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# Pathophysiology of inner ear dysfunction in the squirrel monkey in rapid decompression



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LANDOLT, JACK P., KENNETH E. MONEY, E. D. L. TOPLIFF, A. D. NICHOLAS, JERRY LAUFER, AND WALTER H. JOHNSON. *Pathophysiology of inner ear dysfunction in the squirrel monkey in rapid decompression.* J. Appl. Physiol.: Respirat. Environ. Exercise Physiol. 49(6): 1070–1082, 1980.—More than 90 squirrel monkeys with bilateral myringotomies (a small hole in each ear drum) were rapidly decompressed in a hyperbaric chamber according to a special diving profile in which 35% of attempts produced disorders ("hits") confined to the inner ear. Monkeys receiving inner ear hits (as determined by the sudden onset of vigorous head or eye nystagmus during decompression) were tested and killed at times ranging from 1 h to more than 12 mo following the dive. Histologically, in monkeys killed 1 mo or less after the hit, hemorrhage and/or a deep purple-staining precipitated material were frequently found in the otic fluid spaces. In those monkeys killed more than 1 mo after a hit, ectopic new bone growth in the arms of the semicircular canals was a common sequela. New bone growth never appeared in the cochlea. In unaffected ears, and in both ears of control animals, the precipitated material was somewhat less than in ears damaged by decompression; and, furthermore, new bone growth did not occur. Behaviorally, the hit monkeys showed vestibular deficits that were consistent with the structural damage revealed by histology.

inner ear decompression damage; decompression sickness; vestibulocochlear dysfunction; simulated deep diving; high-pressure environments; fibroosseous labyrinthitis; inner ear hemorrhage

IT IS NOW WIDELY RECOGNIZED that inner ear (vestibulocochlear) disorders resulting from decompression represent a serious hazard in underwater diving (6–8, 13, 16, 20, 26, 31, 37). For dives to depths as low as (approx) 100 m of seawater (msw), the most common decompression problem is joint bends; but deeper than 100 m the most common problem is inner ear damage. This damage is unrelated to Eustachian tube function, and it occurs in spite of pressure equalization on the two sides of the ear drum.

Recently, a group of audiovestibular scientists, working under the auspices of the Undersea Medical Society for a National Plan for the Safety and Health of Divers in their Quest for Subsea Energy, have recognized the need for, and have given the highest priority to, basic research into otologic decompression sickness in animals (19). The present report is written partly in response to that need.

Why is the inner ear so susceptible to damage from decompression? Part of the answer probably lies in the fact that the inner ear is a system of liquid-filled cavities within rigid bone. The membranous labyrinth is comprised of a series of interconnected ducts and sacs that contain the sensory epithelia of the vestibular apparatus and the cochlea for equilibratory and auditory functions, respectively. Two otic fluids, endolymph and perilymph, are an integral part of the vestibulocochlear complex. The endolymph, which is rich in potassium ions and low in sodium ions, bathes the sensory epithelia within the utricle (the macula utriculi), the saccule (the macula sacculi), and the three semicircular ducts (the cristae ampullares of the anterior, lateral, and posterior semicircular ducts)[1] of the vestibular apparatus, as well as the scala media (the organ of Corti) of the cochlea. The membranous labyrinth is separated from its bony counterpart (and the temporal bone of the skull) by the perilymph, a fluid that is rich in sodium and low in potassium. In the cochlea, the perilymph is found in two compartments: an upper one, the scala vestibuli, and a lower one, the scala tympani. (The scala media is separated from the scala tympani below by the spiral lamina and the basilar membrane, the latter of which supports the organ of Corti.) Additionally, there is a specialized network of vessels that supply and drain the various parts of the inner ear. [More detailed information on the anatomy, and also on the physiology and pathophysiology of the inner ear, may be found elsewhere (35, 38).] Perhaps this unique arrangement of rigid walls surrounding large fluid-filled spaces and intricate vasculature peculiarly predisposes the inner ear to bubble formation and hemorrhage during rapid decompression.

In this paper, the pathophysiological manifestations of inner ear dysfunction are elucidated from experiments in which the squirrel monkey (*Saimiri sciureus*) was used as an animal model. The nature and extent of vestibular dysfunction during and after simulated deep diving is determined by correlating histopathological with nystagmoidal observations (both behavioral and electronystagmographic). Cochlear disorders are determined solely from the observations of histopathology.

To date, only a few studies have used animals to

[1] The membranous tubes are referred to as semicircular ducts, the corresponding bony enclosure as semicircular canals. Semicircular canals is also used as a generic term for the vestibular sensors of angular motion

investigate inner ear disorders in a compressed air environment. Earlier reports from this laboratory (29, 30) provided some preliminary results on the nature of the vestibulocochlear "hits" in monkeys that were exposed to high-pressure situations. McCormick and his colleagues (33, 34) and Long et al. (32) had previously given some insight into cochlear dysfunction in the rapid decompression of the guinea pig. Jensen et al. (25) reported on the spontaneous and postrotatory electronystagmus in guinea pigs following different decompression exposures. Chiappe (9) histologically investigated the inner ear lesions resulting from decompression in guinea pigs and cats in which bottom depth, bottom time, and rate of decompression were varied experimentally. The only other studies in which animals have been used to investigate vestibulocochlear dysfunction are those by a team of German investigators, near the turn of this century, on dogs and guinea pigs in work that was related to caisson disease (1, 2).

## METHODS

*Experimental animal model.* Ninety-one male squirrel monkeys, weighing 423–1,444 g (mean = 664 g), and free from otitis media and other disorders, were subjected to simulated dives in a 300-msw hyperbaric chamber (Bethlehem Corp., 0.173-$m^3$ capacity). A special procedure was followed to prevent otic barotrauma (an injury which results from a failure of the Eustachian tubes to open and equalize middle ear and environmental pressures during compression). One day prior to a dive, the caudal portions of the tympanic membranes in both ears were surgically opened (myringotomy) under light pentobarbital sodium anesthesia. (This was confirmed again at the time of the dive.) Although round and/or oval window rupture is often an indirect sequela of otic barotrauma, histological studies of temporal bone sections from successfully dived monkeys revealed that these windows were intact in every instance. Thus it is unlikely that otic barotrauma is involved in any of the otologic disorders that have occurred during these experiments.

*Vestibular function testing.* Vestibular function was examined before the dive and again at various times after the dive, depending on when the monkey was to be killed for light microscopic histological investigations. These examinations involved visual and electronystagmographic observations of spontaneous and induced nystagmus; judgment of the degree of difficulty in walking and standing; and observation for any signs of vomiting that might occur. Before and immediately after the dive, any behavioral manifestations of vestibular dysfunction were recorded on film (16 mm). During the dive, the monkey was free to move in a small wire-mesh cage; and its behavior was monitored through a glass port in the chamber and recorded on videotape.

Horizontal as well as vertical eye movements were detected by electroencephalogram electrodes, amplified by an AC-coupled dual-channel preamplifier (20-s time constant) and displayed by a strip-chart recorder (Beckman type RS Dynograph) as a permanent record. Electronystagmography was used to record, predive, and postdive, each of spontaneous nystagmus, positional nystagmus [nose up (NU), nose down (ND), right side down (RSD), left side down (LSD), in darkness], and postrotatory nystagmus [head erect (HE), RSD, LSD, following clockwise (CW) and counterclockwise (CCW) rotations in darkness]. (The HE, NU, and ND positions stimulate the lateral canals, RSD and LSD the vertical canals.) Any monkey showing signs of spontaneous or positional nystagmus prior to a dive was not used in the experiment. The animal was subjected to loud noises, when necessary, to maintain a state of arousal during the recording of nystagmus. For each head position, an optokinetic nystagmus was also recorded to permit calibration of the induced slow component of the eye movements. To this end, the monkeys were rotated on a turntable at an angular velocity of 30°/s (eyes open, in daylight) for 30 s in a CW direction and again for 30 s in a CCW direction. Assuming that the monkey is fixating during the slow components of the resulting optokinetic nystagmus, and that the angular speed of eyeball rotation equals the speed of rotation of the table (in the opposite direction), the optokinetic nystagmus allows calibration of the eyeball displacement in terms of degrees per millimeter of chart paper. The speeds of the slow components of the vestibular nystagmus in darkness (in degrees per second) can then be readily determined from the vestibular nystagmograms. [The speed of the slow component of vestibular nystagmus is thought to reflect cupular displacement and is considered to be the most accurate indicator of semicircular canal stimulation (3).]

*Decompression procedures.* A decompression schedule, which had previously produced some vestibular hits in the rhesus monkey, was obtained from the International Decompression Data Bank (courtesy of R. E. Peterson, Institute of Environmental Medicine, University of Pennsylvania, Philadelphia), and modified to reflect the shorter tissue saturation and desaturation times required by the lighter mass of the squirrel monkey. In the early experiments, nitrox (80% nitrogen-20% oxygen) was used as the ambient gas mixture (21 animals); and, in the later experiments, heliox (80% helium-20% oxygen) was used (20 animals). The diving profile commenced with compression of the ambient gas from the surface to 13.9 msw. Compression was taken by nitrogen (or later, helium) at the rate of 32.6 msw/min to a depth of 211 msw. Decompression, after bottom times from 2 to 20 min, varied from 5.7 to 18.1 msw/min up to depths ranging from 9.1 to 61 msw. From there, the animals were brought to surface pressure in discrete small steps. Table 1 shows that, using this first profile, the incidence of vestibular hits is five times greater with heliox than it is with nitrox. It also indicates that there is about a 50% chance of not inducing a hit at all with this profile.

To increase the incidence of discrete vestibular damage, a second diving profile to a greater depth was designed (Fig. 1). The initial compression with air produced an oxygen tension ($Po_2$) of 50.7 kPa (= 380 Torr) at 13.9 msw. Subsequent compression with helium to a depth of 274 msw does not alter the $Po_2$. However, during decompression, supplementary oxygen was necessary to prevent a decrease in the $Po_2$ because of oxygen consumption by the monkey. As indicated in Table 1, this second decompression schedule substantially increased

TABLE 1. *Frequency of occurrence of complications in 91 monkeys undergoing simulated decompression schedules*

| Complication | Breathing Gas Mixture | | | | | |
|---|---|---|---|---|---|---|
| | Nitrox | Heliox | Nitrox or heliox | Heliox | Heliox + nitrox* | Heliox or heliox + nitrox |
| | *Bottom depth: 211 msw* | | | *Bottom depth: 274 msw* | | |
| Vestibular | 1 (5%) | 5 (25%) | 6 (15%) | 14 (35%) | 2 (20%) | 16 (32%) |
| Vestibular and central nervous system | 6 (29%) | 5 (25%) | 11 (27%) | 12 (30%) | 3 (30%) | 15 (30%) |
| Central nervous system | 3 (14%) | 2 (10%) | 5 (12%) | 6 (15%) | 3 (30%) | 9 (18%) |
| None† | 11 (52%) | 8 (40%) | 19 (46%) | 8 (20%) | 2 (20%) | 10 (20%) |
| Sample size | 21 | 20 | 41 | 40 | 10 | 50 |

* Implies a gas change and stop for 10 min at 30.5 msw during the ascent. † Includes a few cases in which there were mild unspecified complications.

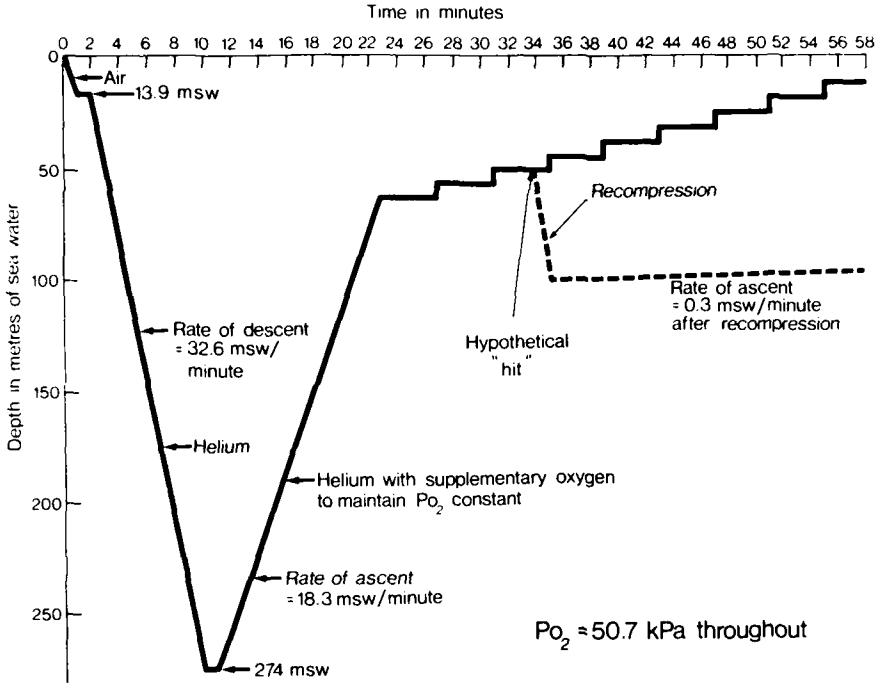


FIG. 1. Diving profile that caused a 35% incidence of discrete vestibular "hits" in squirrel monkeys. Whenever a hit occurred (during ascent from 0.5 msw to the surface), monkey was compressed to twice the depth at which hit occurred and then brought to surface at 0.3 msw/min (see typical profile for a hypothetical hit).

the incidence of discrete vestibular hits (35%), and it also reduced (to 20%) the probability of the procedure having no effect at all on the monkey. Also indicated in Table 1 is the fact that complications involving the central nervous system (CNS) are comparable in both profiles. If decompression produced any CNS complications and/or vestibular hits, the monkey was immediately recompressed to twice the depth (in msw) at which the hit occurred. The recompression was used for the removal of, or as a precautionary measure against, decompression damage in regions other than the inner ear. The procedures were intended to produce inner ear damage for study, without complicating damage elsewhere in the body; and, in most cases, the recompression did prevent damage elsewhere, without reversing the inner ear damage. After the recompression, decompression proceeded at the more conservative rate of 0.3 msw/min to the surface.

The diving profile in Fig. 1 was also used to investigate the incidence of inner ear complication following a change in the chamber gas mixture from heliox to nitrox for 10 min at 30.5 msw ascent (see frequency of occurrence of complications in Table 1).

*Histology.* Monkeys were killed under very deep pentobarbital sodium anesthesia (≃ 1 ml/kg body mass). The chest cavity was opened, the descending aorta was tied, the right auricle was opened for drainage, and the animal's vascular system was washed out with physiological saline introduced by a cannula into the left ventricle under physiological pressure. Then, using the same cannula, the animal was perfused with 10% formalin.

The temporal bones were removed and decalcified in 5% trichloroacetic acid. The tissue was then dehydrated in graded concentrations of alcohol, following which it was embedded in celloidin, according to the method of Igarashi (23). The celloidin blocks were horizontally sectioned at 20 μm, and the sections stained with hematoxylin and eosin. The whole brains were also removed, similarly prepared, and sectioned at 20 μm in the coronal plane [so that subsequent brain pathology could be iden-

tified in relation to comparable sections in an atlas of the brain of the squirrel monkey (17)].

## RESULTS

Monkeys that received inner ear hits were tested and perfused at intervals of from about 1 h to more than 12 mo following a dive. There were no apparent differences in the inner ear deficits (behavioral or histological) obtained with the different ambient gases, gas switching, or type of diving profile; thus all findings may be considered together. No vestibular or CNS disturbances were encountered during descent or at maximum depth; when they did occur, it was always during ascent, between 61 msw and the surface.

In 95% of cases, vestibular dysfunction was identified during decompression by the sudden onset of nystagmus (either in a horizontal or a vertical plane, or about an anteroposterior axis), following which the monkey would become quite unsteady and would have to grasp the wire mesh of the cage to maintain its balance. Other behavioral manifestations of vestibular dysfunction resulting from a successful dive include *a*) emesis and anorexia (2–3 days postdive in 15% of these monkeys); *b*) unsteadiness ("staggers"), either with a tendency to fall in a single direction (40%) or with no predilection for the direction of falling (45%); *c*) head tilt in a preferred direction [30%, occasionally until the animal was killed (up to 7 days postdive)]; and *d*) a tendency to hang upside down in the cage (one case). In general, some form of motor instability was observed in 95% of cases.

For purposes of analysis, the monkeys were arbitrarily segregated into three groups, according to the interval between the dive and the time of death. These groups were *1*) very short-term postdive survival—1 h to 1 day following a dive; *2*) short-term postdive survival—1 day to 1 mo; and *3*) long-term postdive survival—1 mo to 1 year or more. The first of these groups consisted of monkeys that were killed within 1 day of the dive because they showed signs of both peripheral vestibular and central (mainly spinal) lesions. The other groups demonstrated only peripheral vestibular insults and were killed at selected intervals. Additionally, 10 monkeys received various preparative procedures and were used as control animals.

*Inner ear pathology in very short-term postdive survival group.* For all eight monkeys in this group, which were killed within 24 h of the dive, the entries in Table 2 indicate that all of the otic fluid spaces contain a granulated precipitated material that stains a deep purple with hematoxylin and eosin (29). (In Tables 2–4, +++ designates the severest insult, ++ a moderate insult, + the mildest insult, and 0 no insult.) In the cochlea, precipitated material appeared in all scalae and, in some cases, on the tectorial membrane of the organ of Corti. In general, it was loosely packed unless there was concomitant hemorrhage, in which case it was quite compact and more pervasive. In the vestibular apparatus, precipitated material appeared less often in the perilymphatic spaces than in the endolymphatic spaces. It appeared most often in the ampullae, particularly as an agglutinate adhering to the cupulae covering the sensory epithelia of

TABLE 2. *Inner ear histopathology for very short-term postdive survival times*

| Monkey | Depth of Hit on Ascent, msw | Postdive Survival Time, h | Left Side | | | | | | | | | | | | Right Side | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | ASC | | LSC | | PSC | | UTR | | SAC | | COCH | | ASC | | LSC | | PSC | | UTR | | SAC | | COCH | |
| | | | PM | HEM | PM | HEM | PM | HEM | PM | HEM | PM | HEM | PM | HEM | PM | HEM | PM | HEM | PM | HEM | PM | HEM | PM | HEM | PM | HEM |
| 7 | 42.7, 30.5 | 1.5 | +++ | 0 | +++ | 0 | +++ | 0 | ++ | 0 | + | 0 | 0 | 0 | +++ | 0 | +++ | 0 | ++ | 0 | + | 0 | + | 0 | +++ | 0 |
| 10 | 18.3 | 1.5 | + | 0 | +++ | 0 | +++ | + | + | + | + | 0 | 0 | +++ | + | + | +++ | ++ | +++ | + | ++ | + | + | 0 | 0 | 0 |
| 16 | Surface | 2 | +++ | 0 | +++ | 0 | ++ | 0 | + | 0 | + | 0 | + | +++ | +++ | 0 | +++ | 0 | + | + | ++ | 0 | ++ | 0 | + | + |
| 19 | 39.9 | 3.5 | ++ | 0 | + | 0 | ++ | 0 | + | 0 | 0 | 0 | 0 | 0 | ++ | 0 | +++ | 0 | +++ | + | 0 | 0 | +++ | ++ | +++ | ++ |
| 25 | 54.9 | 3 | +++ | ++ | ++ | 0 | 0 | 0 | ++ | 0 | +++ | 0 | 0 | ++ | +++ | +++ | +++ | +++ | + | +++ | 0 | 0 | + | 0 | + | +++ |
| 37 | 24.4 | 24 | + | 0 | 0 | 0 | 0 | + | ++ | 0 | 0 | 0 | ++ | ++ | +++ | 0 | +++ | 0 | 0 | 0 | ++ | ++ | +++ | 0 | ++ | 0 |
| 39 | 24.4 | 24 | +++ | 0 | ++ | 0 | 0 | 0 | + | 0 | + | + | ++ | ++ | +++ | 0 | +++ | + | ++ | 0 | + | + | + | ++ | + | ++ |
| 40 | 30.5 | 2.5 | +++ | 0 | +++ | + | 0 | ++ | + | 0 | +++ | 0 | + | 0 | +++ | +++ | +++ | +++ | 0 | 0 | ++ | ++ | 0 | 0 | +++ | +++ |

Abbreviations: ASC, LSC, and PSC, anterior, lateral, and posterior semicircular canals; UTR, utricle; SAC, saccule; COCH, cochlea; PM, precipitated granulated material; HEM, hemorrhage. Symbols: +++, severest insult; ++, moderate insult; +, mildest insult; 0, no insult.

the cristae ampullares. The left and right labyrinths were equally involved and, in the majority of cases, the precipitate was found in the endolymph and on the cupulae in several ampullae at the same time. The amount of precipitate was considerably reduced in the regions of the saccule and the utricle, where it appeared more often on the macula utriculi than on the macula sacculi. Precipitated material was never found in the cochlear or vestibular aqueducts in this or any other group.

Hemorrhagic incidents occurred more frequently in the cochlea than in the vestibular apparatus in this group of monkeys (Table 2). In the cochlea, hemorrhagic lesions were very discrete and were localized to the stria vascularis (Fig. 2*A*), the vessels lining the top of the scala vestibuli, the collecting venules of the scala tympani, the spiral ligament (occasionally), and, in one instance, vessels to the organ of Corti. [In some instances, hemorrhage caused a partial or complete detachment of the spiral ligament from the outer bony wall, in a manner similar to that reported earlier by Chiappe (9).] In the vestibular apparatus, hemorrhage occurred only in the perilymphatic spaces and even then was mainly confined to the right ear (Table 2). Hemorrhage was never encountered in either the spiral ganglion or the vestibular (Scarpa's) ganglion in any of the groups.

It bears mentioning that most of the monkeys in this group suffered severe CNS (mainly spinal) damage as a result of decompression sickness. On reaching the surface, some were moribund and others appeared to have some paralysis of their limbs. These animals were killed and perfused shortly after the dive.

*Inner ear pathology in short term postdive survival group.* In this group of 11 monkeys, which were killed from 1 to 30 days after the dive, the inner ears were analyzed in great detail (Table 3). None of the four otic fluid spaces (endolymphatic and perilymphatic spaces in the vestibular apparatus and in the cochlea) escaped both hemorrhage and precipitate in all of the monkeys; and, in general, both appeared more in these spaces of the right ears than in the left ears. Compared to the monkeys in the very short-term group, hemorrhage appeared more frequently, and it invariably occurred in the perilymphatic spaces of the vestibular apparatus in this group (Figs. 2*C* and 3*A*).

In both groups, there was blood pooling, to a varying degree, in the regions at which the nerve fibers enter the cristae ampullares and/or the macula utriculi. (In one case, there was gross hemorrhage within the neuroepithelium of the macula utriculi.) However, there was less evidence of gross tissue tearing with concomitant blood vascular disruptions in these regions than there was in the regions along the arms of the semicircular ducts, where hemorrhage was also found in the perilymphatic space. Both blood vessel ruptures and dislodgment of the endosteum were observed along the arms of the semicircular canals (cf. insert Figs. 2*B* and 3*A*). Only occasional

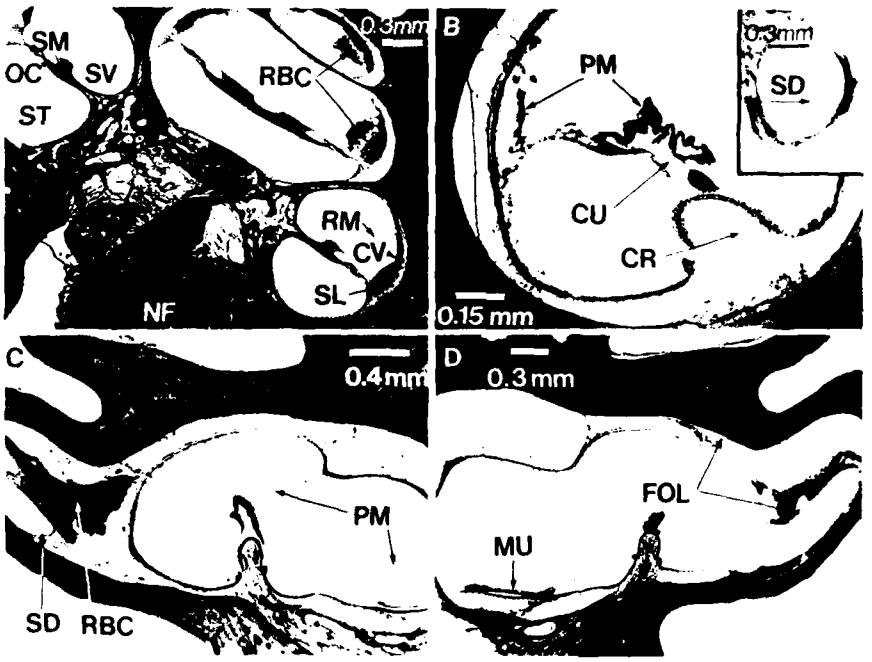


FIG. 2. Histopathology resulting from inner ear decompression sickness. *A*: right cochlea in *monkey 25* (3 h postdive survival) with hemorrhage (RBC) from stria vascularis (CV) in scala media (SM) in middle and apical turns. Also identified are scalae vestibuli (SV) and tympani (ST), organ of Corti (OC), Reissner's membrane (RM), spiral ligament (SL), and nerve fibers (NF). *B*: ampullary contents of anterior semicircular canal in *monkey 12* (48 h postdive survival). Note precipitated material (PM) on cupula (CU) of crista ampullaris (CR) and absence of hemorrhage. Insert illustrates normal appearing semicircular duct (SD). *C*: histopathology of lateral ampulla and semicircular canal, and utricle in *monkey 3* (7 days postdive survival). Note large quantities of PM within ampulla, some of which adheres to CU. Contiguous to SD is a region in which there is a very heavy concentration of RBC. *D*: fibroosseous labyrinthitis (FOL) in perilymphic space in lateral ampulla and semicircular canal in *monkey 68* (290 days postdive survival) illustrating ectopic fibrosis (*light areas* in FOL) and ossification (*dark areas* in FOL). Note macula utriculi (MU), thin neuroepithelium on CR, and darkly stained areas of CU.

TABLE 3. *Inner ear histopathology for short-term postdive survival times*

| Monkey | Depth of Hit on Ascent, msw | Postdive Survival Time, days | Left Side | | | | | | | | | | | | Right Side | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | ASC | | LSC | | PSC | | UTR | | SAC | | COCH | | ASC | | LSC | | PSC | | UTR | | SAC | | COCH | |
| | | | PM | HEM | PM | HEM | PM | HEM | PM | HEM | PM | HEM | PM | HEM | PM | HEM | PM | HEM | PM | HEM | PM | HEM | PM | HEM | PM | HEM |
| X | 12.2 | 8 | 0 | 0 | ++ | ++ | ++ | 0 | 0 | 0 | 0 | 0 | 0 | 0 | ++ | ++ | ++ | ++ | +++ | +++ | ++ | ++ | 0 | 0 | ++ | ++ |
| 2 | 18.3 | 7 | ++ | ++ | 0 | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | +++ | +++ | ++ | ++ | + | + | 0 | ++ | 0 | 0 | 0 | + |
| 3 | 18.3, 6.1 | 7 | ++ | + | 0 | 0 | + | 0 | 0 | 0 | + | 0 | + | 0 | +++ | +++ | ++ | ++ | +++ | +++ | + | + | 0 | 0 | ++ | + |
| 4 | 18.3 | 7 | * | * | * | * | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | ++ | ++ | ++ | ++ | ++ | ++ | 0 | +++ | 0 | 0 | + | + |
| 5 | Surface | 7 | ++ | +++ | +++ | +++ | ++ | ++ | 0 | ++ | 0 | 0 | +++ | + | ++ | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | 0 |
| 11 | 30.5 | 5 | ++ | + | +++ | +++ | +++ | 0 | ++ | 0 | + | 0 | ++ | 0 | +++ | 0 | +++ | + | +++ | 0 | 0 | + | 0 | 0 | + | 0 |
| 12 | 24.4 | 2 | * | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | + | +++ | 0 | +++ | + | +++ | 0 | 0 | 0 | 0 | 0 | ++ | 0 |
| 14 | Surface | 6 | + | + | + | +++ | + | ++ | ++ | 0 | 0 | 0 | ++ | 0 | +++ | +++ | +++ | +++ | +++ | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 20 | 42.7, 18.3 | 6 | ++ | +++ | +++ | +++ | +++ | +++ | ++ | ++ | 0 | ++ | 0 | +++ | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 28 | 34.9, 1.8 | 5 | +++ | + | +++ | 0 | ++ | 0 | + | 0 | + | + | ++ | ++ | +++ | + | +++ | ++ | +++ | ++ | + | + | 0 | 0 | +++ | + |
| 34 | Unknown | 24 | +++ | 0 | + | * | 0 | 0 | ++ | + | 0 | 0 | 0 | 0 | +++ | 0 | ++ | 0 | 0 | 0 | 0 | 0 | 0 | 0 | + | 0 |

Abbreviations and symbols: see Table 2. * Damaged structures during tissue preparation.

red blood cells were found in the vestibular endolymph. In the cochlea, tissue damage and hemorrhage were observed in the basal, middle, and apical turns in all scalae as a result of lesions to the spiral ligament, the blood vessels of the membranous walls, and the stria.

*Inner ear pathology in long-term postdive survival group.* The 11 monkeys in this group were allowed to survive for durations from 38 to 383 days following decompression (Table 4). Though seldom present, only occasional red blood cells (usually hemolyzed) were found, and then only in the perilymphatic vestibular system. The precipitated material was still present in abundance in the endolymphatic vestibular system, where large clumped globules were often evident on and within the cupulae (cf. Fig. 3, *E–G*). The perilymphatic vestibular system was essentially free of this material; and, in most cases, only traces of it were evident in the cochlear, utricular, and saccular regions of the inner ear. Compared to the other two groups, there appeared to be slightly less of the material in this long-term group.

The most surprising and undoubtedly the most important finding of the study was the appearance of connective tissue and new bone growth in tissue-damaged regions that were contiguous to the bony walls of the semicircular canals (Fig. 3, *B–D*). This occurred in 9 of the 11 monkeys in this long-term group. (The two remaining monkeys, which lacked new bone growth, had behavioral symptoms indicative of rather mild vestibular "hits.") The new bone growth gave the appearance of a condition that is termed fibroosseus labyrinthitis (57) and labeled FOL in Table 4. In the decompressed monkeys, this condition appears to start as an infiltration of the perilymphatic vestibular system with fibrous connective tissue about 1 mo after receiving a "serious" vestibular hit. *Monkey 8*, which was killed 38 days after a successful hit (Table 4), indicated such pathology along the arms of the right anterior semicircular canal (Fig. 3*B*). The inner ears in monkeys killed at longer intervals after the dive showed the progressive development of new bone with centers of ossification apparently emanating from the endosteal layer that lines the inner surface of the bony canal (Fig. 3, *C* and *D*). Gradually, the new bone growth develops its own blood supply (Fig. 3, *C* and *D*) and fills the perilymphatic spaces in the region in which the damage first occurred. In some ears, it is then confined locally by the endosteum and the membranous duct of the semicircular canal and spreads no further. In some ears, it fills the local perilymphatic space and also invades the endolymphatic space (Fig. 3*D*); and, in some, it is limited to the perilymphatic space but progressively spreads toward the ampulla and utricle (Fig. 2*D*). When the endolymphatic space is completely filled at any cross section in the semicircular canal, the canal becomes completely insensitive to angular accelerations. When the new bone growth encroached upon the ampullary perilymphatic space, it was observed that, in some instances, the sensory epithelium of the crista was thin and condensed (Fig. 2*D*; cf. Fig. 3, *E* and *F*), lacking hair cells, and that there was a paucity of nerve fibers in the crista. Such cristae were, of course, totally nonfunctional.

The location of new bone and connective tissue growth

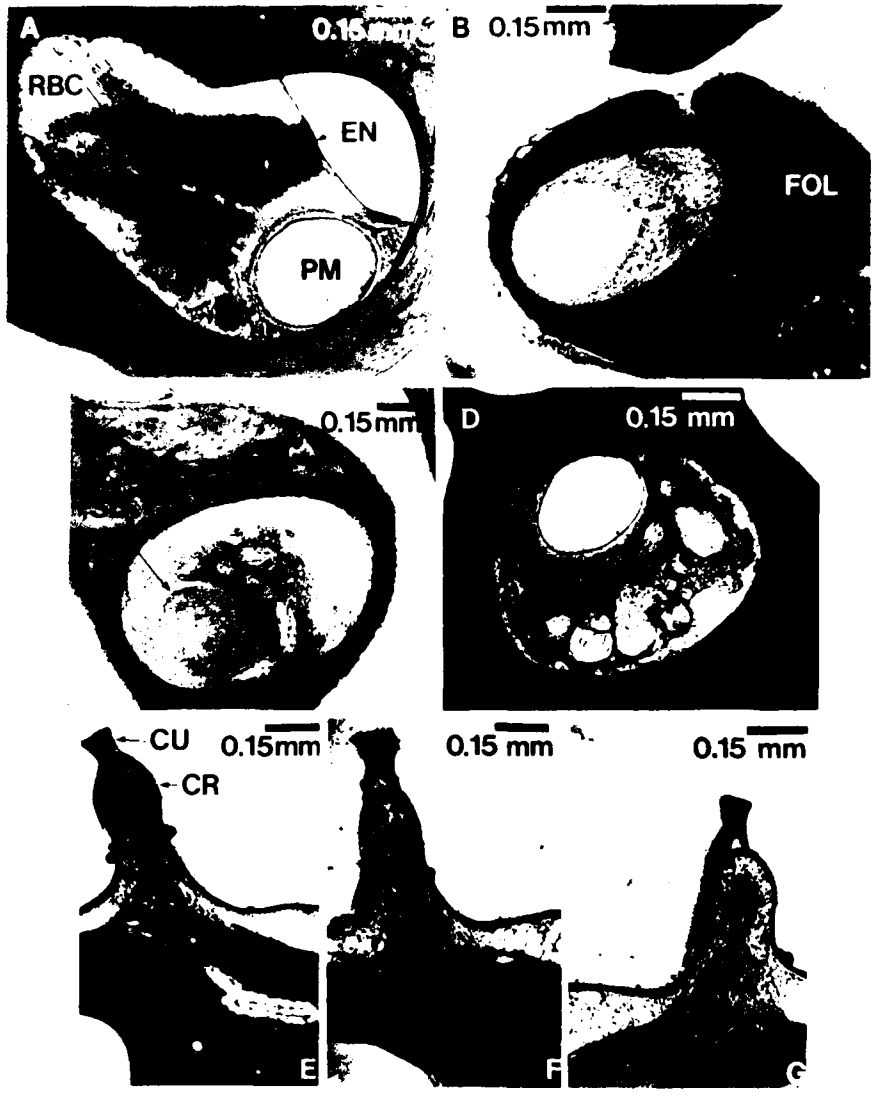


FIG. 3. Inner ear histopathology resulting from decompression sickness. *A*: hemorrhage (RBC) in perilymphatic space and precipitated material (PM) in endolymphatic space in left anterior semicircular canal in *monkey 20* (6 days postdive survival). Also identified are semicircular duct (SD) and partially detached endosteal layer (EN) of the semicircular canal. *B*: fibroosseous labyrinthitis (FOL) (mainly in the form of ectopic fibrosis) in perilymphatic space in right anterior semicircular canal in *monkey 8* (38 days postdive survival). *C*: FOL in both perilymphatic and endolymphatic spaces in right posterior semicircular canal in *monkey 51* (56 days postdive survival). New bone formation (*darker regions*) appears to originate from EN, SD and blood vessels (*arrow heads*) are also identified. *D*: highly vascularized FOL (mainly in the form of new bone growth), in perilymphatic space in left anterior semicircular canal in *monkey 68* (290 days postdive survival). *E*: normal crista ampullaris (CR) and cupula (CU) of lateral semicircular canal illustrating thick neuroepithelium. *F*: darkly stained X-shaped precipitated material within CU of CR in right lateral canal in *monkey 24* (379 days postdive survival). *G*: precipitated material on CR and CU, and within CU in left lateral canal in *monkey 24*. Note thin neuroepithelium.

in the vestibular apparatus provides an indication of a point of initial insult. Accordingly, Table 5 documents these results for both left and right labyrinths. Of pertinence are these findings: *1*) in some monkeys, only a single canal was damaged during decompression (right labyrinth in *monkeys 8, 33*, and *62*); *2*) in some monkeys, more than one canal was affected in the same labyrinth without any concomitant damage in the other labyrinth (right labyrinth in *monkeys 24* and *32*; left labyrinth in *monkeys 36* and *68*); *3*) in other monkeys, damage occurred in both labyrinths (*monkeys 51* and *52*); *4*) in three canals (2 in *monkey 36*; 1 in *monkey 51*), the endolymphatic space as well as the perilymphatic space were penetrated by new bone growth and fibrous connective tissue; and *5*) in four canals (2 in *monkey 36*; 2 in *monkey 68*), bone and connective tissue progressed beyond the initial area of insult in the canal to a degree that encroached on the membranous ampullae.

In the nine monkeys that showed fibroosseous labyrinthitis, 13 canals in right ears and 8 canals in left ears (7 anterior, 8 lateral, and 6 posterior) were affected (cf. hemorrhagic sites in the canals in Table 3).

TABLE 4. *Inner ear histopathology for long-term postdive survival times*

| Monkey | Depth of Hit on Ascent, msw | Postdive Survival Time, days | Left Side | | | | | | | | | | | | Right Side | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | | ASC | | LSC | | PSC | | UTR | | SAC | | COCH | | ASC | | LSC | | PSC | | UTR | | SAC | | COCH | |
| | | | PM | FOL | PM | FOL | PM | FOL | PM | FOL | PM | FOL | PM | FOL | PM | FOL | PM | FOL | PM | FOL | PM | FOL | PM | FOL | PM | FOL |
| 8 | 12.2 | 38 | +++ | 0 | + | 0 | ++ | 0 | 0 | 0 | + | 0 | + | 0 | +++ | ++ | ++ | 0 | + | 0 | ++ | 0 | 0 | 0 | + | 0 |
| 24 | 61.9 | 379 | ++ | 0 | +++ | 0 | + | 0 | 0 | 0 | + | 0 | 0 | 0 | +++ | ++ | ++ | ++ | + | + | + | 0 | 0 | 0 | ++ | 0 |
| 32 | 18.3, Surface | 211 | + | 0 | ++ | 0 | ++ | 0 | 0 | 0 | 0 | 0 | + | 0 | +++ | ++ | ++ | ++ | ++ | ++ | 0 | 0 | + | 0 | +++ | 0 |
| 33 | 6.1, 18.3 | 93 | + | 0 | + | 0 | ++ | 0 | 0 | 0 | + | 0 | + | 0 | +++ | ++ | ++ | ++ | ++ | 0 | 0 | 0 | ++ | 0 | + | 0 |
| 36 | 6.1, 18.3 | 184 | +++ | +++ | +++ | ++ | + | +++ | + | 0 | 0 | 0 | + | 0 | +++ | ++ | + | 0 | ++ | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 42 | 24.4 | 141 | + | 0 | +++ | 0 | ++ | 0 | 0 | 0 | 0 | 0 | + | 0 | 0 | 0 | 0 | 0 | ++ | 0 | + | 0 | 0 | 0 | ++ | 0 |
| 47 | 9.1, 30.5 | 108 | 0 | 0 | + | 0 | ++ | 0 | + | 0 | + | 0 | 0 | 0 | + | ++ | + | 0 | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| 51 | 12.2 | 56 | + | 0 | 0 | ++ | +++ | ++ | 0 | 0 | 0 | 0 | 0 | 0 | + | ++ | + | 0 | ++ | +++ | 0 | 0 | 0 | 0 | + | 0 |
| 52 | 36.6 | 126 | + | 0 | +++ | ++ | ++ | 0 | ++ | 0 | + | 0 | + | 0 | + | 0 | ++ | ++ | + | 0 | + | 0 | 0 | 0 | + | 0 |
| 62 | 24.4 | 383 | +++ | 0 | +++ | 0 | + | 0 | ++ | 0 | 0 | 0 | 0 | 0 | +++ | ++ | 0 | 0 | ++ | ++ | + | 0 | 0 | 0 | = | 0 |
| 68 | 30.5 | 290 | + | +++ | + | +++ | ++ | 0 | 0 | 0 | 0 | 0 | + | 0 | 0 | 0 | 0 | 0 | ++ | 0 | 0 | 0 | 0 | 0 | + | 0 |

Abbreviations: FOL, fibroosseous labyrinthitis; other abbreviations and symbols defined in Table 2.

Fibroosseous labyrinthitis never appeared in the cochlea and it entered the vestibule only occasionally, by spreading from the canals. Furthermore, except for one case with a distended Reisner's membrane and another with a detached stria vascularis in an apical turn, all cochlear structures appeared intact and functional, in spite of the obvious bleeding into cochlear perilymph that occasionally occurred. Moreover, a reduction in the number of cells or loss of cellularity was never indicated in either Scarpa's ganglion or the spiral ganglion.

*Electronystagmographic studies.* Monkeys that received discrete vestibular hits and were observed for spontaneous and positional nystagmus immediately after the dive invariably showed vigorous eye movements. In most cases, regardless of head position, the eyes beat constantly in the same direction [spontaneous nystagmus—see LBN (left-beating nystagmus) component in all head positions for the positional nystagmuses in Fig. 4*B*]. In a few monkeys, the nystagmus immediately after the dive was direction changing [e.g., DBN-UBN (downbeating nystagmus, upbeating nystagmus] components in the positional nystagmuses in Fig. 4, *A* and *B*). These positional or spontaneous nystagmuses usually disappeared after about 3 wk (Fig. 4*A*), but occasionally a residual nystagmus remained long after the decompression (e.g., DBN component to ND position, 126 days postdive in Fig. 4*B*).

Invariably, there was a partial or complete loss of response to postrotatory stimuli in the inner ear-damaged monkeys immediately after the dive and for several days afterward (Fig. 4, *A* and *B*). The postrotatory nystagmus was diminished in frequency, amplitude, and duration. There was partial or complete recovery as time passed; but, in some monkeys, a preponderance of nystagmus in certain directions remained. The postrotatory results in *monkeys 51* (Fig. 4*A*) and *52* (Fig. 4*B*) demonstrate these features.

In the case of *monkey 51*, at 5 days postdive, the postrotatory nystagmuses to horizontal rotations with head erect (as exemplified by the maximum velocity of the slow component of the nystagmoid beats) had de-

TABLE 5. *Distribution and appearance of new bone growth in specific semicircular canals in long-term postdive group*

| Monkey | Left Labyrinth | Right Labyrinth |
|---|---|---|
| 8 | | ASC(p) |
| 24 | | ASC(p), LSC(p), PSC(p) |
| 32 | | ASC(p), LSC(p), PSC(p) |
| 33 | | ASC(p) |
| 36 | ASC(e,p)*, LSC(p), PSC(e,p)* | |
| 51 | LSC(p), PSC(p) | ASC(p), LSC(p), PSC(e,p) |
| 52 | LSC(p) | LSC(p) |
| 62 | | PSC(p) |
| 68 | ASC(p)*, LSC(p)* | |
| Total no. of canals | 8 | 13 |

ASC, LSC, and PSC, anterior, lateral, and posterior semicircular canals; e and p, endolymphatic and perilymphatic spaces. * Ampullary and utricular perilymphatic spaces also encroached upon by new bone growth and fibrous connective tissue.

creased to 24% of their predive values. There was no improvement at the time of death, 56 days postdive. The perilymphatic spaces of the lateral semicircular canals in both labyrinths of this monkey were occluded with bone (Table 5), and this might have decreased the sensitivity of the canals either mechanically or chemically. No obvious neuroepithelial damage was evident in this monkey.

In response to rotations that stimulate the vertical canals (RSD and LSD in Fig. 4), the postrotatory nystagmuses, which were completely obliterated 5 days postdive in *monkey 51*, showed good recovery at the time of death. Interestingly, there was a 33% directional preponderance of UBN over DBN with RSD rotations. Directional preponderance was considered to be present if the maximum speeds of the slow components of the nystagmus from CW and CCW rotations differ by more than 20% (11). Directional preponderances as high as 45% were found in some monkeys in the long-term group. In *monkey 51*, there was extensive damage to the vertical semicircular canals.

The history of the postrotatory nystagmus in *monkey 52*, up to the time of death (126 days postdive), was similar to that of *monkey 51* (Fig. 4*B*). As in *monkey 51*, the perilymphatic spaces in both lateral canals of *monkey 52* were invaded by fibroosseous material (Table 5); and, in both monkeys, the level of nystagmus at the time of

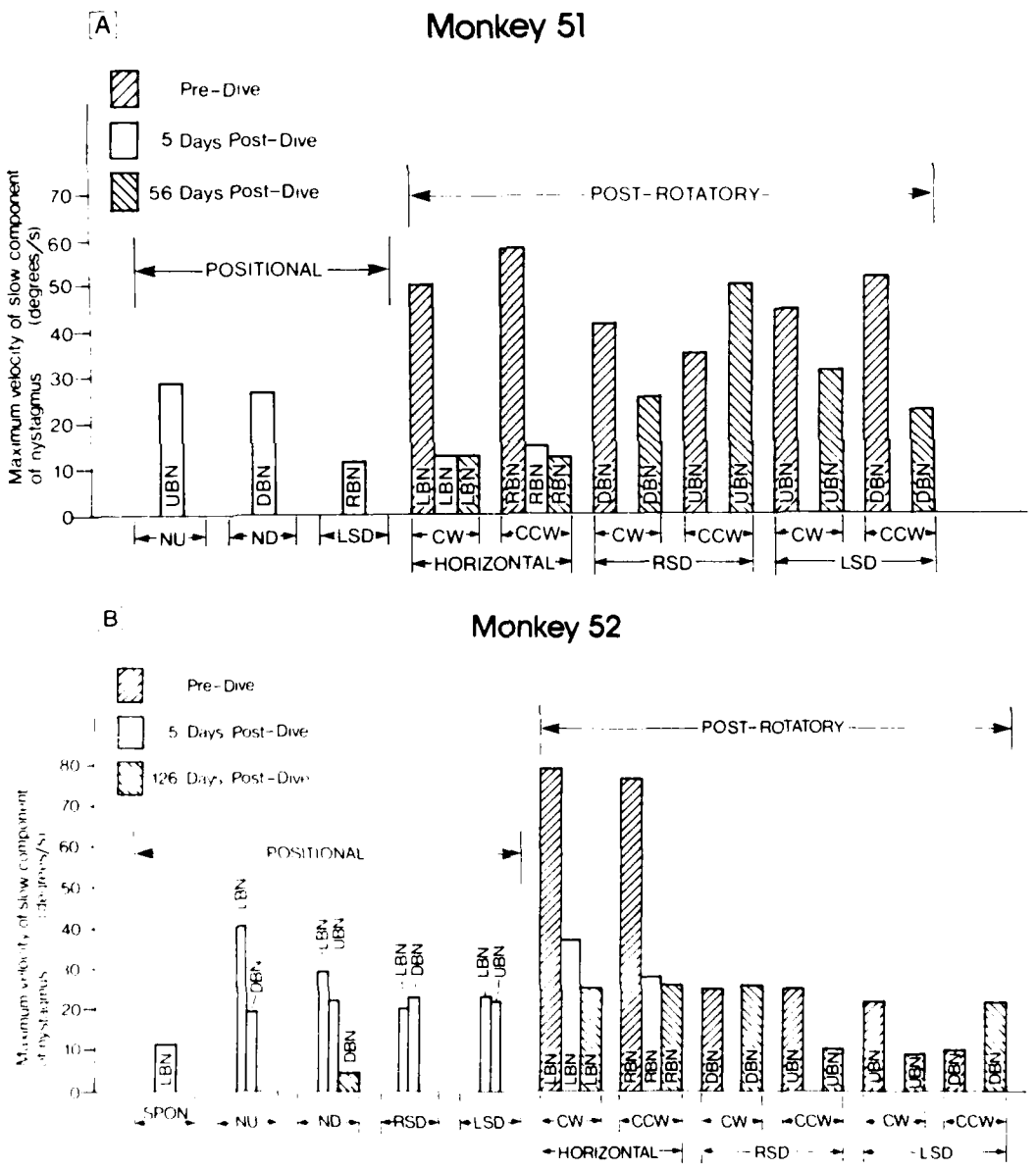


FIG. 4. *Bar graphs* illustrating composite electronystagmographic records in *monkey 51* (*A*) and *monkey 52* (*B*). UBN-DBN (up-beating and down-beating nystagmus) components are detected as vertical eye movements; LBN-RBN (left-beating and right-beating nystagmus) components as horizontal eye-movements. Horizontal refers to postrotatory nystagmus in head-erect (HE) position. Spon implies spontaneous nystagmus obtained during HE position. Other symbols are defined in text.

death was much reduced and was at essentially the same level as it had been immediately postdive (cf. Fig. 4, *A* and *B*). Again, in both monkeys, there was a complete absence of postrotatory nystagmus to vertical canal stimulation shortly after the dive, with essentially full recovery at the time of death. *Monkey 52* had a preponderance of up-beating nystagmus in one kind (LSD) of rotatory test before the dive, but it had a preponderance of down-beating nystagmus (44% and 42%) in both (LSD and RSD) tests after the dive.

*Control monkeys.* In many of the monkeys that suffered inner ear decompression damage, only one ear was affected, while the other ear was entirely normal and served as a control. However, it was thought wise to further control the histological findings by preparing 10 monkeys without any exposure at all to diving. These animals were used to determine whether or not the type of fixative or the myringotomy or both influenced the histological findings. Three of the monkeys were killed without myringotomy (2 formalin fixed, 1 Heidenhain-Susa fixed). The intervals from myringotomy to death in the remaining 7 monkeys were 0, 3 days (2 monkeys), 8 days, 9 days, and 60 days (2 monkeys). In these control animals, there was no new bone growth or invasion of connective tissue; only occasional red blood cells outside blood vessels were encountered. Precipitated material occurred somewhat less in frequency and amount and in different locations (e.g., only occasionally, and in traces, on the cupulae) compared with the dived monkeys. The intact monkeys were not noticeably different from the myringotomized monkeys.

*Brain histology in dived monkeys.* The postdive behavioral changes in posture and nystagmus were consistent with the anatomic damage revealed by histology and were readily explained by that damage; but it was nevertheless necessary to investigate the brains to ascertain whether any central lesions were contributing to the behavioral results. Serial sections of the brains of 22 representative animals, including some from each of the three groups, were independently studied in detail by a neuropathologist (N. B. Rewcastle).

Lesions were found in 7 of the 22 brains, and all 7 of those monkeys were short- or very short-term survival monkeys. Lesions in areas of the brain that are of importance to auditory or vestibular function were found in only two of the seven brains (both from the very short-term squirrel monkey group).

Only monkeys that were recognized behaviorally as having inner ear damage without apparent central lesions were assigned to the long-term survival group for extended study; and, in fact, none of these animals were found to have brain lesions. Apparently, with decompression sickness in squirrel monkeys, it is common to have discrete inner ear damage with no brain lesions, common to have death occur (presumably because of brain lesions), but unusual to have brain damage without obvious behavioral signs of it.

## DISCUSSION

Several conclusions can be drawn from this research. *1*) Compared with other bodily structures, the inner ear in the squirrel monkey is unusually susceptible to damage from decompression, as it is in humans. *2*) Vestibulocochlear disorders resulting from decompression are essentially of peripheral origin unless the CNS involvement is extensive and obvious. *3*) Cochlear disorders tend to be vascular lesions in any turn, mainly located in the stria vascularis and the spiral ligament. *4*) Vestibular lesions appear most frequently along the arms of the semicircular ducts. *5*) Vestibular lesions appear to be more permanent than cochlear lesions, since extensive slow fibrosis and new bone growth in the otic fluid spaces (principally along the arms of the semicircular ducts) are the normal sequelae to vestibular decompression damage.

Cochlear lesions are likely attributable to bubble formation and expansion with consequent blockage and or rupture of microvessels, causing hemorrhage or blood-protein exudation. Vestibular lesions may result from vascular blockage and rupture or from fluid shifts that cause tearing of the blood vessels supplying the semicircular ducts (which would also cause the sedimentary precipitated material to move within the ampulla and adhere to the cupula), or from both. The connective tissue formation and new bone growth in the semicircular canals are probably produced by osteoblasts that have differentiated in response to irritation or tearing of the endosteal layer that lines the surfaces of the semicircular canals. It is noteworthy that gross tissue damage is seldom produced in the nerve fibers, ganglia, or neuroepithelia of the inner ear.

A comparison of these findings to those of Chappe (9) is informative. Decompressing animals at rates from 0.13 to 10.01 msw/s, he determined that the severity of the inner ear lesion is contingent mainly on the speed of decompression. Rapid rates of decompression produced vascular lesions with extensive hemorrhaging; slow rates produced mild congestion of the intact blood vessels with associated "albuminous" exudation. Other observations included *1*) hemorrhaging into the interstices of the vestibular and cochlear nerves and their ganglia; *2*) endosteal hemorrhaging of the semicircular canals; *3*) congestion and/or hemorrhaging of the stria vascularis and the spiral ligament; *4*) hemorrhaging in the regions of the semicircular ducts; *5*) lesions in the secondary tympanic (round window) membrane; *6*) scattered blood clots in the endolymphatic and perilymphatic areas in different turns in the cochlea; and *7*) occasional destruction of the organ of Corti. Jensen et al. (25) have indicated that there is a critical decompression rate below which spontaneous nystagmus is not elicited. Both McCormick et al. (33, 34) and Long et al. (32) have reported hemorrhage in the scalae. Those observations are clearly similar to much of what is reported herein.

*Inner ear pathology resulting from microcirculatory changes in decompression.* The accepted theory for the cause of decompression illness is that inert gases (e.g., nitrogen and helium) come out of solution with decreasing pressure and form bubbles in the body tissues and bloodstream. Experiments using the techniques of Doppler ultrasonics have shown convincingly that intravascular bubbles do form during rapid decompression (43). It appears likely, then, that these bubbles "increase in

size in situ by the accretion of fresh gas from their surroundings" (22) and subsequently block the microcirculation of the inner ear, causing local hypoxia, tissue damage, and infarction. Under extreme conditions, during which the bubbles can grow without interference, tissue tearing with resultant hemorrhage can occur. Hill (22) indicates that bubbles occur more frequently in areas having slow circulation; e.g., bubbles are found more often in the white matter of the cervical cord (where the circulation is quite sluggish) than in the gray matter (which has good circulation). It seems likely, then, that regions such as the stria vascularis, in which the blood flow rate is very slow (despite the large number of vessels), would be particularly susceptible to bubble formation and growth in situ, with consequent blood vessel rupture and hemorrhage. Interestingly, localized blockage of any set of capillaries in the cochlea may be compensated for by increased flow in other sets of capillaries (since there are eight parallel capillary beds, one of which may have the bypass characteristics of an arteriovenous shunt mechanism). This may explain the discrete nature of the tissue damage found in the cochlea. Furthermore, such a mechanism might allow blood vessel blockage to persist for long periods of time, with the likelihood of causing damage to the endothelial cells of the capillary wall and other sequelae (see below).

Intravascular bubbles or blood rheologic factors (6, 12, 18, 36, 44–46) could lower the rate of blood flow and cause vascular stasis. Since the shear rates fall abruptly in the postcapillary segments and the venules, the apparent viscosity of the blood there will rise and cause it to become sluggish (10). Normally, movement of material between the vascular and extravascular spaces is controlled by a balance of the oncotic pressures (which move material between blood and tissue) and the hydrostatic pressures (which move blood and material within the vessels), according to Starling's law. However, if the venous ends become blocked and there is no collateral circulation (as appears to be especially likely in the auditory and vestibular apparatuses—see Ref. 21), then the hydrostatic pressures in the precapillary ends and the arterioles would increase over that found under normal conditions. Such an increase in pressure would result in the transudation of fluids and macromolecules (such as the blood plasma proteins) into the extravascular spaces there.

With prolonged blockage, the postcapillary segments and the venules would be deprived of oxygen, and the consequent endothelial cell deterioration would lead to increased vascular permeability and concomitant exudation of blood serum proteins into the extravascular spaces there. Zweifach (47), in studying the transcapillary fluid exchange during microocclusion experiments in single capillaries in the mesentery of the rabbit, found that there are "pores" or pathways between the endothelial cells through which whole plasma is filtered and exuded. He found this to occur most frequently on the venous side of the capillary network (and in the venules, which are known to be permeable to proteins). Interestingly, the microvascular leakage of protein that results from thermal injury or shock may be due to the action of one or more chemical mediators (possibly the kinins or prostaglandins—see Ref. 39). Should such a mechanism also be at work in the inner ear following rapid decompression, then the use of an appropriate inhibitor of whatever mediator causes the exudation might have value in decompression illness therapy.

Given the fact that precipitated material may appear in the otic fluid spaces without necessarily any evidence of hemorrhage, it follows that the transudation of plasma proteins from the arterial end of the capillary bed is a likely initial event. Should prolonged vascular stasis develop, then the exudation of protein resulting from a loss of endothelial cellularity (likely, at the venous ends) would become the major mechanism by which precipitated material enters into the otic fluid spaces (unless a blood vessel ruptures). Interestingly, McCormick et al. (33) concluded that the exudation of blood proteins is responsible for the precipitated material in the scalae of rapidly decompressed guinea pigs showing cochlear dysfunction.

The results herein, and other considerations, suggest that some of the precipitated material in the scalae and the vestibular perilymph was produced from a transudation-exudation of blood proteins resulting from blood stasis and/or blood vessel rupture that occurred during rapid decompression. The fact that some precipitated material is also present in the otic fluid spaces in control animals suggests that there are also other contributory factors involved. In this regard, vasoconstriction (possibly humoral) of vestibulocochlear vessels as a result of shock- or fright-related factors (e.g., the confinement of, handling of, and experimentation on normally feral monkeys) may also be a causative factor.

Temporal bone sections from patients with acoustic neuroma show a granular eosinophilic precipitate in the otic fluid spaces [e.g., see Fig. 2 in Silverstein and Schuknecht (42)] that is remarkably similar to the material reported herein. Silverstein's finding (40), that perilymphatic protein concentrations are as much as 15 times higher than normal in patients with acoustic neuroma, is also pertinent. Blood serum samples diluted to the same concentrations as in the otic fluids of these patients reveal an almost identical array of proteins in the two types of samples. This finding is consistent with what might occur if a slowly enlarging tumor progressively impairs the inner ear vessels and results in the leakage of blood serum proteins through their walls into the fluids. (The degenerated remnants of any sensory cells destroyed by the hypoxia resulting from circulatory interruption would also be present in endolymph.) Other studies show that experimental interruption of the inner ear blood supply is often characterized by a dense eosinophilic precipitate in the endolymph and perilymph in histological sections (24, 41). Likewise, biochemical analysis of the inner ear fluids from labyrinths in which the blood supply has been deliberately impaired shows a marked elevation of protein (41).

It might be mentioned that the likely reason why decompression illness results in precipitated material and hemorrhage in both the perilymph and endolymph spaces in the cochlea but only in the perilymphatic spaces of the vestibular apparatus is that there is a distinctly larger microcirculatory supply contiguous to the scalae

and vestibular perilymphatic spaces than there is in the vestibular endolymphatic spaces.

Though it is likely that bubbles originate intravascularly (4), the possibility that bubble formation may also occur extravascularly, e.g., in the otic fluid spaces, should not be discounted. Were this to happen, it seems plausible that such bubbles could cause the mechanically "soft" labyrinthine structures to shift relative to their bony counterparts with consequent tearing of the anchoring connective tissue matrix and possible blood vessel rupture and hemorrhage. Likewise, extravascular bubbles between rigid bone and the flexible blood vessels could compress arterioles, venules, and capillaries. This type of blockage in the venules would cause congestion and extravasation from the capillaries. This is particulary pertinent to the vestibular apparatus, in which some of the small vessels enter the vestibule through channels in the endosteal layer lining the semicircular canal, and shifts of the sort envisaged could cause tissue disruptions and hemorrhage with concomitant inner ear dysfunction. Such distortions might well "squeeze" the semicircular duct causing gross fluid shifts with resultant deposition on the cupula of the precipitated material that would normally lie as a sediment in the endolymph.

The cells lining the walls of the semicircular ducts play a major role in creating and maintaining the large differences in ionic concentrations of the endolymph and perilymph (endolymph 140–150 meq/l of $K^+$, 15–25 meq/l of $Na^+$; perilymph 5–8 meq/l of $K^+$, 140–150 meq/l of $Na^+$—see references in Ref. 35). Experiments have shown that, when the blood supply to the cells lining the walls of the ducts is blocked, the ionic concentrations in the endolymph and the perilymph will be equalized. Most of this diffusion occurs during the first 0.5 h of vascular interruption, and it is essentially complete after 1.5 h (15). A high-potassium concentration is essential for normal functioning of the hair cells; an increase in the endolymphatic sodium concentration will irreversibly damage them. However, should the endolymphatic potassium leak into the perilymph, then a continuous depolarization of the nerve would occur, effectively creating a nerve block, and thereby giving erroneous information to the CNS and causing severe symptoms of vertigo and nystagmus (14). (The invasion of blood and/or precipitate into the otic fluid spaces may also directly alter the otic fluid chemistry; this would give rise to physiologically altered inner ear function.) Interestingly, most monkeys suffering from decompression damage in the inner ear show a spontaneous nystagmus that allows the diagnosis of the inner ear hit. This spontaneous nystagmus begins suddenly during the decompression and may persist for one or more days.

The proliferation of fibrous and osseous tissue in the otic fluid spaces is not an uncommon sequela to certain types of labyrinthitis, e.g., the formation of new bone growth in the basal turn of the cochlea following meningococcal labyrinthitis (38). Interestingly, Igarashi *et al.* (24) found ectopic fibrous and osseous proliferation resulting from severe striad and spiral ligament pathology following artificial microembolism of the labyrinthine arterial system in the dog. The new bone formations appeared to originate from the periosteum (herein called endosteum) near the stria vascularis. Pertinent, also, is the observation by Kimura and Perlman (28) that arterial obstruction causes much more rapid and severe damage to the cochlea than does venous obstruction. Ectopic fibrosis and ossification were not evident in the cochlea even after 5 mo of venous obstruction, whereas destruction of arterial cochlear vessels was followed by complete ossification in 6 mo.

In a second study, Kimura and Perlman (27) reported that severe hemorrhage into the perilymphatic spaces of the vestibular apparatus only occurs after permanent venous obstruction, never after arterial obstruction. Hemorrhage into the semicircular canals occurred as early as 3 h after venous obstruction, followed by fibrosis of the perilymphatic space 2 wk later, and then varying degrees of ossification were observed up to 6 mo after venous obstruction (when the animals were killed for observation). The new bone formation started from the endosteum of the canal, developed toward the semicircular duct, and in some instances completely obliterated the endolymphatic space with or without noticeable changes in the crista. Ectopic fibrosis and ossification were not reported for the ampullae, utricle, or saccule. However, lesions to the end organs in both the cochlea and the vestibule were frequently observed. Clearly, many of the observations by Kimura and Perlman (27, 28) parallel those observed in this study.

In all likelihood, the initial event in discrete inner ear damage in decompression is interference by bubbles with venous drainage of the inner ear. Interference with arterial supply seems less likely considering the histological picture of the resulting damage, and also considering the likelihood of extensive central damage if bubbles were present in the arterial blood. Considering also the possibility of extravascular bubbles, venous obstruction would be more likely than arterial obstruction because of the lower pressure on the venous side.

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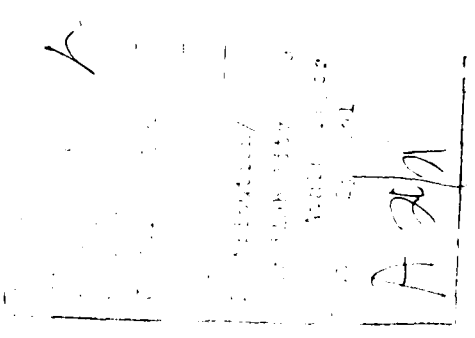

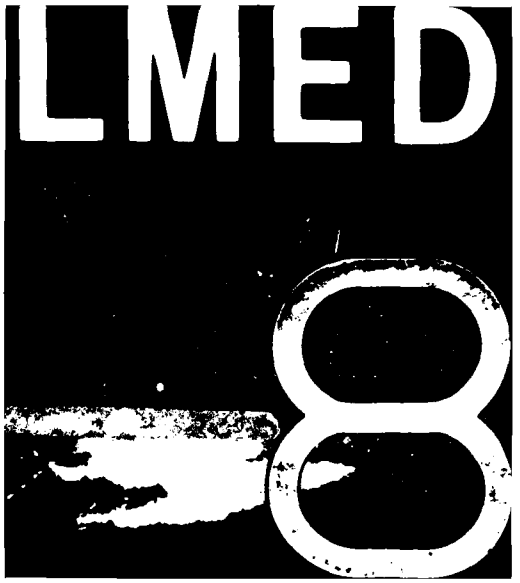
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8