Smokers' Faces
Who Are The Smokers?

The staid peer-review periodical, the British Medical Journal, recently featured a picture quiz entitled, "Smokers' Faces: Who are the Smokers?" The faces depicted included that of the late famed Hollywood screen star, William Holden. The quiz was published as an adjunct to the report, "Smoker's Face: An Underrated Clinical Sign?" The author, Dr. Douglas Model, reported that in his study group, approximately half the cigarette smokers who had smoked for ten years or more were identified by their facial features alone. "Smokers' face" was defined as one or more of the following: (1) lines or wrinkles on the face; (2) a gauntness of facial features with prominence of the underlying bony contours; (3) an atrophic, slightly pigmented gray appearance of the skin and; (4) a plethoric, slightly orange, purple and red complexion. Confounding factors such as exposure to the sun, age and a recent change in weight were evaluated in both the study and control groups. Only cigarette smoking, and not these additional factors, accounted for the relationship between smoking habits and facial features.

It is strange that this physical sign is not noted in standard textbooks of medicine. Model notes that the relationship between smoking and the complexion was first suggested in 1866. Confirmatory data were provided by Ippen and Ippen in 1965 and by Daniell in 1971.

It is important to emphasize a physical diagnostic sign that is underutilized. However, there is a more subtle psychologic bonus to be derived from these observations. Smokers frequently require demonstration of the physical effects of smoking to assist them in stopping this habit. Thermography and spirometry offer potential value, but these methods have not yet achieved widespread clinical acceptance. Perhaps physicians could motivate patients in their efforts at smoking cessation by pointing out these dramatic effects on the complexion.

Predictably, women are particularly impressed with this information; however, one should not underestimate the impact of these data upon men. I was recently invited to be the guest speaker on a question-and-answer radio program in San Diego, California. The subject was the dangers of smoking and smoking cessation techniques. The moderator, a professional announcer in San Diego, was a chain smoker and he seemed singularly unimpressed by my description of the deleterious effects of smoking upon the cardiovascular and pulmonary systems. However, one listener phoned in to ask if it were true that smoking may be responsible for premature wrinkling and lining of the face. When I responded that her information was entirely correct, the announcer snapped to attention. He whispered to me urgently, "Is this really one of the effects of smoking? If so, I'm going to give it up immediately!"

Ah, vanity, vanity. My 50-year-old radio host would consider facial wrinkling an urgent reason for smoking cessation, but not emphysema, lung cancer or coronary atherosclerosis! Nevertheless, we, as clinicians, welcome with gratitude any information which will motivate our patients to stop smoking. I was delighted to see the confirmatory data by Model with a re-emphasis on an underrated clinical sign. For some years, my wife and I have been playing an "elevator game." There is a characteristic deep cough and a typical huskiness of voice in the heavy smoker. As we ride in elevators, we have attempted to guess by the voice and the cough which of the passengers will take out a cigarette as they leave the elevator. We have been correct in a surprisingly large number of instances. The third stigma of the cigarette smoker, the smokers' face, has also been an important clue in our pastime. I wonder if cigarette smokers know how easily their habit can be detected by even the most casual observer?

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REFERENCES
1 Model D. Smokers' faces: who are the smokers? Br Med J 1985; 291:1755

Ventricular Ectopy and Diuretic-Induced Hypokalemia
An Alleged Association In Need of Clinical and Experimental Scrutiny

Few issues of medical therapeutics have stirred more intense and heated debate than the one pertaining
to the prevention or treatment of diuretic-induced hypokalemia.\textsuperscript{1,3} Proponents argue that such hypokalemia, in addition to inducing other less dangerous sequelae (eg, glucose intolerance, hypercholesterolemia), generates potentially malignant ventricular ectopy (VE) both in the basal state and following acute myocardial infarction.\textsuperscript{4} They have extended a strong recommendation, therefore, for a liberal policy of administering potassium supplements and/or potassium-sparing agents to prevent or treat mild, diuretic-induced hypokalemia.\textsuperscript{2,5} Opponents have countered that for the large majority of patients on diuretic therapy the degree of potassium depletion accrued is only mild and the resultant morbidity usually inconsequential.\textsuperscript{1} They have pronounced the existing evidence on the arrhythmogenicity of hypokalemia as tenuous and inadequate at best and, quite ironically, have called attention to the small but real risk of morbidity and mortality from hyperkalemia, a complication emerging from treatments prescribed to avert diuretic-induced hypokalemia.\textsuperscript{1,3} They have concluded, therefore, that such hypokalemia is usually benign and advocate no need for specific therapy for most patients on diuretic therapy.\textsuperscript{1}

Those not directly involved in this on-going debate remain understandably perplexed at how the two sides could interpret the same data base such that they end up arriving at diametrically opposed conclusions and recommendations. We believe that this state of interpretive schism is reflective of the inadequacy and inconclusiveness of the currently available evidence on the alleged arrhythmogenicity of diuretic-induced hypokalemia and that the recommendation for a liberal treatment policy stems largely from a cautious stance towards a lingering uncertainty.\textsuperscript{2,5} We wish to present a brief account in support of such a belief.

Millions of hypertensive patients with or without associated cardiac conditions are currently receiving therapy with diuretic drugs for the management of their hypertension and/or congestive heart failure. Hypokalemia (serum potassium of <3.5 mEq/L) is seen in about 20-40 percent of patients receiving up to 100 mg of hydrochlorothiazide daily and in 40-60 percent of patients receiving 50 mg daily of chlorthalidone.\textsuperscript{6,6} Less than 7 percent of patients receiving thiazides feature a decrease in serum potassium below 3.0 mEq/L.\textsuperscript{7,8} The mean decrement in serum potassium produced by thiazides and chlorthalidone is 0.6 mEq/L and the average total body potassium deficit is in the range of 200 mEq, or a 5 percent decrease in total body potassium stores.\textsuperscript{7,8} Minor ECG repolarization changes are commonly found in such patients. Whereas hypokalemia is uniformly accepted to predispose to digitalis toxicity, the association of hypokalemia with VE in the nondigitaled patient remains hotly debated. Cogent arguments against a proven association have been advanced in a recent, comprehensive review of the older literature.\textsuperscript{1} Nonetheless, two recent studies utilizing continuous ambulatory ECG monitoring or exercise stress testing have detected an increased incidence of VE in patients with diuretic-induced hypokalemia.\textsuperscript{9,10} Yet, three independent, recent investigations employing experimental designs similar to those above were unable to find such an association.\textsuperscript{11,12,13} Despite their contradictory findings, all these studies have generally employed asymptomatic hypertensive patients; indeed, two studies have ruled out even underlying silent coronary artery disease in their subjects by conventional exercise stress testing, but still arrived at antithetic conclusions.\textsuperscript{9,13} The reasons for this discrepancy remain mysterious. The explanation may lie partially with the fact that the above-cited studies generally employed a small number of patients and that the duration of diuretic-induced hypokalemia was variable but, by and large, short. Notwithstanding, the Medical Research Council study included both short-term and long-term observations on 155 patients with mild hypertension randomly assigned to therapy with thiazide diuretic or placebo and was unable to uncover a cause-and-effect relationship between hypokalemia and VE.\textsuperscript{14} Thiazide-induced hypokalemia of six-month duration did not result in increased VE.\textsuperscript{15} Moreover, ample evidence suggests that treatment with thiazide diuretics given for one to several years does not further augment the initial mild total body potassium deficit.\textsuperscript{15,16}

It is far more difficult to demonstrate causality between hypokalemia and VE in patients with pre-existing cardiac pathology. Presumably, such an association was found in one study of eight patients with left ventricular hypertrophy, advanced age and abnormal baseline chest films, ECGs and Holter monitoring.\textsuperscript{18} However, if one considers the frequent phenomenon of VE in apparently asymptomatic patients\textsuperscript{16} and the increased ectopy inherent to ventricular hypertrophy,\textsuperscript{17} it becomes a cumbersome task to identify the component of VE deriving from hypokalemia itself. The suggestion has been made that the increased mortality noted in patients with baseline ECG abnormalities in the Multiple Risk Factor Intervention Trial was due to their vigorous therapy with diuretics.\textsuperscript{18} Yet, increased mortality did not correlate with hypokalemia in that trial.

Most of the literature focusing on the alleged association between VE and hypokalemia has reported an augmented frequency of premature ventricular beats and/or the occurrence of ventricular couplets and rare short runs of ventricular beats, but without much more identifiable morbidity or mortality. However, some studies have reported increased prevalence of ventricular tachycardia and ventricular fibrillation in patients with acute myocardial infarction who on
presentation were found to be hypokalemic and/or receiving maintenance diuretics.\textsuperscript{4,10-21} Although this morbid association with hypokalemia may indeed be real, one should keep in mind the intrinsic high frequency of VE in the setting of acute myocardial infarction, the presence of spontaneous oriatrogenic changes in acid-base status (leading to secondary alterations in the prevailing serum potassium level) and the precipitation or worsening of hypokalemia by the heightened adrenergic activity commonly noted in patients admitted with heart attacks.\textsuperscript{32,33} In point of fact, most of the studies designed to investigate the association of VE with hypokalemia in this setting have not considered vigorously the influence of confounding variables and, rarely, when this was done,\textsuperscript{41} it was not carried out systematically in a prospective manner.

On the basis of our scrutiny of available evidence, we believe that the existing controversy about the potential arrhythmogenicity of diuretic-induced hypokalemia of the magnitude encountered clinically cannot be resolved by merely interpreting the data base at hand. In addition, we feel that resorting to more gathering of retrospective data is bound to confuse the issue further. What is sorely needed is carefully designed, prospective studies aimed at dissecting this complex issue to its individual components. It is of prime importance to investigate prospectively the potential arrhythmogenicity of diuretic-induced hypokalemia \textit{per se} in a large number of asymptomatic hypertensive patients devoid of identifiable cardiac pathology. Patients recruited in such a study should be screened for the possible presence of silent coronary artery disease by exercise stress testing. Left ventricular hypertrophy should be searched for by conventional echocardiography, instead of merely relying on insensitive modalities such as chest radiography and standard 12-lead ECG.\textsuperscript{13,17} Patients with congestive heart failure, cardiomegaly, and baseline ECG changes should also be excluded from such a study.\textsuperscript{13,18}

The independent role of age\textsuperscript{19} should be explored by proper stratification of data. The duration of hypokalemic state should be taken into consideration, and data should be treated as a continuum regarding both serum potassium values and frequency and severity of VE. The independent or contributing role of hypomagnesemia could be explored in such a study, although hypokalemia was not associated with hypomagnesemia in a recent investigation.\textsuperscript{18}

Objections have been voiced in reference to the validity of semiquantitative classifications of arrhythmias often used in the literature.\textsuperscript{24} It will be advisable in the future to utilize more sophisticated approaches in the serial assessment of arrhythmias.\textsuperscript{26} Due to the inherent variability of VE noted in serial ambulatory ECG recordings,\textsuperscript{26,27} future studies should consider such multiple tests preferably of 48 hours in duration.\textsuperscript{13}

Investigation of the role of diuretic-induced hypokalemia in association with other pathology in the causation of VE should follow a careful study design. Of particular importance for the implementation of investigational protocols in this area is a careful characterization of the study groups (with and without hypokalemia) in reference to a large number of variables with appropriate stratification for age, associated morbidity, size of acute myocardial infarction, therapy at the time of onset of VE, etc.

What should the clinician do in the midst of this controversy which does not appear to be nearing its resolution in the immediate future? We believe that patients receiving digitalis should be watched carefully so that their normokalemia can be insured. In addition, patients with severe potassium depletion (unlike the one seen often with diuretic therapy) and documented high grade VE should be treated with potassium supplements, or potassium-sparing diuretics. The same recommendation should apply to patients admitted to the CCU with angina or acute myocardial infarction. Regarding the asymptomatic hypertensive patient with diuretic-induced hypokalemia and considering the small but identifiable risk of treatment-induced hyperkalemia,\textsuperscript{30} we believe that the bulk of currently available evidence does not suggest routine prophylaxis for, or therapy of hypokalemia of the degree commonly encountered with diuretic therapy.

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\section*{References}

16 Kennedy HL, Underhill ST. Frequent or complex ventricular ectopy in apparently healthy subjects: A clinical study of 25 cases. Am J Cardiol 1976; 38:141-48
27 Winkle RA. Ambulatory electrocardiography. Mod Concepts Cardiol Dis 1960; 49:7-12

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Everest—the Testing Place

Climbing Mount Everest has always been a symbol of the ultimate in human achievement. It was not surprising, therefore, that when Christopher Pizzo, M.D. of the American Medical Research Expedition to Everest obtained the first alveolar gas samples on the summit in 1981, this stirred the imagination of many people working in lung research.

I was invited to provide this retrospective glance back at the expedition because of the publication of a new book entitled, Everest—The Testing Place (West JB, New York: McGraw-Hill, 1985, $18.95.) The expedition had several notable scientific and mountaineering successes. Five people reached the summit, including the ninth, tenth, and eleventh Americans to do this. Measurements on or near the summit included alveolar gas samples, barometric pressure, temperature, electrocardiogram, exercise ventilation and base excess. Sophisticated laboratories were set up at camp 2 (6,300 m, 20,700 ft) and base camp (5,400 m, 17,700 ft) and an extensive series of physiologic measurements were carried out, including: exercise capacity, control of ventilation, sleep studies, hemotologic changes, effects of hemodilution, metabolic and endocrine studies, and psychometric tests.

Not surprisingly, the extensive results from the expedition raised as many questions as they gave answers. How could climbers on the summit tolerate an arterial Po2 level of less than 30 mm Hg, an arterial Pco2 level of only 7.5 mm Hg, and an arterial pH level of over 7.7? Why was metabolic compensation of the respiratory alkalosis so slow at these altitudes? How were the Sherpas able to maintain an even-breathing rhythm during sleep, whereas all the Americans had striking periodic breathing? Why did reducing the degree of polycythemia by hemodilution not reduce exercise tolerance? Does that mean that the polycythemia of high altitude is an inappropriate response? Why was muscle protein catabolism apparently increased at these altitudes, resulting in a marked loss of muscle mass? What was the reason for the increased serum concentration of thyroid hormones, the changes in insulin response to glucose loading, and the increase in growth hormone in some subjects?

The wealth of scientific information that was obtained tends to obscure the human adventure of the expedition. Everest is a dangerous place, and we had our share of drama. When Chris Pizzo set out for the summit from the highest camp, he could not find his ice ax because it was buried by snow and ice as a result of recent storms. Having nothing better, he started climbing with a tent pole. After about two hours, he was astonished to come across an ice ax which had been abandoned some two years ago by a climber who died on the mountain. This near-miraculous find enabled us