NUCLEAR MEDICINE RESEARCHERS SCALE TO NEW HEIGHTS

To conduct their studies on high altitude illnesses, nuclear medicine investigators have set up labs on the rugged tips of mountains. Who has reached the highest peak?

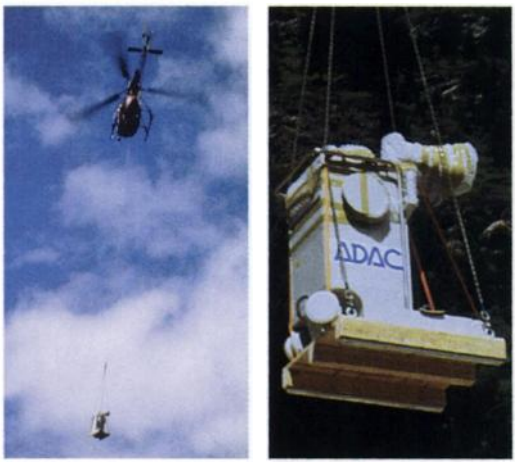
MOST MOUNTAIN CLIMBERS plant a flag to stake their claim on a mountain summit. High-altitude nuclear medicine researchers install imaging cameras to mark their turf above the clouds. Last summer, Peter Bartsch, MD, a professor of sports medicine at the University of Heidelberg, Germany had a gamma camera transported by helicopter to the top of a mountain peak in the Italian Alps in order to conduct studies on high-altitude pulmonary edema (HAPE). He proudly claimed his research laboratory—nestled 14,954 feet above sea level—on Monte Rosa as "the highest alpine hut in Europe." His research colleague even proclaimed that they had performed the "highest-level" nuclear medicine research in the world. Little did they know that one innocuous comment would bring out the measuring tapes of other nuclear medicine researchers whose labs are perched on mountaintops.

The Mysteries of Mountain Sickness

Nuclear medicine physicians have been conducting studies at high altitudes since the 1950's. Using radionuclides thousands of feet above sea level, they are able to learn about the physiological changes that occur on plasma volume, red-blood-cell counts and blood vessel functioning at altitudes where oxygen is less abundant. Many researchers are attempting to identify the mechanisms behind HAPE, while others are studying populations that live in mountainous terrains to better understand how the body adapts to high altitudes.

Unlike Bartsch, most of these researchers haven't transported gamma cameras to their labs. Instead, they conduct their studies using radioimmunoassays on serum samples or by recording emissions using sodium iodide crystal counting detectors.

Bartsch began conducting high altitude nuclear medicine studies ten years ago to explore the mechanisms behind high altitude illnesses, which can affect mountain climbers, hikers, or skiers who ascend too quickly to heights above eight to ten thousand feet. By leading research expeditions to Monte Rosa every summer, he studied the effects of mountain sickness, which usually causes short-lived symptoms such as headaches, nausea and dizziness. He also studied the more serious HAPE, which is longer lasting and manifests itself by severe breathlessness, coughing and the production of frothy phlegm. However, it wasn't until this past summer that Bartsch and his research team decided to install a gamma camera to perform nuclear medicine studies to better understand these conditions.



Ulrich Noelpp, PhD, the University of Heidelberg

Last summer this gamma camera was transported by helicopter to the top of Monte Rosa in the Italian Alps. Researchers used the camera to perform radiotracer studies of high-altitude pulmonary edema.

Physiologists who study the effects of mountain sickness know that the low atmospheric pressure at high altitudes can lead to reduced oxygen concentration in the blood, which in turn causes an abnormally high perfusion in the lungs and brain in those who are susceptible. This perfusion can

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Marcus E. Raichle, MD, Mallinckrodt Institute of Radiology

High in the Karakoram mountains at the Pakistani-China border, Marcus E. Raichle, MD, of the Mallinckrodt Institute of Radiology in St. Louis, had a ^{133}X brain scan to study cerebral blood flow in acute mountain sickness.

ment a policy requiring states to re-examine their current guides and make adjustments as needed. HCFA probably won't make a decision on this issue for several months.

Medicare Codes:The Good News and Bad. Last December 8, HCFA published the Medicare Fee Schedule for 1995. The rule contained both good news and bad news for nuclear physicians. For the good news, Medicare will now reimburse physicians for a SPECT study when it follows a whole-body planar study under the category called -51 modifier, traditionally used for surgical codes. In the past, some Medicare carriers refused to pay for a second nuclear medicine procedure performed on the same day. Effective January 1 of this year, all Medicare carriers must now fully cover the more expensive of the two procedures and provide a 50 percent payment for the less expensive test. HCFA notes that this policy change is based on recommendations from the ACNP and SNM.

For the bad news, HCFA finalized its proposal to get rid of the two billing codes, 78890 and 78891, by assigning them "B" status. The codes had previously existed to compensate for separate generation and interpretation of computer data when a primary diagnostic test did not already include a quantitative component. HCFA said that nuclear physicians were incorrectly billing computer studies as stand-alone codes about 90 percent of the time. According to the agency, total expenditures for these codes were $1.6 million annually. SNM and ACNP persuaded HCFA to reallocate the funds and keep them within nuclear medicine codes. Although nuclear physicians will no longer be able to bill for these computer applications, they may gain small increases in reimbursements for other procedures.

Review of RBRVS. HCFA will conduct the first five-year review of the physician component of the Resource Base Relative Value Scales (RBRVS) this year. These numbers determine how much Medicare carriers should reimburse physicians based on the procedure and the amount of time and effort it takes to perform. Last November, the agency published a notice in the *Federal Register* inviting specialty societies to delineate codes which they believe are misvalued. The Society and College submitted two codes that they think are undervalued. The codes are for parathyroid imaging and lymphatic imaging.

The organizations decided to recommend re-adjustment only for those procedures where they felt they had the strongest case for increasing the RBRVS. The reason they didn't want to recommend a slew of codes for review is because HCFA not only has the prerogative to increase the values but also to decrease them. (HCFA has asked its carrier medical directors to nominate codes which they believe are over-valued.) HCFA will review all nominations from specialty medical societies and refer a small number of them to the American Medical Association for survey, review and a recommendation. Note: The process will be budget-neutral so that for every code raised, either one will be lowered or all the codes will go down slightly. Overall, the SNM and ACNP feel that most nuclear medicine codes are correctly valued.

Sandra K. Bilko, Director of Reimbursement Policy
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High Altitude Nuclear Medicine

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lead to a lung edema and, in rare cases, a cerebral edema, which may result in seizures, hallucinations, coma, brain damage and even death. "The crucial role of elevated blood pressure in the development of HAPE was demonstrated in previous investigations," said Ulrich Noelpp, PhD, a physicist who was part of Bartsch's research team. But, he said, researchers still aren't certain how this vasoconstriction of pulmonary arterioles leads to edema formation.

One of the leading theories suggests that vasoconstriction is not homogeneous, so some blood vessels may constrict more or less than others. This would result in overperfused areas, which can lead to edema, according to Noelpp. To test this hypothesis, Bartsch's team at Monte Rosa conducted a prospective study last July on 22 mountaineers, 5 of whom developed HAPE.

The researchers conducted gas exchange studies, chest radiographs and lung perfusion scans using ^{99m}Tc macroaggregated albumin. They also performed special "lung-water" studies using ^{123}I-antipyrine which enabled them to determine the amount of water in the lungs by measuring radiotracer transit time. Preliminary results showed no significant differences in the lung perfusion studies between the mountaineers who did get HAPE and those who did not.

Who Has Scaled the Highest Mountain?

A postcard sent overseas from one researcher to another sparked a playful debate via the global Internet electronic mail (e-mail) over who has climbed to the highest peak to practice nuclear medicine. After receiving the card from Noelpp last August, Trevor Cradduck, PhD, a medical physicist at Victoria Hospital in Ontario immediately posted a bulletin on Internet: "Today I received a postcard from Ulrich Noelpp sent from an alpine hut perched (somewhat precariously, according to the picture) on a rocky ridge at 4559 meters [14,954 feet] high in the Italian Alps. Ulrich claims that this must surely be the highest level of nuclear medicine practiced anywhere in the world! Do we have any dissenters, or can we allow Ulrich to submit his claim to the *Guinness Book of World Records*?" Within a few days, Cradduck received several e-mail replies naming other high-altitude researchers who conduct their studies where the air is thin. ("In fact," Noelpp told *Newsline*, "I never claimed to have conducted the highest nuclear medicine research in the world but, quite humbly, only the highest in Europe.")

One reply on the bulletin board suggested that a Peruvian research site may be a contender for the highest peak. Another e-mailer swore that a research site on the border of China should garner the world record. *Newsline* tracked the most promising leads to determine (at least until someone climbs higher) who has scaled the tallest mountain in the name of nuclear medicine.

The Earliest High Altitude Studies

In the rugged terrain of the Peruvian Andes, Carlos C. Monge, MD, founded the renowned Instituto de Biologia Andina (Andean Biology Institute) in 1940. He was the first to describe chronic mountain sickness (a.k.a. Monge's Disease), which can affect

those who reside permanently at high altitudes, according to Javier Villanueva-Meyer, PhD, an expert on high-altitude studies in South America at the University of Texas in Galveston.

Beginning the first nuclear medicine studies at the Institute in the 1950's, Cesar Reynafarje, MD, conducted research on ferokinetics, plasma volume, red blood cell mass quantitation and red blood cell survival. He and his colleagues performed in vitro nuclear medicine studies with ^{59}Fe, ^{131}I human serum albumin, and ^{14}C. They found that high altitude dwellers had a 30 percent higher blood volume than those who lived at normal altitudes, according to Villanueva-Meyer. They reasoned that the body adapts to high altitudes by increasing the oxygen concentration in its blood supply and by generating a greater number of blood vessels—especially around the heart.

Other researchers have since found that coronary artery disease and strokes are very rare in individuals who live at high altitudes, said Villanueva-Meyer. Unfortunately, no nuclear medicine studies have been done to assess whether there's a link between chronic hypoxia and a lower risk of these illnesses. "Given the current interest in heart disease prevention," he said, "it would make sense to study these populations in more detail."

Conducting nuclear research in other areas, physiologists at the Instituto Boliviano de Biologia de Altura (Bolivian Institute of Altitude Biology) recently studied the effect of testosterone on the ability of men to adapt to high altitudes. They performed a series of radioimmunoassays to measure testosterone concentrations in native Aymara men who lived at high altitudes and compared these measurements with the testosterone levels of urban men who live at sea level. The scientists concluded that very high testosterone levels could compromise adaptation to high altitudes, particularly in older men.

Although the scientific importance of this research goes unquestioned, the work was conducted in a lab that stands about 3000 feet closer to sea level than Monte Rosa. The Peruvian research labs, alas, also fall short by a mere 300 to 650 feet.

The True World Record, Perhaps?

A nuclear medicine practitioner at the Mallinckrodt Institute of Radiology at Washington University in St. Louis responded vigorously to Cradduck's e-mail. "As a member of the team that does hold the world record, I believe this mistaken claim should be refuted!" wrote Marcus E. Raichle, MD.

In 1987, Raichle worked with a group of British and Danish scientists who studied cerebral blood flow in acute mountain sickness. The team trekked to the Karakoram mountains at the Pakistani-China border, whose grand height is recorded at 17,800 feet above sea level. They measured changes in brain emissions using ^{133}Xe and an array of six collimated sodium iodide crystal detectors. The researchers found that headaches and central nervous system disorders caused by acute mountain sickness don't result from increased cerebral blood flow since the climbers who had symptoms had the same increase in cerebral blood flow as those who had none. They also confirmed that administering carbon dioxide (CO_2) at high altitudes can rapidly relieve symptoms of acute mountain sickness. Brain studies with $^{133}Xe_2$ showed increased cerebral blood flow in some climbers who inhaled the CO_2, which indicates that they had an improved oxygen delivery to their brains. In terms of the nuclear medicine world record, Raichle and his colleagues had indeed surpassed Noelpp's self-proclaimed record by 2854 feet!

No one has yet reported a nuclear medicine study that tops the Karakoram expedition, but one astute Internet correspondent pointed out that it should perhaps be qualified as the "earthbound" record. Sylvain Houle, MD, of the Clarke Institute's PET Centre in Toronto, noted that scientists from the National Aeronautics and Space Administration (NASA) performed radiotracer studies aboard spacecraft to study the effects of weightlessness in space.

During a mission launched on October 18, 1993, astronauts were injected with three radionuclides: ^{125}I, to determine plasma volume; ^{35}S, to measure extracellular fluid space; and ^{59}Fe, to study erythrokinetics and red-blood-cell volume. However, "no radiation detection devices were used, other than the crew's personal occupational dosimeters," said a NASA spokesperson. With plans to build an international East-West space station over the next seven years, researchers may soon have the means to land gamma cameras at high altitudes via spaceships rather than helicopters.

Lawsuit Over NRC Rule

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laws less strict to comply with this rule—which is crazy considering that Agreement States have one-third the misadministration rate as NRC states," she says.

The final rule also defines who is qualified to practice nuclear pharmacy and includes labeling requirements for radionuclides which are independent of the FDA's requirements. "The NRC doesn't have the jurisdiction to make these regulations," said Marcus. "The agency says it's going to supersede the board of medicine, supersede the board of pharmacy and override state law."

Although Marcus raises persuasive arguments, some nuclear medicine experts feel she is being unrealistic and is waging a quixotic battle against windmills. "I think the lawsuit is much ado about nothing," said Barry Siegel, MD, director of the division of nuclear medicine at Mallinckrodt Institute of Radiology and chairman of the Advisory Committee on the Medical Uses of Isotopes. "Carol [Marcus] thinks getting anything less than what she asked for is a resounding defeat. But I think it's a good rule considering where the NRC was when we started."

Society leaders are hoping that filing the petition for review will spur fruitful negotiations with the NRC allowing the issues to be settled out of court. Cost is definitely a factor on their minds. According to Nichols, the petition for review has already cost about $1000 in legal fees. Formal negotiations with the NRC, the next step, could run up to $7500. Presenting an oral argument and filing a brief in court could cost up to $50,000.

The Concern Over Licensing Fees

The factor that will play a major role in determining the direction of the lawsuit: the yet-to-be-published regulatory guides. These guides, which accompany every final rule, outline the details