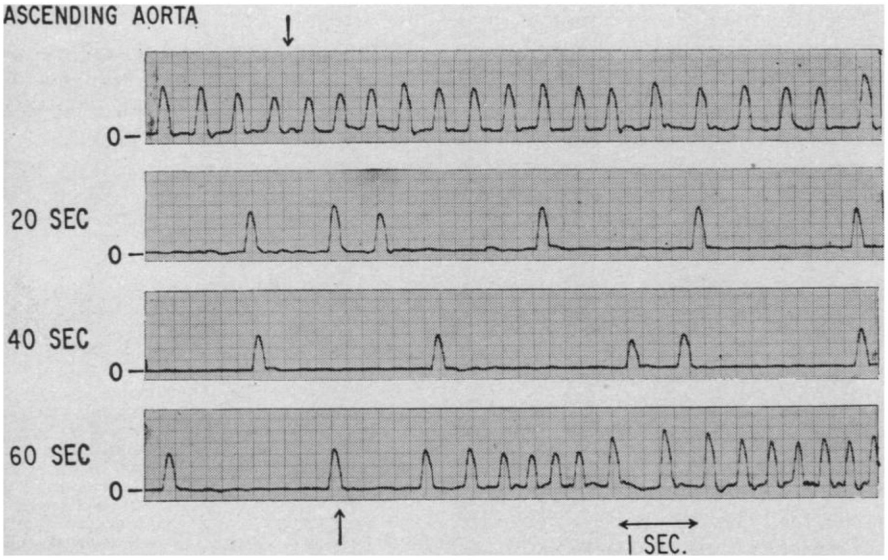

Fig. 2. Blood flow in the ascending aorta of a dog during an experimental dive of 1 minute.

Animal Studies

During the course of an expedition to Guadalupe Island, Mexico, several physiological studies were performed on northern elephant seals, *Mirounga angustirostris*. Measurements of arterial blood pressure, made by earlier workers with mercury manometers (*6*), were repeated by us using modern strain-gauge equipment (*11*). Animals were captured on the beach and were transported to a research ship anchored offshore. They were restrained on an immersible platform by means of padded metal straps and could thus be submerged at will either in the sea itself or in a canvas tank on the ship's deck. A polyethylene cannula was inserted under local anesthesia (Xylocaine) via a hind flipper artery directly into the abdominal aorta to about the level of the kidneys.

One record obtained on a young adult male elephant seal weighing 820 kilograms is shown in Fig. 1. The intense bradycardia, sometimes as low as six beats per minute, is clearly apparent throughout the 20-minute dive. Systolic pressure, which before the dive was about 110 to 130 millimeters of mercury, became somewhat irregularly elevated, varying from about 120 to 160 mm-Hg while the animal was quiet. In the much-prolonged diastolic phase, pressure fell very slowly and was maintained about 80 to 100 mm-Hg, as in the resting nonsubmerged state. Occasional struggling elevated these values, but it can be seen that the mean arterial pressure was hardly changed throughout the dive.

The energy for maintaining diastolic pressure is provided by the stretching of the arterial walls during and immediately following systole. This function is probably aided in the marine mammals by the presence of a highly elastic bulbous enlargement of the aorta just where it leaves the left ventricle. This enlargement almost doubles the diameter of the ascending aorta and has been seen by us in every marine mammal examined, including the northern elephant seal *Mirounga angustirostris*, harbor seal *Phoca vitulina*, California sea lion *Zalophus californianus*, Pacific bottle-nosed dolphin *Tursiops gilli*, pilot whale *Globicephala scammoni*, gray whale *Eschrichtius gibbosus*, and Cuvier's beaked whale *Ziphius cavirostris*.

The intense, immediate bradycardia with maintained arterial pressure suggested a decreased cardiac output and peripheral vasoconstriction, both under exquisite control. Clearly, dynamic measurements of cardiac output and blood flow distribution were required for elucidation of these major circulatory events.

The development of modern electronic blood-flow measuring devices which can be surgically implanted provided the means for obtaining dynamic and quantitative measurements of blood flow in individual vessels in seals and dogs. The Franklin pulsed ultrasonic flow meter (*12*) was used in studies in this laboratory. Surgery was performed aseptically under fluothane anesthesia in seals, and pentobarbital (Nembutal) in dogs. The snug-fitting plastic transducer cylinder, divided for convenience into halves, was placed around an artery and tied. The animals were then allowed to recover until they were, to all outward appearances, normal, intact animals. Recovery usually required 1 week, although some measurements were obtained as early as 1 day after surgery. Other records were obtained for several weeks after recovery (*13*).

Our first measurements were of cardiac output in a California sea lion *Zalophus californianus* which was trained to immerse its head upon command (*14*). Right ventricular output was recorded directly by means of a flow transducer mounted on the pulmonary artery. The output decreased with heart rate, stroke volume remaining unchanged. Other experiments were performed on dogs to test the response of terrestrial animals in the unfamiliar diving situation. Blood flow in the ascending aorta was recorded while the dog's head was immersed for 1 minute or less in a water-filled rubber sack. Sample records are shown in Fig. 2. [This and other figures in which blood flow records are presented show relative measures of flow. It has previously been shown that the pulsed ultrasonic blood flow meter is a linear device (*12*).] Heart rate slowed despite vigorous struggling which contrasted with the general quiet attitude of the seal under similar circumstances. It will be noted that, as was seen earlier in the sea lion, the stroke volume, represented by the area under the blood-flow curves, remained essentially unchanged during immersion. Cardiac output, therefore, decreased in proportion to rate. This pattern was observed in 12 asphyxia experiments in two dogs.

Blood Flow Distribution

Blood flow was measured in harbor seals (*Phoca vitulina*) in the renal artery, terminal abdominal aorta, and the common carotid artery. Measurements were obtained in dogs in the superior mesenteric artery, renal artery, and the terminal abdominal aorta. Blood flow in the left circumflex coronary artery of a greyhound dog was measured during immersion of the head. Two young adult harbor seals weighing 30 and 35 kilograms and five adult dogs which ranged in weight from 15 to 25 kilograms were used.

The general features of blood-flow changes in the abdominal aorta and

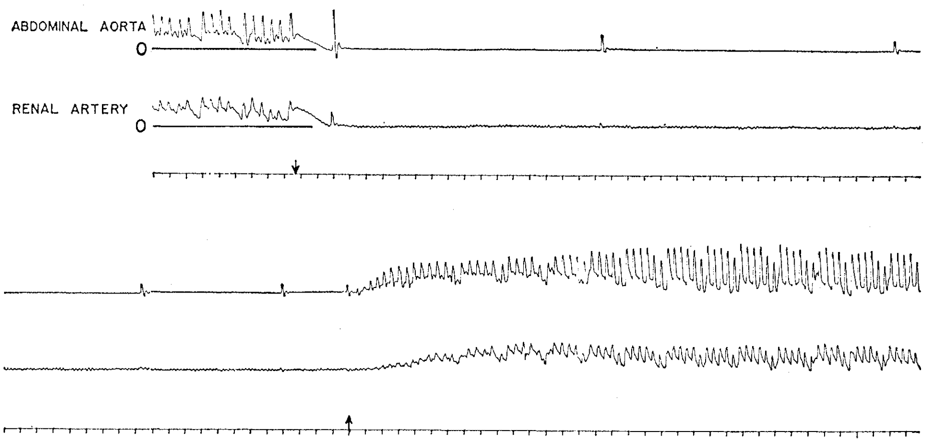

Fig. 3. Blood flow in the abdominal aorta and renal artery of a harbor seal *Phoca vitulina* at the beginning and end of an 8-minute dive (indicated by arrows). Time marks are in seconds.

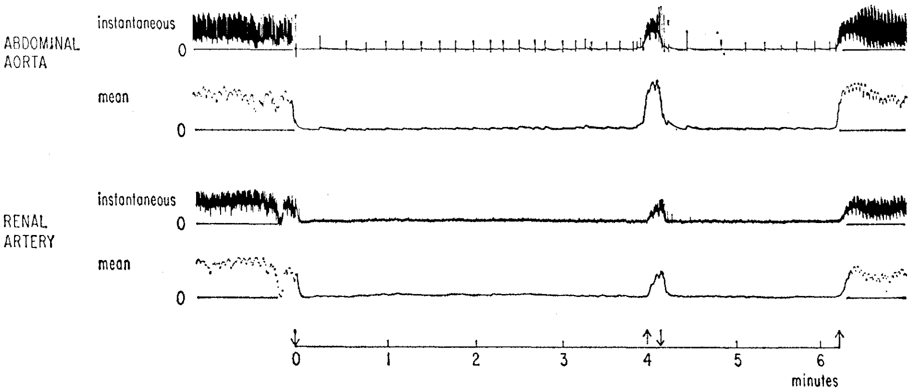

Fig. 4. Instantaneous and mean blood flow in the abdominal aorta and renal artery of a harbor seal *Phoca vitulina* during an experimental dive. The animal was brought to the surface for 10 seconds at 4 minutes, then submerged for an additional 2 minutes.

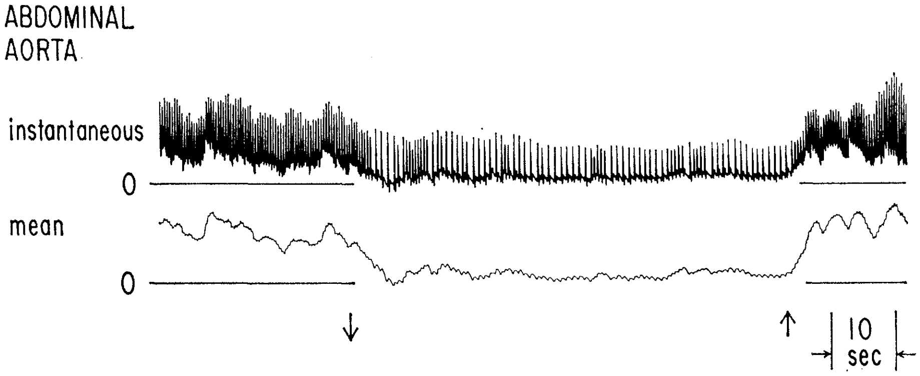

Fig. 5. Instantaneous and mean blood flow in the abdominal aorta of a harbor seal *Phoca vitulina* trained to dive on command. Immersion period is indicated by arrows.

renal artery of the harbor seal during a dive are shown in Fig. 3. This was a forced dive in which the animal lay quietly restrained underwater for 8 minutes. The beginning and end of that dive are shown in the figure. The striking bradycardia, with a change from 100 to four beats per minute, and the simultaneous fall of blood flow are clearly seen. A transient reversal of flow in the abdominal aorta immediately after each heartbeat indicated oscillation of blood within this vessel as it was pumped into the tightly constricted elastic arterial tree. Both flows returned promptly to previous levels after the dive. Approximately 50 such dives, extending in time to a maximum of 15 minutes, were performed in the two seals, always with similar pronounced changes in blood flow.

Figure 4 illustrates another record of blood flow obtained in the abdominal aorta and renal artery and shows both instantaneous and mean blood flow. The flow records, which were recorded on tape, were directed to a simple analog computer to obtain information on mean blood flow. The animal was first submerged for a period of 4 minutes. The prompt and intense bradycardia and decrease in blood flow occurred as before. Then, at 4 minutes the seal's head was raised above water for 10 seconds. Blood flow was promptly restored, then abruptly decreased again upon reimmersion. The promptness of the response to reimmersion argues for precise neural control overriding the influence of accumulated metabolic vasodilator substances. At the end of the completed dive a slight overshoot in blood flow occurred in both circuits.

It was subsequently found that both sea lions and harbor seals have much more profound heart slowing when they are forced to submerge than when they have been trained to dive on command, either by head immersion alone or by whole body dives (*15*). Abdominal aortic blood flow in trained animals was still drastically reduced, however, by the nearly complete elimination of steady diastolic flow (Fig. 5).

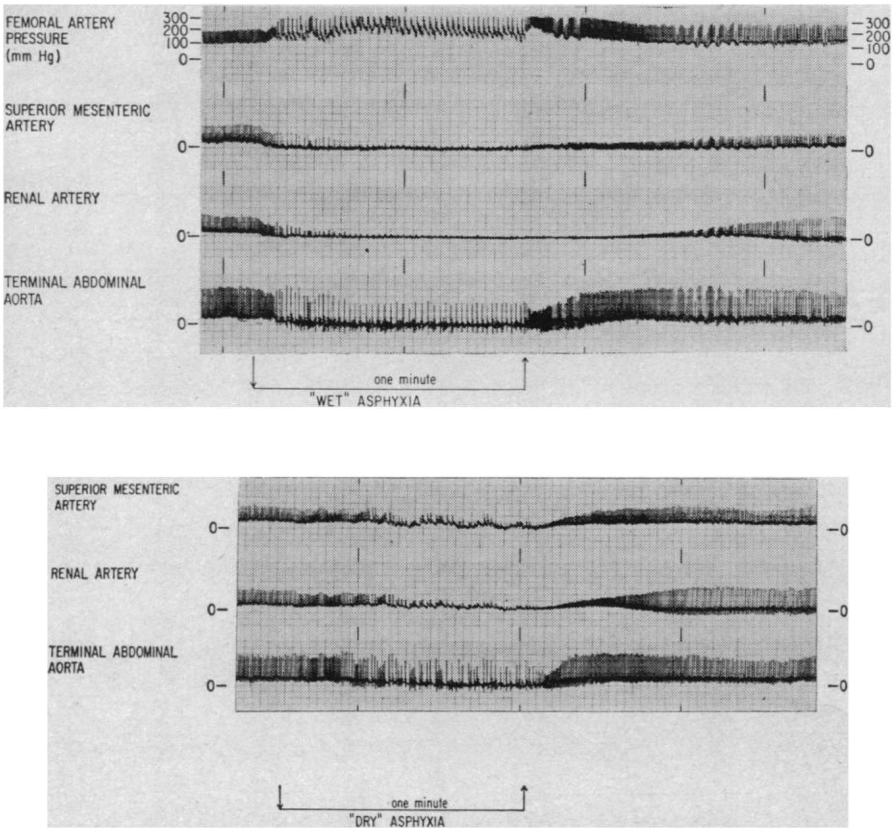

Fig. 6. (Top) Arterial blood pressure and blood flow in the superior mesenteric and renal arteries and the abdominal aorta of a dog during head immersion of 1 minute. (Bottom) Blood flow measured in the same dog during asphyxia without immersion.

In Fig. 6 (top) blood-flow records from a dog are presented. The dog's nose and mouth were immersed for 1 minute of "wet asphyxia," and the usual bradycardia, this time a decrease from 150 to 45 beats per minute, was produced. Blood flow fell nearly to zero in the superior mesenteric and renal arteries and was considerably decreased in the terminal abdominal aorta. It is noteworthy that despite the dog's struggles, heart slowing occurred and blood flow was reduced in the abdominal aorta. The elevation in arterial blood pressure was probably associated with this struggling. Prompt and complete recovery followed the period of head immersion.

Figure 6 (bottom) shows a record obtained from the same dog before, during, and after 1 minute's "dry asphyxia" produced by holding a rubber glove tightly over its head. It can be seen that the responses were not as profound as with water. These experiments, with minor variations, were performed a total of 20 times on five dogs, with similar results.

The changes in blood flow distribution during diving rank with response to vigorous exercise in magnitude of physiological displacement. In fact, these flow changes are the greatest which have been measured under physiological conditions by the direct methods employed here (*16*).

In two experiments, dogs in which measuring instruments had been implanted were treated with 0.1 milligram of atropine per kilogram of body weight in an attempt to block the parasympathetic outflow to the heart via the vagus nerve. After administration of the drug, the heart rate increased from 150 to about 300 beats per minute. The tachycardia persisted unchanged during 1 minute's "wet asphyxia" produced as before. This blocking of diving bradycardia was demonstrated years ago by Richet (*2*), but it is of note that, despite the tachycardia, blood flow in the mesenteric and renal arteries and abdominal aorta was still somewhat reduced during immersion. Atropine thus produced some separation of the circulatory responses mediated by the sympathetic and parasympathetic divisions of the autonomic nervous systems.

That the intense peripheral vasoconstriction during diving is selective in nature is suggested by the record of flow in the common carotid artery in the harbor seal (Fig. 7). During this dive of 8 minutes the flow was considerably reduced in the carotid artery, but it was sustained at a higher level than in the other arteries in which it was measured. It cannot be stated with certainty that the sustained flow in the common carotid is related to the maintenance of cerebral blood flow in this animal, though it is suggested.

Figure 8 shows a record of aortic pressure and blood flow in the left circumflex coronary artery of a greyhound dog while its head was immersed for 30 seconds. The blood flow in the coronary circuit was only slightly reduced during the procedure; thus continued oxygen supply for heart muscle is assured as long as adequate amounts remain in the circulating blood.

The changes that occurred during diving were easily abolished with anesthesia. In several experiments in dogs and seals, even light anesthesia with pentobarbital or sedation with phenylcyclidine (Sernylan) eliminated both the bradycardia and peripheral vasoconstriction during experimental asphyxia, either "wet" or "dry."

Studies on Humans

Although clarification of the diving response has been accomplished through the study of comparative marine physiology, some of the circulatory events can also be traced in man. Bradycardia of diving was first observed in man by Irving in his 1940 study of an experienced swimmer (*17*). Heart slowing of 50 percent was commonly seen. Recent workers have elaborated upon this finding (*18*).

Scholander and his co-workers studied the experienced trochus-shell divers in the region of Thursday Island near Cape York, in northern Australia. Electrocardiograms and blood-pressure measurements were obtained (*10*). Bradycardia of diving was routinely observed. Blood pressure measured during quiet dives near the surface was generally well maintained. Cardiac arhythmias during the dives were commonly seen by these workers and were subsequently studied by Olsen, Fanestil, and Scholander (*19*). In another study, brachial artery pressure was measured directly by catheterization during underwater dives preceded by hyperventilation (*20*). A slight increase in pressure was noted, but delayed run-

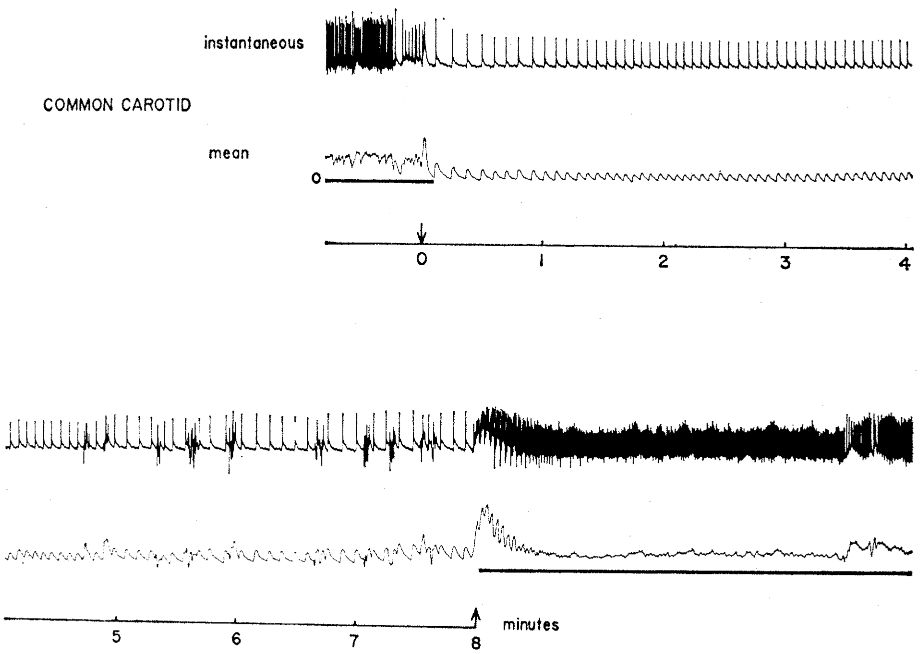

Fig. 7. Blood flow in the common carotid artery of a harbor seal *Phoca vitulina* during an 8-minute dive.

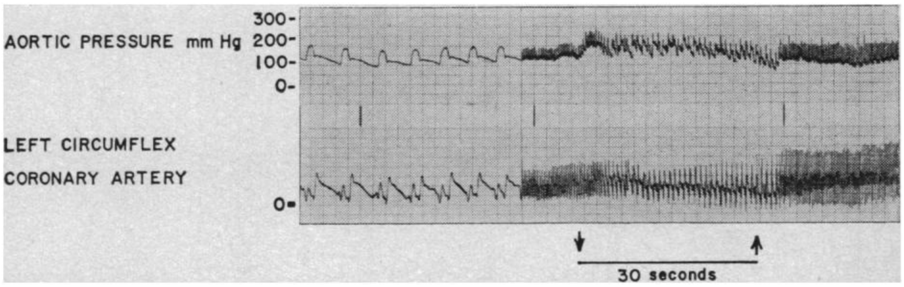

Fig. 8. Aortic pressure and blood flow in a coronary artery of a dog during an immersion of 30 seconds.

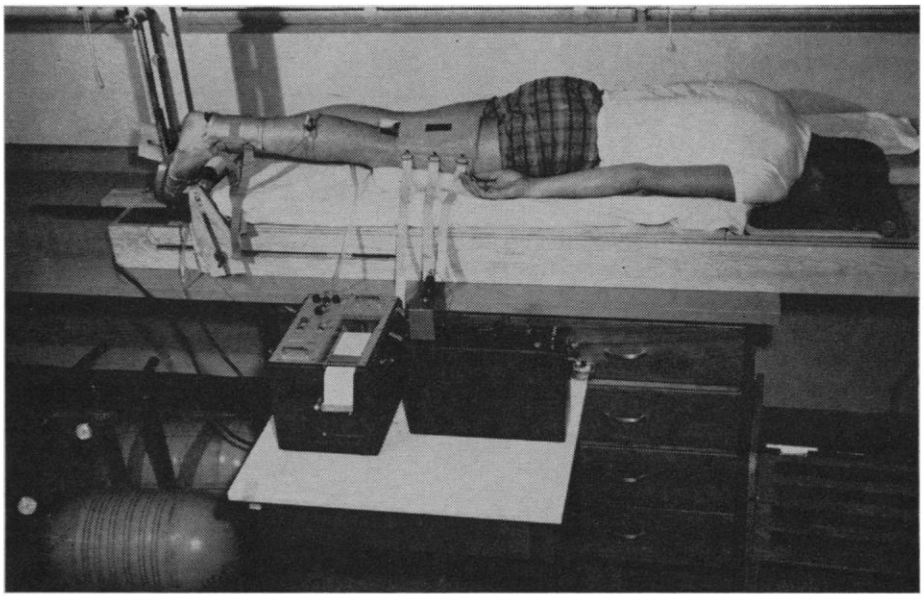

Fig. 9. Experimental subject during face immersion. A mercury-in-rubber plethysmograph is mounted on the right calf.

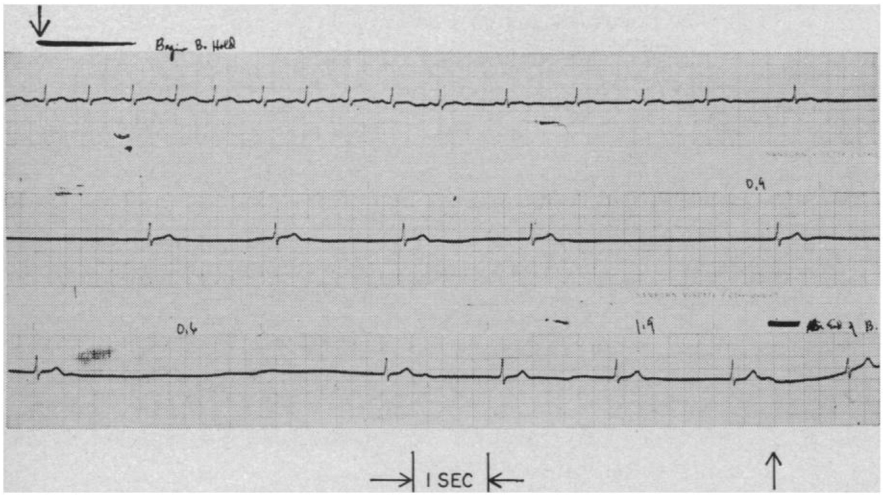

Fig. 10. Electrocardiogram of a subject during face immersion demonstrating unusually profound bradycardia.

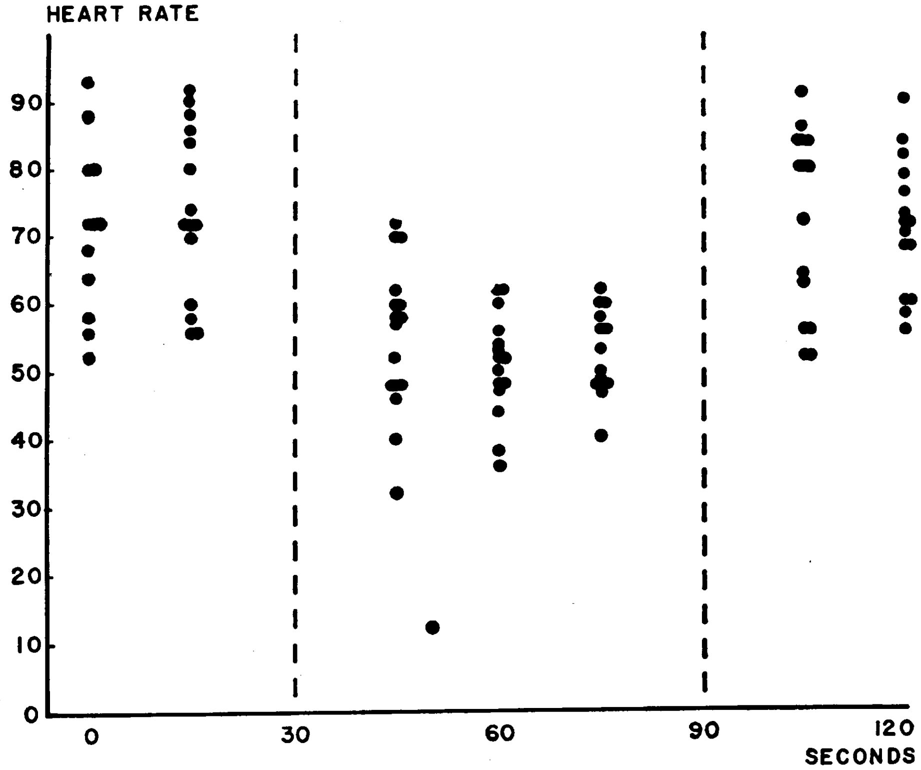

Fig. 11. Heart rate in human subjects before, during, and after face immersion. The period of immersion is indicated by dotted lines.

off during diastole was always observed as the heart slowing progressed.

Studies were undertaken in our laboratory to determine whether circulatory changes occurred in human limbs during dives (*21*). Nine young men of varying diving experience were the subjects. It was soon discovered that the full bradycardia of diving could be produced as well by immersion of the face alone as by immersion of the entire body (Fig. 9). Blood-flow measurements in the calf of the leg were obtained with a Whitney mercury-in-rubber plethysmograph (*22*).

During experiments, an arterial-occlusion cuff at the ankle was inflated to a pressure of 200 mm-Hg to exclude the foot circulation from the measurements. A venous-occlusion cuff situated above the knee was inflated to a pressure of 50 mm-Hg to produce limb filling under the plethysmograph. The limb was elevated slightly above heart level so that filling after venous occlusion could proceed with the limb initially drained of venous blood. In some experiments the subject was requested to perform mild standard exercise by pushing repeatedly against a spring-loaded foot pedal to a cadence established by a metronome. Face immersion "dives" customarily lasted for 1 minute. They were performed after a moderate inspiration or expiration without hyperventilation.

All subjects experienced bradycardia during the dives, sometimes with dramatic effects. In one experiment a subject held his face underwater for 30 seconds beginning at the end of expiration. He began the procedure with a heart rate of approximately 90, which slowed to 13 beats per minute (Fig. 10). Subjects varied widely in the response, their heartbeats usually slowing to about two-thirds of the resting value (Fig. 11). By contrast, bradycardia was generally slight or absent during breath-holding in air. Figure 12 shows a plethysmogram recorded continuously for 1 minute before, during, and after face immersion. The rate of limb filling after venous occlusion (blood flow) is indicated by the steepness of the curves. In this subject, limb blood flow fell nearly to zero during the dive. The artifacts produced by inflation and deflation of the venous-occlusion cuff are clearly visible. Changes in heart rate can be seen superimposed on the record. Results of experiments on all subjects are plotted in Fig. 13 (top left). The limb blood flow consistently decreased more during face immersion than during simple breath-holding in air (Fig. 13, top right). Similar results were recently reported by Brick (*23*).

In three of the more responsive subjects, the hyperemia that usually follows exercise was overridden by the effects of face immersion. This is demonstrated in Fig. 13 (bottom right). After 15 seconds of standard foot-pedal exercise without diving or breath-holding, the usual hyperemia and recovery occurred. The subjects also performed the same exercise during a 1-minute period of face immersion. Measurements taken immediately after exercise, but still during immersion, did not show the usual increase in blood flow. The hyperemia was delayed until after the subject had removed his face from the water. It has not been possible to demonstrate any consistent differences between experienced and inexperienced divers in circulatory responses to apneic face immersion.

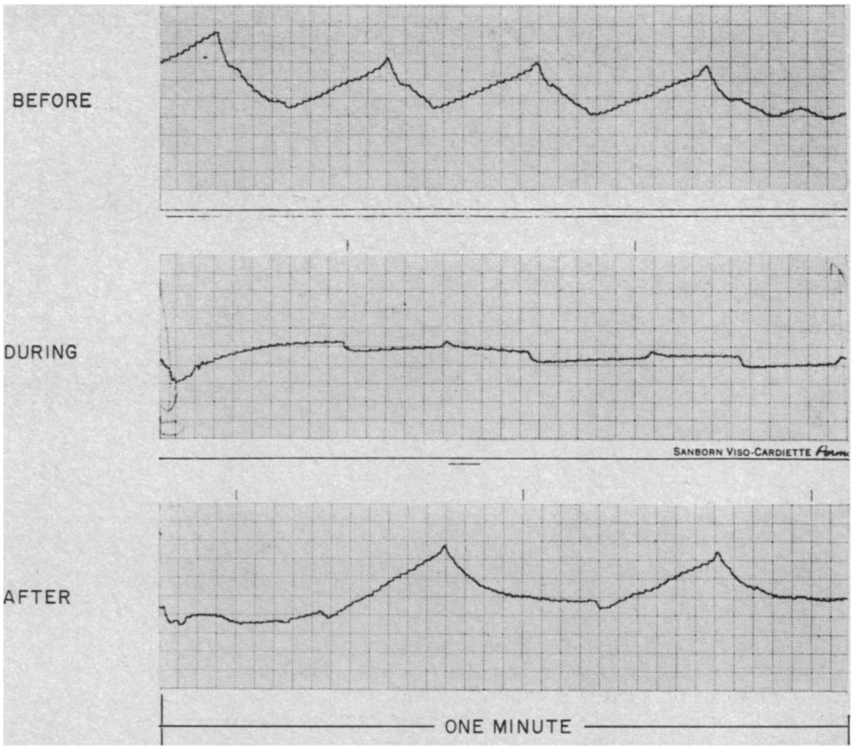

Fig. 12. Plethysmogram recorded continuously for 1 minute before, during, and after face immersion of a human subject.

Some Implications

The results of these various investigations substantiate Irving's hypothesis of conservation of available oxygen through massive peripheral vasoconstriction, particularly in those organs which can tolerate anoxia for prolonged periods. The vigor of the ischemic reactions is particularly impressive, as demonstrated in the harbor seal (Fig. 3). The sudden onset of the reaction suggests that it is initiated by a neural mechanism. Further evidence of strong neural stimulation was shown by the experiment in which a harbor seal which had been immersed for 4 minutes was brought to the surface for 10 seconds with immediate restoration of blood flow, then reimmersed for two more minutes (Fig. 4). The second immersion was promptly followed by intense bradycardia and nearly complete cessation of blood flow. Thus, at a time when vasodilatation would be expected to result from the accumulation of metabolic products during prolonged ischemia, this reaction was completely dominated by the vasoconstriction of diving.

It has been seen that the vasoconstrictive reaction occurred in dogs and man, although it was not as intense and its onset appeared not to be as abrupt as in the harbor seal. Nevertheless, the response to immersion was profound, with flow in some arteries falling almost to zero. The terrestrial animals cannot match the acknowledged superiority of the various seals (*5, 24*) in storing oxygen bound to both hemoglobin and myoglobin. The seals are also less sensitive to accumulation of carbon dioxide (*25*) and tolerate well the build-up of anaerobic metabolic products (*5*). These factors, combined with the more highly developed circulatory control of the aquatic mammals, appear adequate to explain the differences between them and the terrestrial species, but the quantitative relationships and control mechanisms are still unclear.

In the animals examined, immersion of the head in water led to a more pronounced response than did simple breath-holding alone. Other investigators have reported similar findings in ducks (*26*) and man (*23*). Water immersion alone, without breath-holding, has been shown to produce some heart slowing in both ducks and man (*27, 23*), and a specific sensory pathway from the beak of the duck has been described (*28*). The nature of the postulated receptor organ is unknown. Direct stimulation of regions deep within the brain have produced cardiovascular responses resembling those of diving in ducks (*29*) and elephant seals (*11*).

Metabolic Considerations

When a tissue is deprived of oxygen for a prolonged period its metabolism decreases, as is evidenced by a decrease in temperature. The diving animal experiences a similar decrease in total body metabolism and an associated decrease in temperature (*30*). It has also been demonstrated that the excess oxygen consumption after a quiet dive in a harbor seal was insufficient to account for the oxygen which would have been consumed had the animal continued without diving at its previous metabolic rate (*5*), a strong indication that the "oxygen deficit" incurred during the dive was only partially repaid.

The similarity between the diving phenomena and the physiological events associated with hibernation is impressive. In at least two species, the ground squirrel and the hedgehog, circulatory changes preceded (and probably initiated) metabolic changes in both onset of and arousal from hibernation (*31, 32*). Thus, during the onset of hibernation, heart rate fell before body temperature began to decline. Similarly, during arousal from hibernation, the heart rate increased before body temperature rose. Arterial blood pressure was lowered during hibernation, but peripheral resistance was elevated, as shown by the slow decline in diastolic pressure between heartbeats (*32*). Thus, pressure was maintained relatively well despite profound bradycardia and, presumably, much decreased cardiac output. Selective vasoconstriction during arousal from hibernation was demonstrated by x-ray visualization of radio-opaque substances injected into the heart (*33*). Normal circulation was more rapidly reestablished in the head than in the more peripheral parts of the body during awakening. These findings suggest a coordinated, precisely controlled mechanism in hibernation similar to, but having a much longer time course than, those seen in diving.

Responses to compensated shock also bear a resemblance to the diving adjustments. Kidney blood flow sometimes decreases during hemorrhagic

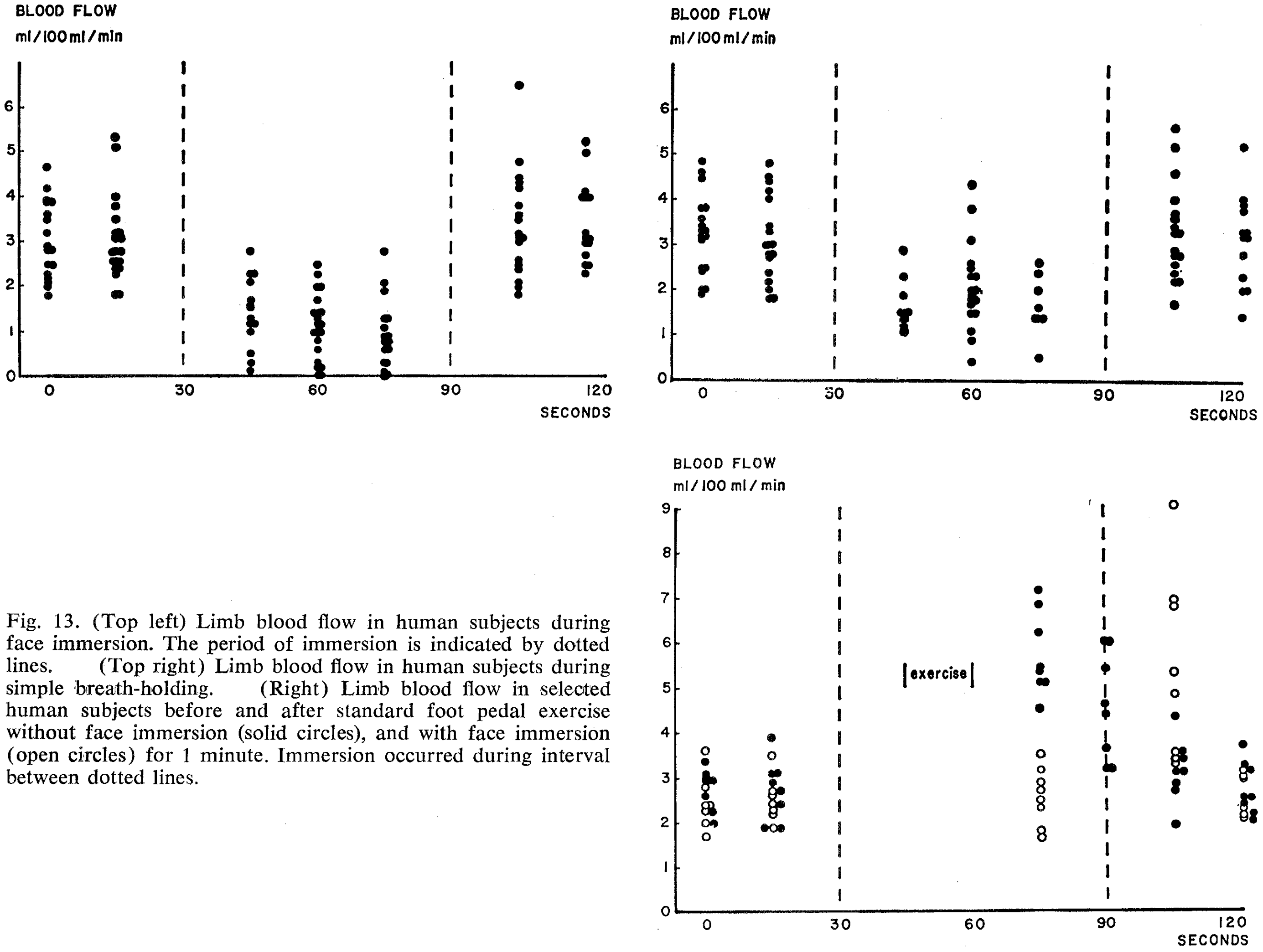

Fig. 13. (Top left) Limb blood flow in human subjects during face immersion. The period of immersion is indicated by dotted lines. (Top right) Limb blood flow in human subjects during simple breath-holding. (Right) Limb blood flow in selected human subjects before and after standard foot pedal exercise without face immersion (solid circles), and with face immersion (open circles) for 1 minute. Immersion occurred during interval between dotted lines.

shock, but it has been learned only recently that the mesenteric circulation is also drastically reduced (*34*). As with the response to apneic diving, the circulation in the kidney and intestine was reduced while adequate arterial pressure and perfusion were maintained in organs more vital for survival. Such results, however, must be cautiously interpreted because of the enormous variety of possible circulatory responses during shock (*35*).

It has been commonly observed for many years that very young animals are considerably more resistant to asphyxia than are adult animals. This is particularly true in those species born in a relatively immature state. Newborn puppies, for instance, survived for 20 to 50 minutes, depending on temperature, in an atmosphere in which oxygen was totally lacking (*36*). It was demonstrated many years ago by Bohr (*37*), working with the diving birds murres and puffins, and later by Scholander with the gray seal (*5*), that survival time in an atmosphere of 100 percent nitrogen was considerably shorter than survival time during water immersion, probably because of oxygen washout in vital tissues and dependence upon aerobic metabolic pathways. A better model, perhaps, showing a parallel in anaerobic capability with the newborn infant, would be the diving fresh-water turtle. It survived equally well for periods up to 27 hours underwater or in 100 percent nitrogen (*38*). Elimination of anaerobic processes by iodoacetate poisoning drastically shortened survival time underwater (*39*), just as it did in newborn rats in a nitrogen atmosphere (*40*).

Cardiac and liver stores of carbohydrate are important for the survival of the newborn (*41*), and it seems clear that the maintenance of cerebral circulation for the transport of metabolizing substances is essential for its life. Thus, the newborn *in extremis* might be expected to respond to asphyxia in a manner similar to that seen in experimental animals during breath-holding dives. This may be the explanation of the commonly observed fetal and newborn bradycardia associated with difficult or prolonged labor.

Preliminary experiments on newborn calves were recently performed in our laboratory. Under local anesthesia (Xylocaine), a Franklin ultrasonic Doppler flow transducer (*42*) was implanted on the superior mesenteric or renal artery. We were usually able to obtain blood flow records within 2 hours after birth. Experimentally induced asphyxia at that time resulted in little change in heart rate and blood flow. Such changes as did occur were delayed until the animal was in a state of severe distress. The calf remained relatively unresponsive to induced asphyxia until about the tenth day, when prompt bradycardia and decreased blood flow occurred. This finding suggests that the conversion from primary dependence upon an anaerobic metabolic response of infancy to a circulatory adjustment mechanism may have occurred during that time.

The circulatory system plays a major, possibly dominant role in adjustment to the general phenomenon of asphyxia. Apneic diving is a special, highly developed instance of this. The associated changes in cardiac function and peripheral circulation are among the most profound ever demonstrated by naturally occurring stimuli. Their study aids in defining the range of physiological responses. Quantitative description of such responses is a necessary step toward the goal of understanding the nature of general cardiovascular control mechanisms and their integration with other physiological systems.

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Relativistic Quantum Field Theory

Julian Schwinger

The relativistic quantum theory of fields was born some thirty-five years ago through the paternal efforts of Dirac, Heisenberg, Pauli and others. It was a somewhat retarded youngster, however, and first reached adolescence seventeen years later, an event which we are gathered here to celebrate. But it is the subsequent development and more mature phase of the subject that I wish to discuss briefly today.

I shall begin by describing to you the logical foundations of relativistic quantum field theory. No dry recital of lifeless "axioms" is intended but, rather, an outline of its organic growth and development as the synthesis of quantum mechanics with relativity. Indeed, relativistic quantum mechanics—the union of the complementarity principle of Bohr with the relativity principle of Einstein—*is* quantum field theory. I beg your indulgence for the mode of expression I must often use. Mathematics is the natural language of theoretical physics. It is the irreplaceable instrument for the penetration of realms of physical phenomena far beyond the ordinary experience upon which conventional language is based.

Improvements in the formal presentation of quantum mechanical principles, utilizing the concept of action, have been interesting by-products of work in quantum field theory. Both my efforts in this direction (*1*) and those of Feynman (*2*) (which began earlier) were based on a study of Dirac concerning the correspondence between the quantum transformation function and the classical action. We followed quite different paths, however, and two distinct formulations of quantum mechanics emerged which can be distinguished as differential and integral viewpoints.

In order to suggest the conceptual advantages of these formulations, I shall indicate how the differential version transcends the correspondence principle and incorporates, on the same footing, two different kinds of quantum dynamical variable. It is just these two types that are demanded empirically by the two known varieties of particle statistics. The familiar properties of the variables q_k, p_k, $k = 1 \, . \, . \, n$, of the conventional quantum system enable one to *derive* the form of the quantum action principle. It is a differential statement about time transformation functions,

$$\delta\langle t_1|t_2\rangle = (i/\hbar)\left\langle t_1\left|\delta\left[\int_{t_2}^{t_1} dtL\right]\right|t_2\right\rangle \quad (1)$$

which is valid for a certain class of kinematical and dynamical variations. The quantum Lagrangian operator of

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The author is professor of physics at Harvard University, Cambridge, Massachusetts. This article is the lecture he delivered in Stockholm, Sweden, 11 December 1965 when he received the Nobel Prize in physics, which he shared with Richard Phillips Feynman and Shinichero Tomonaga. It is published here with the permission of the Nobel Foundation and will also be included in the complete volumes of Nobel lectures in English, published by the Elsevier Publishing Company, Amsterdam and New York.