Rethinking the Hit

By Andrea Zaferes

Reviewed by Bill Hamilton, Ph.D., and Karen Van Hoesen, MD

- Bubbles are not the only cause of damage. The immune response and its domino effect on blood chemistry changes may lead to further damage even after the bubbles are gone.
- The importance of early treatment. The longer you wait for DCS treatment the more blood chemistry changes you will have.
- How complement system activation may acclimate you to resist DCS.
- How the immune system response may cause injuries to the brain or lungs.
- Possible individual differences in susceptibility to DCS.
- Possible future tests and treatments for DCS.

Glossary of Medical Terms

Anaphylatoxin: A substance believed to be the cause of anaphylactic shock, which results as a reaction of an antibody to a specific foreign invader.

Antibody: A substance that reacts with an antigen.

Antigen: A substance that, as a result of coming in contact with appropriate antibodies, elicits an immune response, inducing a state of sensitivity and/or resistance to foreign invaders.

Basophil: A type of phagocytic white blood cell.

Blood brain barrier (BBB): A barrier believed to be made up of walls of capillaries that surround the brain's membranes. The barrier normally prevents many chemicals and disease-causing organisms in the blood from entering the central nervous system.

Complement system: The series of 20 proteins that aid T- and B-leukocytes in the immune system.

Complement activation: Activation of complement proteins by the immune system in response to foreign invaders

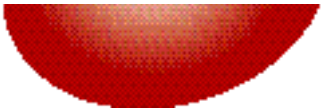
Endothelium: A layer of flat cells lining especially blood and lymphatic vessels and the heart.

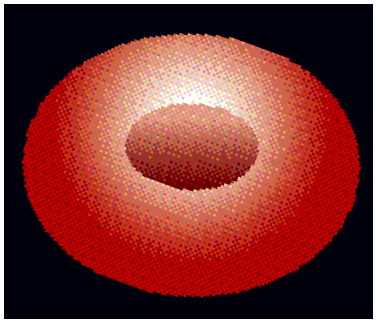
Erythrocytes: Red blood cells.

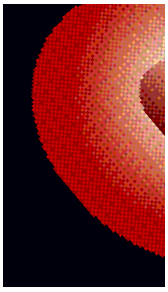
Granulocytes: White blood cells that mature into phagocytic cells, including neutrophils, eosinophils and basophils.

High-Pressure Nervous Syndrome: Changes in the electrical activity of the brain when divers are subjected to depths in excess of 600 feet / 183 meters on helium-oxygen mixes. Symptoms include tremors of the hands and jerky movements of the limbs, dizziness, nausea, decreased alertness and a tendency to sleep if the diver does not remain active. Symptoms can be controlled by using very slow descent rates and adding a small amount of nitrogen to the breathing mix.

Bubbles in the blood stream may cause the binding of red blood cells to proteins. Such a reaction results in a series of effects possibly leading to brain, spinal cord and/or lung injury.







Decompression sickness, or DCS, is no simple illness. Rather it is a conglomeration of symptoms that occur when gases dissolved in body fluids under pressure are released too rapidly, forming bubbles in tissues as well as in blood and lymphatic systems.

Injuries caused by the mechanical effects of the bubbles begin a cascade of factors producing greater tissue damage. These factors may be responsible for brain, spinal cord and lung injury not easily explained solely by mechanical damage from gas bubbles. Complement activation of the immune system may be responsible for some symptoms such as itching, pulmonary swelling, small blood vessel leakage, increased blood viscosity, clotting and much more.

The metaphor of a battlefield can be used to describe the human body's immune response. Foreign invaders, such as bacteria, cause the body to mobilize several defense strategies:

1. The invaders are sought out, recognized and destroyed by roaming soldiers. White blood cells, or leukocytes, such as phagocytic macrophages, granulocytes and monocytes, ingest the invaders.
2. Soldiers recognize the invaders, flag them, then go back to their base to help produce other soldiers trained to recognize invaders by their banners, or antigens. They target and destroy even more invaders. These trained soldiers, or antibodies, recognize specific invaders and point them out to the phagocytes.
3. Specially trained soldiers weaken the invaders by activating complement.

Histamine: A substance that increases the permeability of capillaries and blood vessels.

In vitro: In an artificial environment, referring to a process or reaction occurring in a test tube or culture media.

In vivo: In the living body, referring to a process or reaction occurring therein.

Interstitial: Spaces or interstices in the tissue structure.

Ischemia: Local anemia due to mechanical obstruction, mainly arterial narrowing, of the blood supply.

Leukocytes: White blood cells.

Lysosome: A cell particle containing enzymes capable of destroying the host cell or other cells when those cells need to be removed from the body.

Mast cells: Defense cells normally found outside of blood vessels that rush to invasion sites to release histamines that dilate the vessels, increasing local blood flow.

Macrophages: Large phagocytic cells that help ingest invading cells and alert other portions of the immune system to the invaders.

Monocytes: A relatively large cell that constitutes 3 to 7 percent of the white blood cells in circulating blood, which is normally found in the lymph nodes, spleen, bone marrow and loose connective tissue.

Myelin: The material enveloping nerve fibers.

Neutrophils: A phagocytic white blood cell formed by granulocytes.

Phagocytosis: The process of ingestion and digestion by phagocytes of bacteria, bits of dead tissue and foreign invaders.

Venules: Venula; Capillary vein; a minute vein.

4. Cells damaged by invaders send out distress signals, calling for more soldiers to come and fight the invaders, producing inflammation, complement activation and activating the clotting mechanism.
5. Cells widen the rivers of the blood system, the venules and capillaries, so more soldiers can rush to the site. Histamine dilates the venules and capillaries.
6. Cells in the attacked, damaged area can build fortresses of clots that serve to plug up holes to keep out additional invaders, decrease fluid loss and capture invaders for the arriving soldiers to destroy. The clotting mechanism is in full swing.

An introduction to these immune system functions will give you the necessary knowledge to comprehend how the system may respond to the possible effects of "invading" gas bubbles.

Immune System Organs

(*See "Immune System Organs" diagram to the right*)

Bone Marrow: The "stem cell" originates in the bone marrow. It is the origin of all other types of blood cells, which comprise the immune system's defense network. Stem cells mature in different parts of the body, depending on which type of blood cell they mature into. It is presumed that B-cells reside in bone marrow after maturing.

Thymus: Stem cells that migrate from the bone marrow to the thymus mature into T-cells. Mature T-cells then go from the thymus to the spleen and the lymph nodes.

Lungs: The lungs filter out diseases and prevent them from entering the body via the gas we breathe, and filter bubbles from the blood passing through them.

Spleen: The spleen is home to T-cells, B-cells and macrophages, the white blood cells that kill and eat dead cells and foreign cells marked by other immune system cells. Blood and lymphatic fluid that flows through the spleen are cleane of foreign matter, such as infectious cells and dead cells.

Intestines: Parts of the intestines, known as Peyer's Patches are part of the Retriculoendothelial System, which includes cells in spleen, liver, lymph nodes, bone marrow, lungs and intestines responsible for cleaning the blood of foreign matter. Macrophages within these patches eat bacteria, old blood cells and foreign particles.

Liver: The liver cleans the blood of infectious cells, dead cells, and foreign matter.

Tonsils: Act as filters for disease organisms trying to enter the body through the mouth.

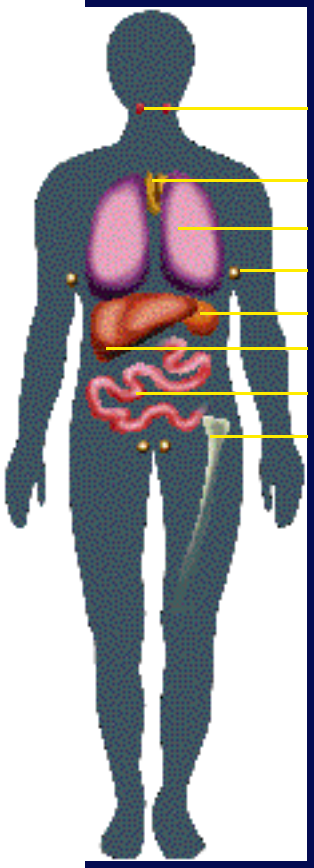
Lymph nodes: A reservoir of B-cells and T-cells, which are deployed when foreign cells are detected.

Blood Cell Production

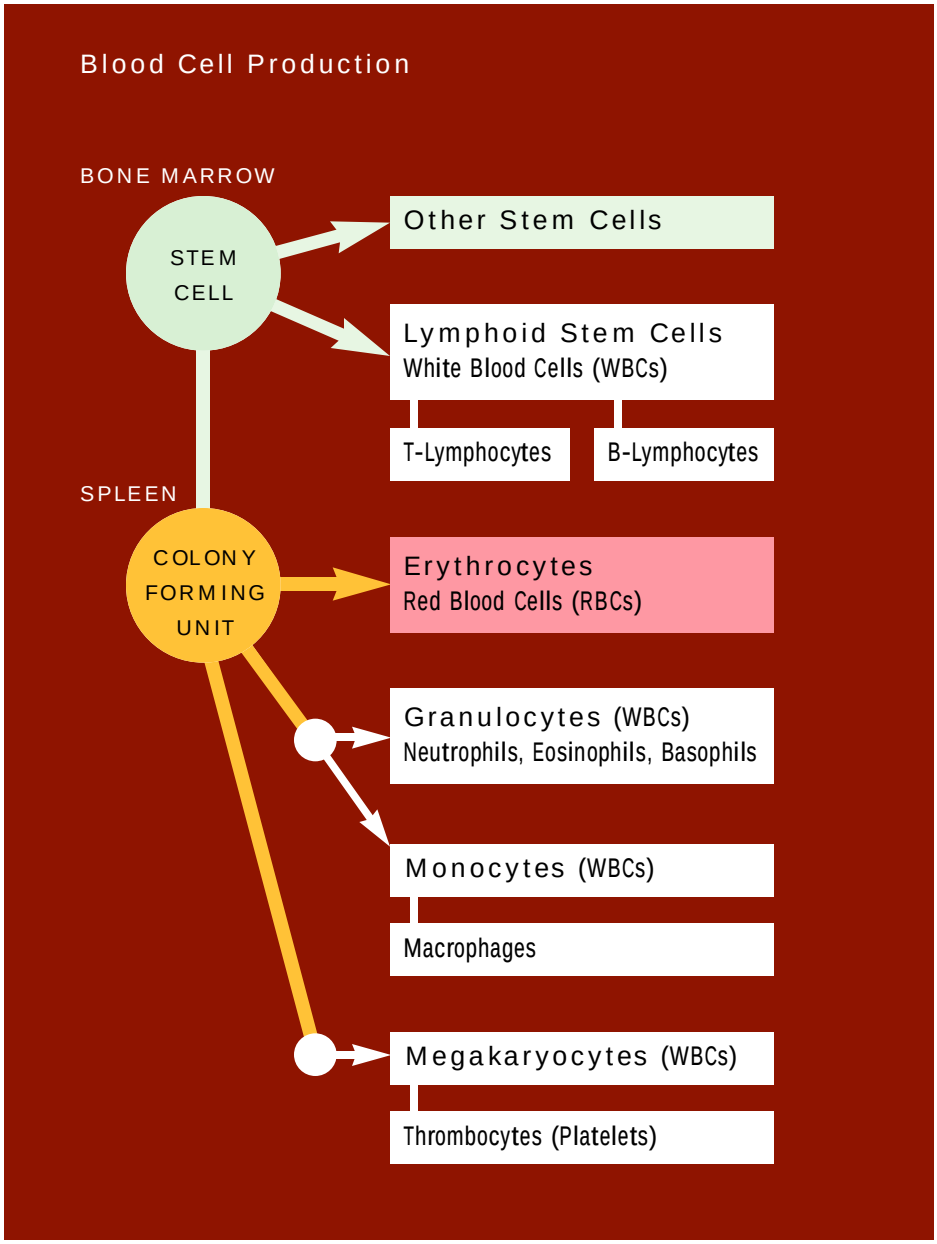
(*See "Blood Cell Production" diagram on opposite page*)

All cells in the blood originate from the bone marrow's pluripotential hemopoietic stem cells. PHSCs form all types of blood cells, including:

1. More PHSCs, which are retained in the bone marrow.
2. Lymphoid stem cells that form the white blood cells T-lymphocytes and B-lymphocytes.
3. Colony forming unit-spleen cells. These ultimately differentiate into:
   A. Red blood cells called erythrocytes.
   B. White blood cells called granulocytes that further differentiate into such phagocytic cells as neutrophils and monocytes. These go on to become phagocytic macrophages.
   C. White blood cells called megakaryocytes that fragment into platelets, or thrombocytes.



White blood cells, or leukocytes, are the mobile defense cells that circulate in both the blood and the lymphatic systems. Leukocytes seek out areas of inflammation, which are the damaged battle zones. Granulocytes live



for four to eight hours in circulating blood and for four to five days in the tissues. Monocytes live for 10 to 20 hours in the blood, but when they reach the tissues, they can swell up to five times their size and become macrophages, which can live for months and even years. Macrophages can grow to 80 micrometers, large enough to be seen by the naked eye.

Lymphocytes pass from the drainage of lymph nodes into the circulatory system, and return to the tissues a few hours later. Lymphocytes repeat this journey for months or sometimes years. Platelets are replaced every 10 days by the production of 30,000 platelets formed every day for each microliter of blood. Each microliter of blood normally contains about 300,000 platelets.

The Humoral Immune Response

(*see "Humoral Immune Response" diagram on page 29*)

Soldiers arrive, destroy the invaders and reproduce to continue the fight. The body has soldiers born to recognize antigens, or the flags carried by foreign invaders. The soldiers are Y-shaped proteins called antibodies. Antibodies are immunoglobins, which are produced by B-lymphocytes, or B-cells.

Specific antibodies react to the antigen's 3-D shape and electrical charges and can use their Y-shaped locks to clump the foreign invaders together. Two antibodies of the IgG type can activate the complement system. Both processes serve to attract and aid the white blood cells, phagocytic neutrophils and macrophages. Phagocytes ingest and destroy the invaders and further stimulate the immune system process.

The phagocytes recognize the antigen-antibody complex and sticks it to its surface. Phagocytosis, or ingestion, of the complex follows. The lysosome, inside the macrophage, releases digestive enzymes that destroy the invader.

The macrophage frees the antigens and pushes them to its plasma membrane where the antigens again serve as flags alerting the immune system. The macrophages travel with their antigen flags throughout the body. When they reach the B-lymphocyte-filled lymph nodes, the B-cells that recognize the specific antigen bind their antibodies to it. This stimulates the B-cells to divide and form clone cells with the aid of T-lymphocytes, creating more antibodies targeted to a specific antigen. This flood of antibodies into the blood is the primary immune response. The second time an antigen invades the body, it responds more quickly since it already has developed antibodies. This is the secondary immune response.

Complement Activation

There are 20 different proteins in the complement system, which bind to cells flagged by the antibody. The 11 most important proteins, labeled C1 to C9, B and D, are present in blood plasma and the plasma that leaks from capillaries into tissues. Normally inactive, these proteins are activated by classical and

alternative pathways (*See "Classical Pathway, Alternative Pathway, and Complement Activation" diagram to the right*"). The classical pathway is activated by an antigen-antibody reaction. A part of the antigen-antibody complex binds with C1, which begins a cascade of complement activation reactions such as the following:

Two IgG antibodies are held together by a C1 protein. Part of C1, called C1s, splits into C2 and C4. C2 and C4 bind to the invader, resulting in the splitting of C3. C5 then joins C2, C3, C4. These four complement enzymes attract C6 and C7. C5 then moves to a new place on the invader taking C6 and C7 with it. C8 and C9 join the C5 group and form a ring that eats through the invader's tough membrane, destroying the invader. The activation of C1 thus results in a large increase in enzymes that help prevent damage by the invaders.

Alternative pathway activation occurs without the antibody-antigen reaction when the invader provides a suitable complement activation site, for example, in red blood cells. Shastri, Logue and Lundgren (1991) found increased complement activation when red blood cells were present. The nitrogen bubbles caused the binding of C3 complement to the blood cells. Thus, the quantity of C3 bound in these cells could measure the degree of complement activation by nitrogen bubbles in decompressing divers.

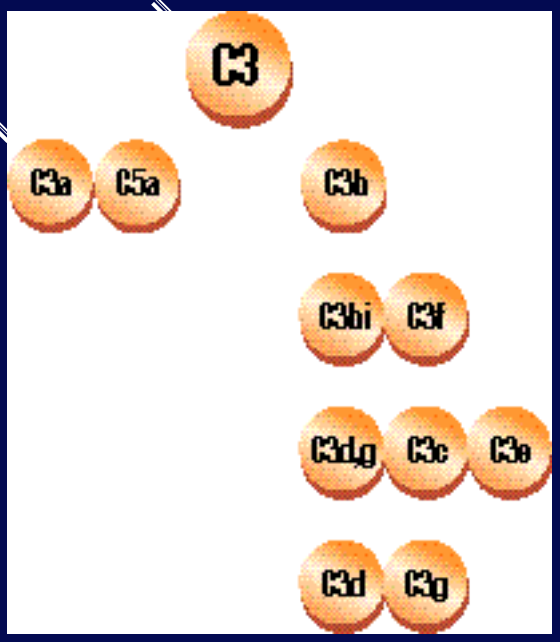
Complement fragments stimulate phagocytic cells, components of the blood that ingest invaders by rupturing their membranes. Stimulated phagocytes migrate to other areas seeking invaders. Some fragments change the invaders' surfaces causing them to stick together, while others neutralize the invaders. Mast cells, defense cells normally found outside blood vessels, rush to invasion sites to release histamines that dilate the vessels, increasing local blood flow, or inflammation. Dilation of the veins

Classical Pathway, Alternative Pathway, and Complement Activation

- An immune response triggered by bacteria or other invader flagged with antigens activates the CLASSICAL PATHWAY.

- An immune response triggered by an injury, such as a cut or the formation of bubbles, where no antigens are present activates the ALTERNATIVE PATHWAY.

- Both pathways lead to responses creating a suitable complement activation site, activating the key complement protein C3 and subsequent fragments and attractions.



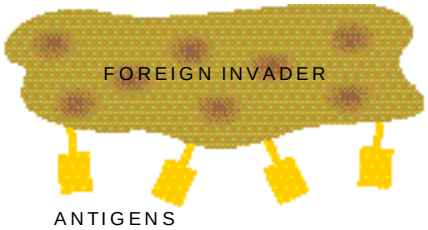
- The above cascade of various proteins results in inflammation and capillary damage, which could play a significant role in the DCS process.

- The proteins in this cascade are just one example of many combinations and types of proteins fragmented and attracted by complement activation.

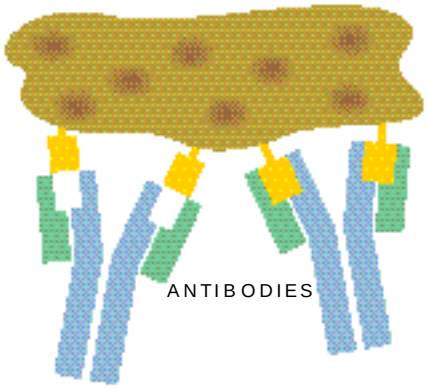
◄ The differentiation between the classical and alternative pathway is important. It is the knowledge of the classical pathway that lead to vacines, which are injections of antigens, designed to create and memorize a certain immune response. Research will try to discover if the immune system reacts differently to different gases. An indication of different responses may mean that the classical pathway is being activated. Could this lead to possible vacinations for DCS?

✎ Marked proteins. By testing for the quantity of marked proteins found in the blood after a complement activation, researchers can evaluate the severity of the immune system reponse that has taken place.

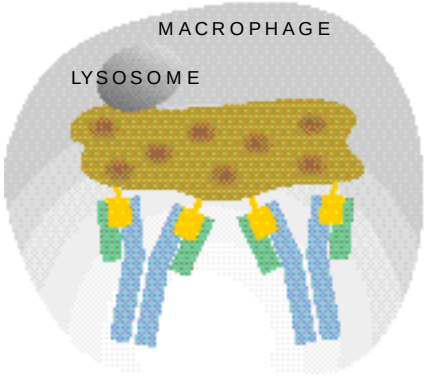
Humoral Immune Response



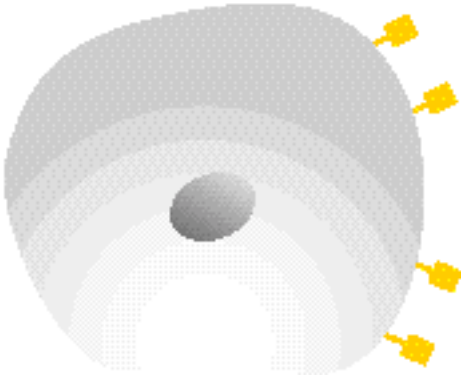
A foreign invader's antigens alert the body's immune system.



Antibodies, "Y" shaped proteins called immunoglobins that are produced by B-lymphocytes, recognize and attach to the antigens.



Phagocytosis: Macrophages recognize and surround the antigen/antibody complex. The macrophage's lysosome releases digestive enzymes that destroy the invader.



The macrophage frees the antigens and pushes them to its surface where they serve as a flag, signaling the immune response and aiding in the recognition of the next invader.

ILLUSTRATION: MING-YEN TUNG

and capillaries also leads to leakage of proteins that coagulate, trapping invaders in the local tissue sites.

Research in the past decade suggests that complement activation and the resultant inflammation and capillary damage could play a role in the DCS process.

Inflammation

Inflammation is a series of changes that tissues go through as a result of injury. (*See "The Effects of Immune Response to Bubbles" diagram on pages 32-33.*)

1. The complement reactions and damaged tissue attract mast cells, which are normally found on the outside of blood vessels, under the skin and in connective tissue. Mast cells release histamine, which increases blood flow to the tissues by dilating venules and capillaries.
2. Products of inflammation, such as histamine, make capillaries' interior walls, or endothelium, sticky. Neutrophils, the phagocytic white blood cells formed from granulocytes, stick to the capillary walls in a process called margination. Margination causes the endothelium cells to separate from each other. It is interesting to note that hyperbaric oxygen reduces neutrophil adherence to the interior walls of venules in tissue that is becoming anemic due to blockage by bubbles. It also reduces the delivery of leukocytes and neutrophils to the area.
3. The separated endothelium cells increase capillary wall permeability, allowing fluid, leukocytes and clotting molecules to leak out of the blood vessels into the interstitial space of the damaged tissue. This increases fluid and clotting in the damaged area.
4. Clotting begins when a blood vessel wall is damaged. The injured

cells release substances that attract platelets. The injury exposes collagen, a protein made of bundles of tiny fibers that form connective tissue. Platelets contact the collagen and disintegrate, forming a temporary plug in the injured vessel. Platelets release serotonin, which constricts the vessel. This decreases blood loss and flow, while barricading foreign invaders from the site. Two results of the clotting process are pain and further swelling.

5. Histamine, serotonin and bradykinin could temporarily increase barrier permeability, while complement activation could play a role in destruction of the sheath around nerve fibers, or myelin. Myelin destruction results in nerve damage.
6. Inflamed tissue releases substances that cause chemotaxis, the chemical attraction of neutrophils and macrophages that attack the invaders in the inflamed area. Some of these substances are complement activation products, products of the damaged tissues and products of the clotting mechanism.

Neutrophils invade the inflamed area in about an hour, but macrophages can provide aid within minutes, since they are already present in nearby tissues. Recompression treatment with hyperbaric oxygen within the first two hours of DCS manifestation may help prevent or decrease the blood chemistry changes, thereby decreasing the additional tissue damage.

How Bubbles Affect Proteins

(See "Denaturization" diagram below)

Complement activation caused by the blood-DCS-bubble interaction may be due to the modification of blood proteins that occurs at the blood-gas interface, where electrochemical forces denaturize proteins, or cause them to change their shape and electrochemical nature. Hydrophilic portions of the protein molecules are drawn away from the gas bubble, while the hydrophobic portions are drawn to the bubble. When this denaturized protein molecule comes into contact with cell membranes, it could result in the accumulation of globules of free fats and the release of fatty acids from cell membranes and subsequently form fat emboli, which could cause further damage.

Remote Damage

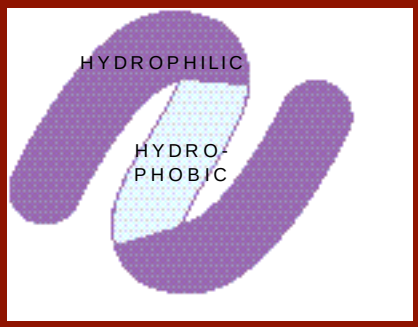
Complement activation damage can occur in tissues remote to local bubble sites. This damage can occur even after DCS bubbles have disappeared, which may explain delayed DCS symptoms. Individuals with greater sensitivity to complement activation may be at greater risk for DCS manifestation and/or more severe DCS injury. Some of these injuries might not even be fully treatable by hyperbaric oxygen. Someday, research might result in tests for physiological decompression stress when DCS symptoms are not apparent, as well as tests for discovering which divers are at greater risk for DCS.

Immune system reactions to decompression bubbles result in further disruption of blood flowing to the site, leading to tissue damage and cell death at the site and in more remote sites because of impaired circulation. Such damage may have its greatest effect in the central nervous system, where even small decreases in circulation can result in serious problems.

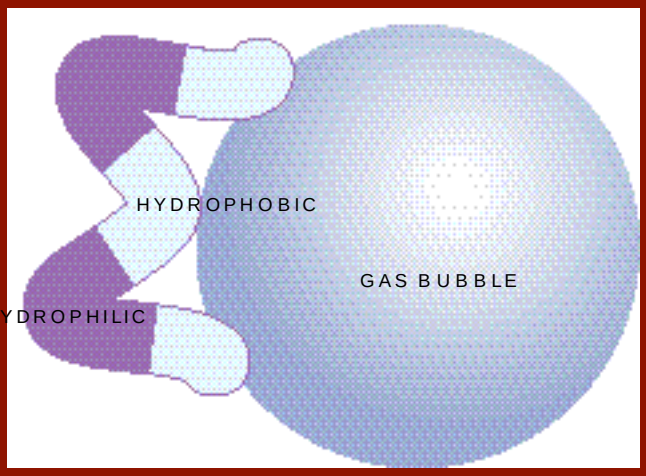
How Bubbles Affect Proteins — Denaturization

A protein molecule is made up of hydrophilic sections which are attracted to fluid, and hydrophobic sections which are attracted to gas.

NORMAL: When in blood the protein molecule's hydrophobic sections are surrounded by its hydrophilic sections which are in contact with the surrounding fluid.



FLUID

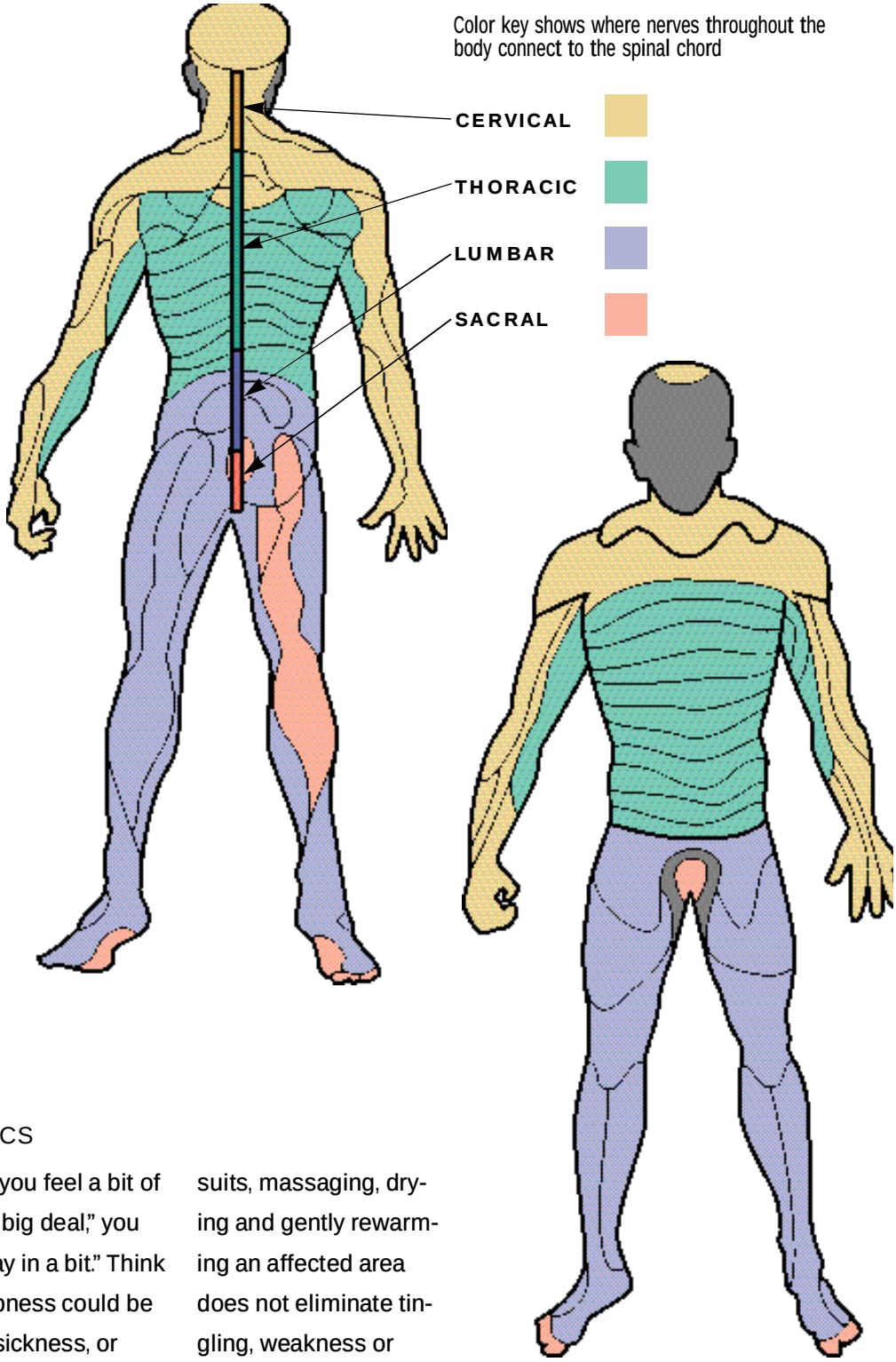


DENATURED: When the protein molecule comes in contact with a gas bubble it becomes denatured. Its shape and electrochemical nature is changed: the hydrophobic sections of the molecule come in contact with the gas whereas the hydrophilic sections move in the opposite direction to remain in contact with the fluid.

This, in turn, adds only more weight to the need for more research in the emerging field of diving medicine and biochemistry.

Leakage of fluids through capillary walls increases hemoconcentration, or the percentage of cells in blood, and is thought to contribute to DCS shock. This means an increased blood viscosity with less fluid circulating in the blood, since only blood fluid, not blood cells, leak through the damaged capillary walls. Increased hemoconcentration is manifested in both arterial gas embolism and DCS. And in the case of arterial gas embolism, it is correlated with the eventual neurologic outcome.

The capillary permeability increase could explain clinical features of DCS that are less likely to result from vascular blockage. For example, the loss of plasma from capillaries may significantly increase hemoconcentration and shock following DCS. This, in a less serious form, is probably the cause of "inappropriate fatigue," a symptom of DCS. It also helps to underscore the need to avoid dehydration, and explains why rehydration often improves DCS during treatment.

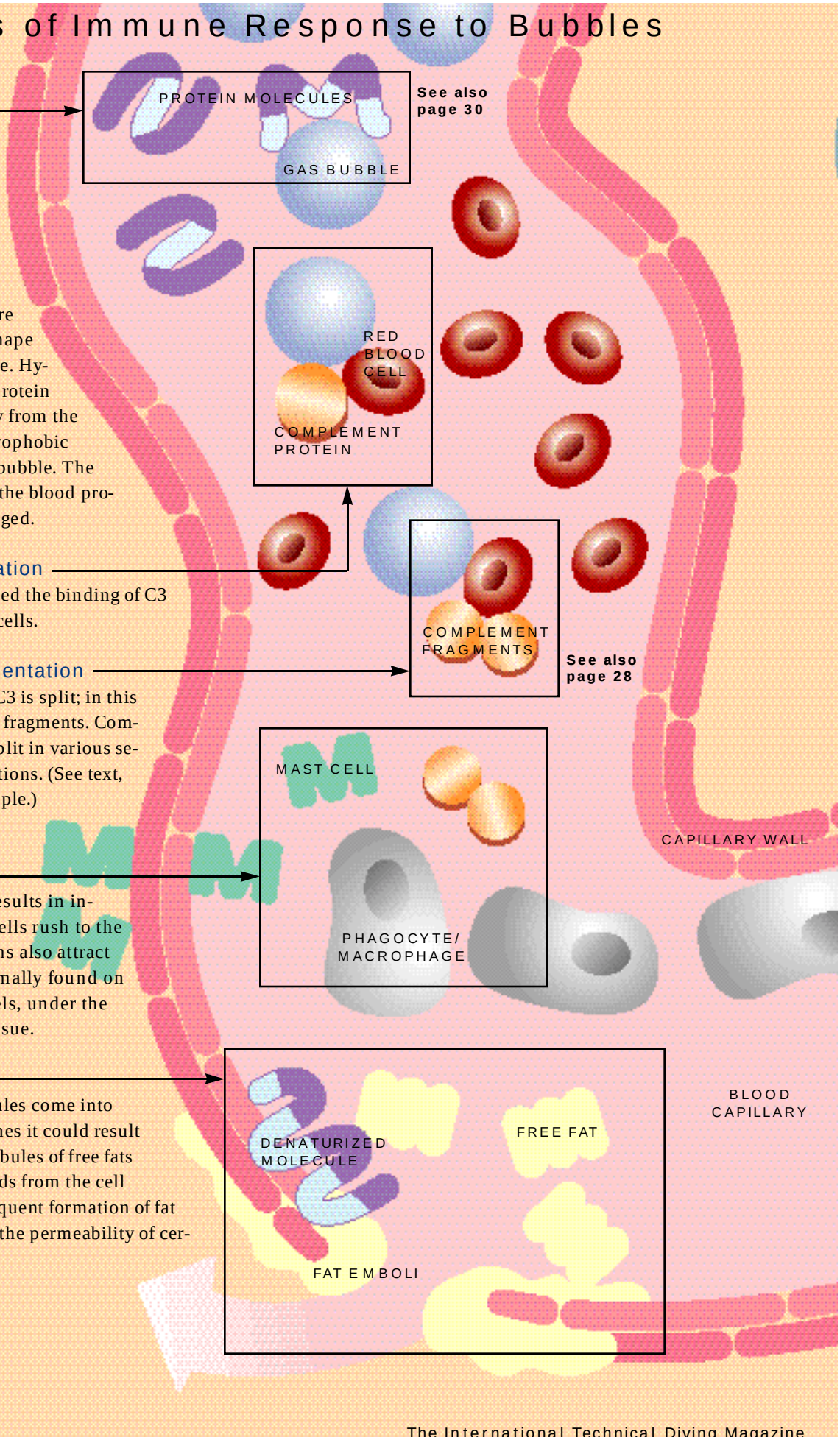


FIELD NEUROMAN

There's nothing too mild about DCS

It's been a few hours after a dive, and you feel a bit of a tingling sensation in your pinky. "No big deal," you think. "It's just a 'skin' hit that'll go away in a bit." Think again. Any tingling, weakness or numbness could be a symptom of type II decompression sickness, or DCS, that affects the neurological and/or cardiorespiratory systems. Nerves going to your pinky, for example, join the spinal cord in the neck, so tingling in your little finger could be the first sign of neurological damage that could progress to full paralysis from the neck down. Never ignore even subtle problems. If removing such circulatory obstructions as straps and suits, massaging, drying and gently rewarming an affected area does not eliminate tingling, weakness or numbness within five minutes, the possibility of DCS should be investigated and treated. Denying these symptoms could do more than just end your diving career. It could end your ability to walk, have sex or even think clearly.

The Effects of Immune Response to Bubbles



1. Denaturization

Complement activation caused by the blood-DCS-bubble interaction may be due to the modification of blood proteins that occurs at the blood-gas interface, where electrochemical forces denature proteins, changing their shape and electrochemical nature. Hydrophilic portions of the protein molecules are drawn away from the gas bubble, while the hydrophobic portions are drawn to the bubble. The electrochemical nature of the blood protein molecule is now changed.

2. Complement Activation

The nitrogen bubbles caused the binding of C3 complement to the blood cells.

3. Complement fragmentation

The complement protein C3 is split; in this example into C3a and C5a fragments. Complement proteins can be split in various series of complex fragmentations. (See text, page 28, for another example.)

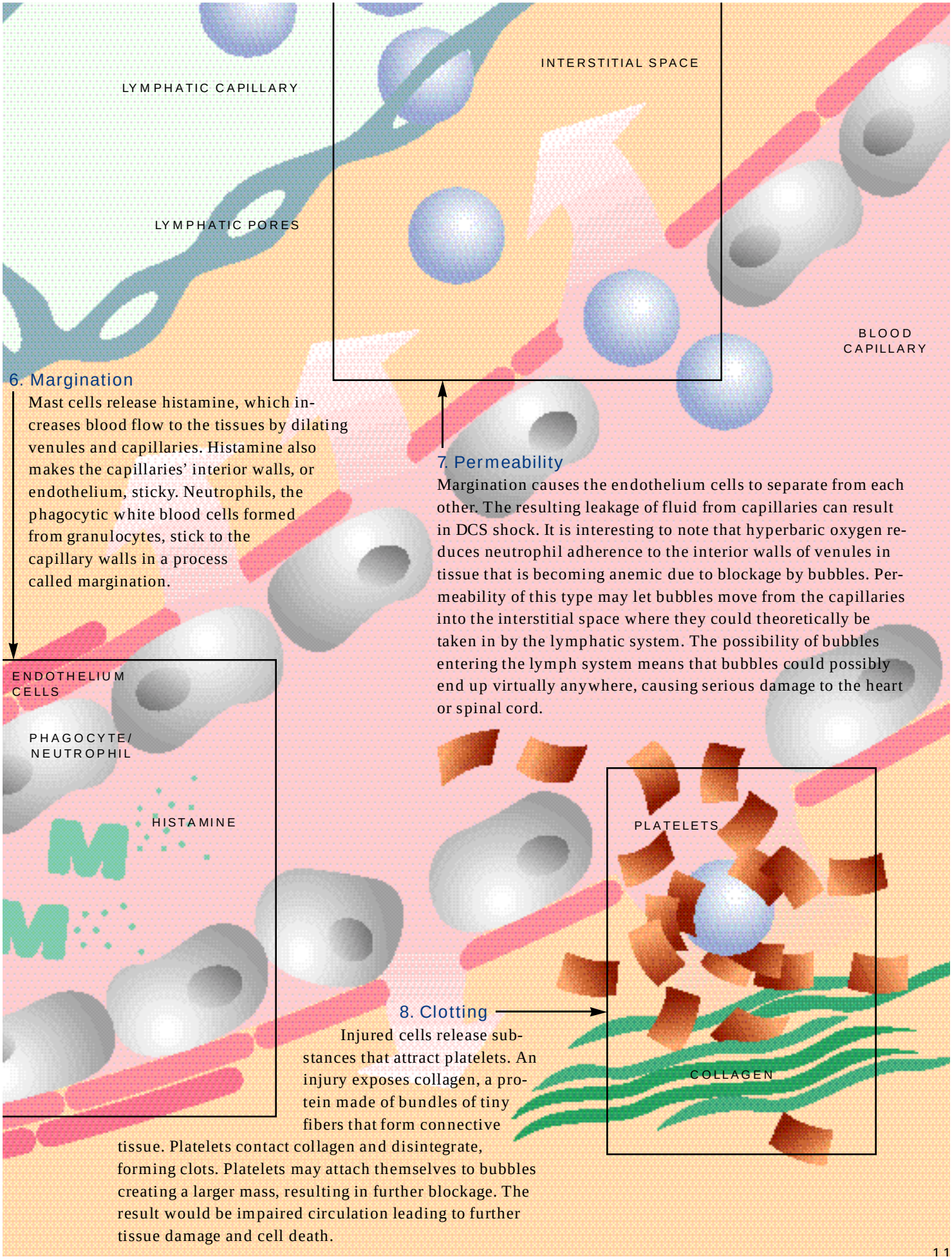
4. Stimulation of the immune response

Complement activation results in inflammation. Phagocytic cells rush to the site. Complement reactions also attract mast cells, which are normally found on the outside of blood vessels, under the skin and in connective tissue.

5. Permeability

When denaturized molecules come into contact with cell membranes it could result in the accumulation of globules of free fats and the release of fatty acids from the cell membranes and the subsequent formation of fat emboli. This can increase the permeability of certain barriers.

DIAGRAM/ILLUSTRATION:
DUVAN HOFFMANN AND MING-YEN TUNG



6. Margination

Mast cells release histamine, which increases blood flow to the tissues by dilating venules and capillaries. Histamine also makes the capillaries' interior walls, or endothelium, sticky. Neutrophils, the phagocytic white blood cells formed from granulocytes, stick to the capillary walls in a process called margination.

7. Permeability

Margination causes the endothelium cells to separate from each other. The resulting leakage of fluid from capillaries can result in DCS shock. It is interesting to note that hyperbaric oxygen reduces neutrophil adherence to the interior walls of venules in tissue that is becoming anemic due to blockage by bubbles. Permeability of this type may let bubbles move from the capillaries into the interstitial space where they could theoretically be taken in by the lymphatic system. The possibility of bubbles entering the lymph system means that bubbles could possibly end up virtually anywhere, causing serious damage to the heart or spinal cord.

8. Clotting

Injured cells release substances that attract platelets. An injury exposes collagen, a protein made of bundles of tiny fibers that form connective tissue. Platelets contact collagen and disintegrate, forming clots. Platelets may attach themselves to bubbles creating a larger mass, resulting in further blockage. The result would be impaired circulation leading to further tissue damage and cell death.

Bubbles on the Move

Blood consists of plasma, a clear, watery fluid that contains red blood cells, white blood cells, protein molecules, glucose, platelets and other molecules and cells. Plasma carrying oxygen and nutrients passes through capillary walls to the interstitial space to supply cells with these vital molecules. Large protein molecules and red blood cells do not normally pass through to the interstitial space unless the capillary wall permeability is increased by such processes as complement activation or physical damage (*See "The Effects of Immune Response to Bubbles"*).

Such increased permeability may allow bubbles into interstitial spaces. Bubbles that enter or form in interstitial spaces are too large to be re-absorbed by the blood capillary are possibly removed by the lymphatic capillaries, which are found in almost all tissues. Theoretically if bubbles were to get into the lymph system they could end up almost anywhere, in more dangerous areas such as the heart or spinal cord, possibly causing even more serious injuries.

Let us consider gas bubbles' effect on the blood-brain barrier or the blood-lung barrier, which prevent certain substances from entering these organs. Denaturized proteins result in the release of fatty acids, increasing the permeability of these barriers and allowing harmful molecules to enter these organs. Increased permeability of the blood-brain barrier can result in focal swelling and possibly the cerebral features of DCS, changes in cerebral blood vessels and spinal cord myelin and axon damage.

Hills & James demonstrated in 1991, that micro DCS bubbles increase blood-brain barrier permeability, resulting in local swelling and possibly the cerebral features of DCS, changes in cerebral blood vessels and spinal cord myelin and axon damage.

Skin biopsies of swine inflicted with skin DCS showed leukocyte-mediated inflammation. Neutrophils were found adhered to blood vessel walls, causing congestion. The authors concluded that the skin lesions may reflect similar changes in the vasculature of the spinal cord and other target organs of DCS. White blood cells may thus be an important indicator in decompression sickness.

Early Treatment

As technical diving extends the recreational diving limits with deeper and/or longer duration dives, knowledge of the complexity of DCS becomes increasingly important. Participants frequently pursue the sport without the surface support, equipment and lengthy training available to commercial and military divers. Technical divers must understand the risks of not having surface support equipment such as on site recompression chambers and diving medical offices.

The longer you wait for treatment the more blood chemistry changes you will have due to the immune response. It is important to seek treatment in less than two hours from DCS manifestation. An understanding of immune response to DCS may lead to the development of better industry mechanisms to achieve immediate treatment.

Acclimatization; a possibility warranting further research

Eleven U.S. Navy divers performing a 28-day saturation dive to a pressure of 1,000 feet seawater / 305 meters seawater were tested for increased levels of C3a and C5a fragments. No correlation was found between high-pressure nervous syndrome experienced by some of the divers and the levels of the fragments. However, the three divers with Type I DCS characterized by skin bends fatigue or pain only had significantly higher levels of C3a and C5a.

C3d levels in divers exposed to a 20-minute, 170 fsw / 52 msw dry chamber dive or to two such dives with a six-hour surface interval were studied by Zhang and others in 1991. Their goal was to develop a measure of decompression stress other than DCS symptoms for low-risk recompression dives. Red-blood-cell-bound C3d was chosen because it is one of the final cleavage products of complement C3, the key protein arising from both the alternate and classical pathways of the complement cascade. They demonstrated that C3d did not increase after the single dive, but it did significantly increase after the repetitive dive. No divers presented DCS symptoms, although half reported itching during or after decompression from the first and second dive. This could have been due to platelet aggregation followed by histamine release that was not related to complement activation.

The fact that C3d activation was greater after the second dive supports the hypothesis of Ward and his associates that complement is depleted by repetitive diving, even when DCS is not present. Low-grade complement activation on such dives may not be enough to initiate DCS, but could result in complement depletion that may protect divers from DCS after subsequent dives. For example, divers subjected to six 30-minute repetitive dives with a maximum depth of 2.0 atmospheres absolute over three days showed an approximate one-half reduction of C5a produced in plasma samples after completing all dives, compared with predive samples. Complement C3a did not show significant differences after the dives.

Rabbits were shown to become 30 percent less sensitive to DCS if they were subjected to a series of low-pressure profiles before severe-pressure tests. Sensitivity of the rabbits was graded on the susceptibility to complement activation as defined by their C5a levels. Seven out of seven high-sensitivity rabbits subjected to the se-

vere profiles developed DCS. A second group of 13 high-sensitivity rabbits was subjected to four low-pressure dives. Only three of them developed DCS after subsequent severe-pressure dives. Complement activation sensitivity was reduced by exposure to low-pressure profiles, which in turn significantly reduced the rabbits' susceptibility to DCS.

Possible Individual Differences in Susceptibility

Complement sensitivity could explain, in part, individual variation in DCS susceptibility. Ward and others found that sensitive rabbits and divers had higher incidence of DCS than insensitive subjects, and therefore raised the possibility that changes in complement sensitivity could explain individual variation in DCS susceptibility. Sensitivity was defined by the level of C5a increase following plasma incubation with bubbles outside of the body. They also found that cobra venom factor ended the manifestation of DCS in rabbits. ■

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Sources

Additional information about the possible neurological effects of decompression sickness can be found in the following articles, which were used in the preparation of this story:

Barnard E.P., Hanson J.M., Rowton-Lee M.A. et al. Post-decompression shock due to extravasation of plasma. British Medical Journal 1966. 2:154-155.

Buttolph T.B., Broome J.R., Dick E.J., Kang Y.H. Leukocyte-mediated inflammation in porcine model of cutaneous decompression illness. Undersea & Hyperbaric Medicine; 1996. 23 supplement: 38.

Douglas M., Stevens S.L., Gartner D.H., Robinson D.H., Dutka AJ. Complement activation during saturation diving: relationship to decompression sickness and high-pressure nervous syndrome; Undersea Biomed Res., 1991 supplement 18:19

Dux E., Joo F. Effects of histamine on brain capillaries. Exp Brain Research, 1982; 47:252-258.

Hills B.A., James P.B. Microbubble damage to the blood-brain barrier: relevance to decompression sickness, Undersea Biomedical Research. 1991, 18, 2:111-116.

Lee W.H. Jr., Hariston P. Structural effects on blood proteins at the gas-blood inerface. Fed Proc. 1971. 30:1615-1622. Cited in Shastri, Logue and Lundgren (1991).

Lee W.H. Jr., Krumhaar D., Fonkalsrud E.F, et al. Denaturation of plasma proteins as a cause of morbidity and death after intracardiac operations. Surgery, 1961 50:29-39.

Marzetta L., Swoveland P., Myers R., Tehrani M.J. Localization of leukocyte cell adhesion molecules in the spinal cord of rats with decompression sickness. Abstract. Undersea Biomedical Research 1993. 20 supplement: 54.

Shastri K.A., Logue G.L., Lundgren C.E. In vitro activation of human complement by nitrogen bubbles. Undersea Biomedical Research. 18, 3:157-165.

Smith R.M., Van Hoesen K.B., Neuman T.S. Arterial Gas Embolism and Hemoconcentration. Journal of Emerg. Med 1994. 12, 2:147-153.

Suckling A.J., Rumbsy M.G., Bradbury M.W.B. The blood-brain barrier in health and disease. Chichester, England: Ellis Horwood, 1986. Cited in Hills B.A., James P.B. 1991.

Ward C.A., Fraser W.D., McCullough D. Effects of mild pressure profiles in complement activation sensitivity. Abstract. Undersea Biomedical Research. 1993. 20 supplement: 54-55.

Ward C.A., McCullough D., Fraser W.D. Changes in complement activation sensitivity and decompression sickness susceptibility of rabbits from repeated pressure profiles. Undersea Biomedical Research. 1991. 18 supplement: 19.

Ward C.A., McCullough D., Yee D., Stanga D., Fraser W.D. Complement activation involvement in decompression sickness in rabbits. Undersea Biomedical Research. 1990. 17, 1:51-66.

Ward C.A., McCullough D., Fraser W.D. Relationship between complement activation and susceptibility to decompression sickness. Journal of Applied Physiology. 1987. 62:1160-1166.

Zamboni W.A., Wong H.P., Stephenson L.L. Effects of hyperbaric oxygen on neutrophil delivery and pulmonary sequestration in reperfusion injury. Undersea & Hyperbaric Medicine. 1996. 23 Supplement: 54.