

AD-A283 565



1993

Final

Family Practice Rounds

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2510 Kennedy Circle, STE 117
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AL/AO-JA-1993-0089

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Family Practice Recertification

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Decompression sickness is a complex condition that can present a considerable challenge to the health care provider. The mainstay of treatment for decompression sickness is therapeutic recompression therapy while breathing oxygen. The patient should be compressed as soon as possible, however patients should be considered for recompression even after several days delay. Aggressive hydration and high flow oxygen should be instigated, even before starting recompression therapy. The use of hyperbaric oxygen is generally safe, relatively non-toxic at clinical treatment depths, and can be used to treat young children. Pharmacologic agents may be useful adjuncts to recompression therapy but their proper role requires further study. Early consultation with a physician trained in dive medicine should be sought.

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Decompression Sickness, Evaluation and Treatment

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Confusion, headache, and joint pain after scuba diving

PATRICK N. KIMBRELL, MD, ABFP

Patient presentation

T.W., a 27-year-old white woman, came to the family medicine clinic complaining of a severe, generalized headache and fatigue that had persisted for 14 hours. For the last 12 hours, she had also suffered from progressive right shoulder pain, bilateral wrist and ankle pain, and tingling in the feet. She had no history of any significant medical problems or recent acute illness or trauma.

By the patient's own account, she had been scuba diving 18 hours earlier. While her first dive of the day—a 40-minute descent to a depth of some 36 feet of sea water (fsw)—was uneventful, her second dive had ended abruptly. During this 15-minute descent to 40 fsw, she was unable to clear her face mask of water; panicking, she rapidly ascended to the surface.

Only 8 hours before arriving at the clinic, the patient had visited the emergency department of a local hospital where her symptoms were diagnosed as musculoskeletal strain and fatigue. At that time, she was given a prescription for ibuprofen (Ibu-Tab, Motrin, Rufen, etc.) in 800-mg doses to be taken three times daily. She was also taking norgestrel and ethinyl estradiol (Lo/Ovral) once daily on a regular basis.

Diagnosis

Physical examination revealed a slightly confused, slender, young woman with poor concentration. Her vital signs were temperature, 98.2°F; blood pressure, 106/74 mm Hg; pulse, 78 beats per minute; respirations, 24 per minute. Laboratory results showed a complete blood cell count and electrolyte levels in

normal ranges. Pertinent physical findings included poorly localized, deep, throbbing pain, 9/10 in intensity in the joint area of the right shoulder and in both ankle joints; this pain did not worsen with movement. Involved areas were not erythematous, swollen, or tender to the touch. Strength in her right shoulder was decreased compared with that in her left, and the strength of her ankle flexion and extension was decreased bilaterally. Diffuse paresthesia occurred in both feet and extended to the ankles.

Neurologic findings were significant; the patient was well-oriented but appeared to have problems concentrating, demonstrated by her inability to recite serial multiples of seven or repeat simple phrases. Her illness was diagnosed as decompression sickness (DCS), and she was immediately started on 100% oxygen by anesthesia mask. Vigorous hydration with Ringer's lactate was also begun intravenously. She received 325 mg of aspirin orally and was quickly transported to a nearby recompression, or hyperbaric, chamber for definitive treatment. There she received hyperbaric oxygen treatment (US Air Force Table 6), and her symptoms resolved. She was observed overnight in the hospital and discharged the next day after a careful examination showed no residual neurologic or other abnormalities. She was told not to dive or fly for at least 48 hours.

Discussion

DCS, most frequently associated with compressed gas diving, is a medical emergency. In 1992, the illness was treated in approximately 600 patients in North America.^{1,2} With an estimated 2-3 million trained recreational scuba divers in the United States and about 500,000 new divers starting training each year,³ it is becoming increasingly important for primary care physicians to be able to

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References: 1. Study 1097, data on file, 3M Pharmaceuticals. 2. McFadden ER Jr, Gilbert IA. Medical progress: asthma. *N Engl J Med* 1992;327:1928-1937. 3. Shinn C, Williams MH. The adequacy of inhalation of aerosol from canister nebulizers. *Am J Med* 1980;69(6):891-894.

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BRIEF SUMMARY

INDICATIONS AND USAGE: MAXAIR AUTOHALER is indicated for the prevention and reversal of bronchospasm in patients with reversible bronchospasm including asthma. It may be used with or without concurrent theophylline and/or steroid therapy.

CONTRAINDICATIONS: MAXAIR is contraindicated in patients with a history of hypersensitivity to any of its ingredients.

WARNINGS: As with other beta adrenergic aerosols, MAXAIR should not be used in excess. Controlled clinical studies and other clinical experience have shown that MAXAIR like other inhaled beta adrenergic agonists can produce a significant cardiovascular effect in some patients, as measured by pulse rate, blood pressure, symptoms, and/or ECG changes. As with other beta adrenergic aerosols, the potential for paradoxical bronchospasm (which can be life threatening) should be kept in mind. If it occurs, the preparation should be discontinued immediately and alternative therapy instituted.

Facilities have been reported in association with excessive use of inhaled sympathomimetic drugs.

The contents of MAXAIR AUTOHALER are under pressure. Do not use or store near heat or open flame. Exposure to temperature above 120°F may cause bursting. Never throw container into fire or incinerator. Keep out of reach of children.

PRECAUTIONS: General — Since pirbuterol is a sympathomimetic amine, it should be used with caution in patients with cardiovascular disorders, including ischemic heart disease, hypertension, or cardiac arrhythmias, in patients with hyperthyroidism or diabetes mellitus, and in patients who are unusually responsive to sympathomimetic amines or who have convulsive disorders. Significant changes in systolic and diastolic blood pressure could be expected to occur in some patients after use of any beta adrenergic aerosol bronchodilator.

Information for Patients — MAXAIR effects may last up to five hours or longer. It should not be used more often than recommended and the patient should not increase the number of inhalations or frequency of use without first asking the physician. If symptoms of asthma get worse, adverse reactions occur, or the patient does not respond to the usual dose, the patient should be instructed to contact the physician immediately. The patient should be advised to see the Illustrated Patient's Instructions for Use.

The Autohaler actuator should not be used with any other inhalation aerosol canister. In addition, canisters for use with MAXAIR AUTOHALER should not be utilized with any other actuator.

Drug Interactions — Other beta adrenergic aerosol bronchodilators should not be used concomitantly with MAXAIR because they may have additive effects. Beta adrenergic agonists should be administered with caution to patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants, since the action of beta adrenergic agonists on the vascular system may be potentiated.

Carcinogenesis, Mutagenesis and Impairment of Fertility — Pirbuterol hydrochloride administered in the diet to rats for 24 months and to mice for 18 months was free of carcinogenic activity at doses corresponding to 200 times the maximum human inhalation dose. In addition, the intragastric intubation of the drug at doses corresponding to 6250 times the maximum recommended human daily inhalation dose resulted in no increase in tumors in a 12-month rat study. Studies with pirbuterol revealed no evidence of mutagenesis. Reproduction studies in rats revealed no evidence of impaired fertility.

Teratogenic Effects — Pregnancy Category C — Reproduction studies have been performed in rats and rabbits by the inhalation route at doses up to 12 times (rat) and 16 times (rabbit) the maximum human inhalation dose and have revealed no significant findings. Animal reproduction studies in rats at oral doses up to 300 mg/kg and in rabbits at oral doses up to 100 mg/kg have shown no adverse effect on reproductive behavior, fertility, litter size, pre- and postnatal viability or fetal development. In rabbits at the highest dose level given, 300 mg/kg, abortions and fetal mortality were observed. There are no adequate and well controlled studies in pregnant women and MAXAIR should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers — It is not known whether MAXAIR is excreted in human milk. Therefore, MAXAIR should be used during nursing only if the potential benefit justifies the possible risk to the newborn.

Pediatric Use — MAXAIR AUTOHALER is not recommended for patients under the age of 12 years because of insufficient clinical data to establish safety and effectiveness.

ADVERSE REACTIONS: The following rates of adverse reactions to pirbuterol are based on single and multiple dose clinical trials involving 761 patients, 400 of whom received multiple doses (mean duration of treatment was 2.5 months and maximum was 19 months).

The following were the adverse reactions reported more frequently than 1 in 100 patients: CNS: nervousness (6.9%), tremor (6.0%), headache (2.0%), dizziness (1.2%). Cardiovascular: palpitations (1.7%), tachycardia (1.2%). Respiratory: cough (1.2%). Gastrointestinal: nausea (1.7%).

The following adverse reactions occurred less frequently than 1 in 100 patients and there may be a causal relationship with pirbuterol: CNS: depression, anxiety, confusion, insomnia, weakness, hyperkinesia, syncope. Cardiovascular: hypotension, skipped beats, chest pain. Gastrointestinal: dry mouth, glossitis, abdominal pain/cramps, anorexia, diarrhea, stomatitis, nausea and vomiting. Ear, Nose and Throat: smell/taste changes, sore throat. Dermatological: rash, pruritus. Other: numbness in extremities, alopecia, bruising, fatigue, edema, weight gain, flushing.

Other adverse reactions were reported with a frequency of less than 1 in 100 patients but a causal relationship between pirbuterol and the reaction could not be determined: migraine, productive cough, wheezing, and dermatitis.

The following rates of adverse reactions during three-month controlled clinical trials involving 310 patients are noted. The table does not include mild reactions.

PERCENT OF PATIENTS WITH MODERATE TO SEVERE ADVERSE REACTIONS

Reaction	Pirbuterol N = 157	Metaproterenol N = 153	Reaction	Pirbuterol N = 157	Metaproterenol N = 153
Central Nervous System			Gastrointestinal		
tremors	1.3%	3.3%	nausea	1.3%	2.0%
nervousness	4.5%	2.0%	diarrhea	1.3%	0.7%
headache	1.3%	2.0%	dry mouth	1.3%	1.3%
weakness	0%	1.3%	vomiting	0%	0.7%
drowsiness	0%	0.7%	Dermatological		
dizziness	0.6%	0%	skin reaction	0%	0.7%
Cardiovascular			rash	0%	1.3%
palpitations	1.3%	1.3%	Other		
tachycardia	1.3%	2.0%	bruising	0.6%	0%
Respiratory			smell/taste change	0.6%	0%
chest pain/tightness	1.3%	0%	backache	0%	0.7%
cough	0%	0.7%	fatigue	0%	0.7%
			hoarseness	0%	0.7%
			nasal congestion	0%	0.7%

OVERDOSAGE: The expected symptoms with overdosage are those of excessive beta-stimulation and/or any of the symptoms listed under adverse reactions, e.g., angina, hypertension or hypotension, arrhythmias, nervousness, headache, tremor, dry mouth, palpitations, nausea, dizziness, fatigue, malaise, and insomnia.

Treatment consists of discontinuation of pirbuterol together with appropriate symptomatic therapy.

The oral acute lethal dose in male and female rats and mice was greater than 2000 mg base/kg. The aerosol acute lethal dose was not determined.

CAUTION: Federal law prohibits dispensing without prescription.

Store between 15° and 30° C (59° to 86° F).

For Full Prescribing Information, see package insert.

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recognize, evaluate, and treat patients with DCS.

This illness is induced by inert gas bubbles, usually nitrogen, that have formed in the vascular system and tissues in enough volume to interfere with or alter organ or neurologic function. Diving while using compressed air may produce these bubbles. As a diver descends, the partial pressures of oxygen (PO₂) and nitrogen (PN₂) increase in the alveoli. A new tissue equilibrium is established, with higher levels of these gases dissolving in solution (Henry's law). During ascent, partial pressures decrease and the gases start to diffuse from the tissues. Although oxygen is removed through metabolic consumption, diffusion, and blood flow, inert nitrogen can be removed only by the latter two routes. If the rate of ascent exceeds the rate at which the inert gas can be eliminated from the body tissues, nitrogen bubbles may form, causing local symptoms due to vascular occlusion, local tissue distortion or disruption, hypoxia, or activation of the complement system and coagulation cascades.

Clinical manifestations of DCS range from skin eruptions and joint pain to neurologic dysfunction, profound fatigue, and weakness. Cardiovascular shock and death result in rare cases. Symptoms usually occur within 24 hours of a dive and can be progressive if untreated. Symptom onset 36 hours or more after a dive is uncommon. Untreated DCS may lead to significant functional or neurologic disability. Any neurologic finding, especially if progressive, usually signifies increasing severity of illness. Other structures, including the vestibular apparatus and lymphatic system, may also be affected.

Although the illness is more commonly associated with dives deeper than 33 fsw, there is considerable individual variability, and symptoms have been observed after shallower dives.^{4,5} Regardless of the circumstances, time between symptom onset and treatment must be minimized.

Management For nearly 100 years, the standard preliminary therapy for DCS has been 100% oxygen.⁶ The patient should be placed in a supine position, and the oxygen—in a concentration as close to 100% as possible—

administered continuously through a tightly sealed oral-nasal mask until definitive treatment is started. The 100% oxygen increases the concentration gradient for the diffusion of nitrogen from bubbles back into the tissues and blood and then to the lungs where it is expelled.

Nitrogen bubbles may cause platelets and leukocytes to aggregate, leading to microvascular impairment and occlusion. Damage to capillary endothelium leads to increased vascular permeability, and some patients therefore show an increased hematocrit and platelet count. In severe cases of DCS, which are associated with a generalized capillary leak syndrome and hemoconcentration with increased blood viscosity, aggressive hydration is very important. Oral or intravenous hydration allows the continued wash-out of nitrogen from the tissues; at the same time, the process dilutes platelet aggregation and improves vascular flow. Isotonic crystalloid solutions, such as normal saline or lactated Ringer's, are best; glucose solutions are usually avoided. The use of corticosteroids, anticoagulants, and lidocaine HCl is controversial.⁴

If treated soon after the onset of symptoms, less severe cases of DCS may be resolved at this point in therapy. Before treatment is ended, however, consultation is warranted with a physician knowledgeable about recompression therapy, or hyperbaric medicine, the only known definitive treatment for DCS.⁷

Modern recompression therapy almost always employs oxygen-enriched breathing mixtures, or hyperbaric oxygen. When inhaled under pressure, oxygen dissolves in the plasma. At 3 atmospheres of absolute pressure (ATA), or 66 fsw, an arterial oxygen pressure of more than 2,000 mm Hg may be forced into plasma solution. By Boyle's law, recompression therapy also greatly reduces the size of nitrogen bubbles. The simultaneous use of 100% oxygen significantly increases the oxygen gradient, causing the inert nitrogen to diffuse from the bubbles back into the tissues, thus accelerating the rate of bubble nitrogen elimination.

Among its other benefits, therapy with hyperbaric oxygen offers greater oxygen delivery to support ischemic tissue and inhibits the fur-

ther uptake of inert nitrogen⁶; the vasoconstrictive effect of oxygen may also reduce edema in some injured tissues. The optimum pressure for treatment is not known. Although most patients are successfully treated with a single oxygen recompression table to a depth of between 2 ATA and 2.8 ATA, individual responses may vary. Some patients may require repetitive hyperbaric oxygen therapy until symptoms are resolved or incremental benefit ceases.⁴

Conclusion In treating DCS, recompression with 100% oxygen should begin as soon as possible and be considered even after several days' delay.⁴ Aggressive hydration and high-flow oxygen should be initiated immediately. Hyperbaric oxygen is generally safe and relatively nontoxic at clinical treatment depths and can be used in children. Pharmacologic agents may be useful adjuncts, but their role is undefined. A physician trained in dive medicine should be consulted early.

More information on DCS and its treatment, including a list of hyperbaric treatment facilities in your area, is available from the Divers Alert Network, 919-684-2948, or the Undersea and Hyperbaric Medical Society, 301-530-9275. The Divers Alert Network emergency hot line is 919-684-8111. §

Opinions, interpretations, conclusions, and recommendations expressed in this article are the author's and are not necessarily endorsed by the US Air Force.

REFERENCES

1. Bove AA, Davis JC. Diving medicine. Philadelphia: WB Saunders Co, 1990:170-187.
2. Davis JC. Medical examination of sport scuba divers. San Antonio, Tex: Medical Seminars Inc, 1986:1-45.
3. Divers Alert Network. Report on diving accidents, Divers Alert Network 1992, Durham, NC.
4. Moon RE. Treatment of gas bubble disease. *Probl Respir Care* 1991;4(2):232-252.
5. Myers RA. National registry at MIEMSS 1967-1992. Baltimore, Md: University of Maryland, Maryland Institute for Emergency Medical Services Systems.
6. Nichols G. History of diving. *Alert Diver* May-June 1993: 4-7.
7. Thom SR. Hyperbaric oxygen therapy: A committee report. Bethesda, Md: Undersea and Hyperbaric Medical Society, 1992:25-27.