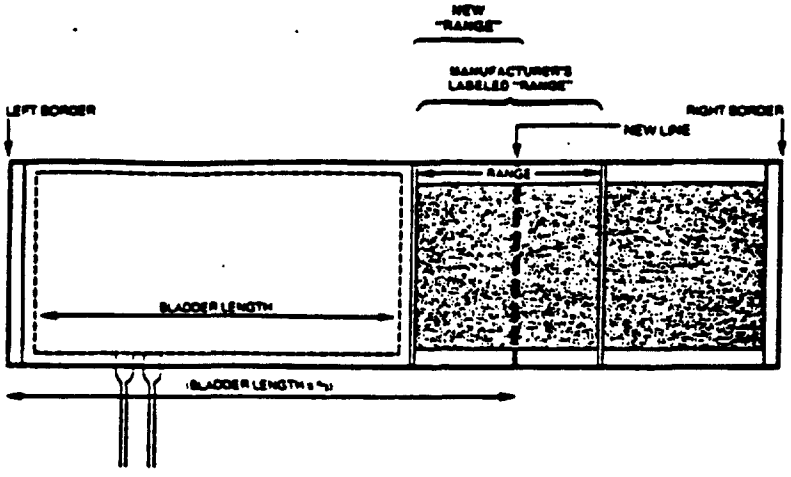


Figure 1. Re-marking of the Inner Surface of Sphygmomanometer Cuff for Proper Fit.

cumference, this range should be shortened by 7.0 cm. Patients with large arms who are "undercuffed" have systolic and diastolic readings that are falsely elevated 5 to 10 mm Hg on the average,[3,4] leading to overdiagnosis and overtreatment of hypertension.[5]

The problem can be remedied by re-marking, with an indelible marker, the right border of the range on a cuff at a point where 75 per cent of the arm's circumference is covered by the bladder. This is most easily done by multiplying the bladder length by 4/3, then marking a vertical line on the cuff at this distance from the left border of the cuff (Fig. 1). Thus, when the cuff is applied snugly to the arm, one will know (without measurement) whether the cuff size is appropriate: if on closure the left cuff border meets a point to the left of the new line, the cuff is adequate; if the left border meets a point to the right of the new line, a larger cuff is required.

Given the awkwardness of the older recommendations regarding cuff size, it is little wonder that most physicians and nurses do not employ objective criteria (manufacturer's markings or others) in selecting a size. Strict adherence to the 1980 criteria can be easily accomplished and will save many large-armed patients from inappropriate antihypertensive treatment.

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1. Kirkendall EM, Fenkuh M, Freis EA, et al. AHA Committee Report: recommendations for human blood pressure determination by sphygmomanometers. Circulation. 1980; 62:1146A-55A.
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## SPUTUM FOR CYTOLOGIC DIAGNOSIS OF LUNG CANCER

*To the Editor:* In a letter in the October 8 issue, Melamed and his colleagues reported that cytologic specimens obtained by pooling sputum produced by spontaneous coughing on the three mornings after aerosol induction contained identifiable cancer cells more frequently than did specimens obtained during induction itself. These authors may have given the erroneous impression that the same is true of specimens from spontaneous coughing (pooled over three days) produced independently of aerosol induction. Our experience from a cooperative study that included the Johns Hopkins Medical Institutions and the Mayo Foundation may be relevant to the interpretation of the data of Melamed et al.

The design of their study and ours required that aerosol induction be performed at the initial visit, with sputum obtained during induction and on the next three mornings, as outlined above. This procedure was repeated annually. In addition, twice a year (at four and eight months), a three-morning pooled specimen was collected that was identical to the above post-induction specimen, except that it was collected with no preceding induction.

Our data show that the post-induction three-day pooled sputum added further diagnostic benefit to that obtained at the time of induction, as in the study by Melamed et al. However, two thirds of all cytologically positive cases of cancer appearing after the initial screening (15 of 23) were detected by the annual induction procedure (induced sputum plus post-induction three-day pooled sputum), whereas only one third (eight of 23) were detected by the procedures at four or eight months with three-day pooled sputum that was not induced. These data clearly show an advantage of performing aerosol induction before obtaining a spontaneous-cough specimen for the detection and diagnosis of lung cancer, at least in a screening situation.

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The above letter was referred to the authors of the letter in question, who offer the following reply:

*To the Editor:* As described in our previous letter, we compared aerosol-induced and three-day pooled spontaneous-cough sputum-collection techniques in an initial screening of men enrolled in a lung-cancer detection program. In the detection of cancer present at enrollment (prevalence cases) the three-day pooled spontaneous sputum was of greater diagnostic value.

Dr. Frost and his colleagues suggest that the three-day pooled spontaneous specimen obtained after aerosol induction may be a better sample than such a specimen produced without aerosol induction. This is an important issue, and these authors' data on cytologically detected lung cancers appearing after initial screening (incidence cases) support this view

Table 1. Cytologic Diagnosis of Lung Cancer (Incidence Cases) by Sputum Sampling.

| No. of Cases | Diagnosis by Sampling Technique | |
|---|---|---|
| | Aerosol induced | Spontaneous cough* |
| 6 | + | Cancer |
| 4 | + | Suspicious |
| 2 | + | Moderate atypia |
| 2 | Negative | Cancer |
| 1 | Moderate atypia | Moderate atypia |
| 1 | Cancer | Cancer |
| 1 | Cancer | Suspicious |
| 1 | Cancer | Not done (x-ray positive) |

*Specimen derived from pooling sputum over three days.

†No sputum induction. Three-day pooled spontaneous sputum specimens only were obtained between annual examinations, as required by the protocol.

We therefore reviewed all our cytologically detected cases of lung cancer appearing after the initial screening (incidence cases). There were 16 such cases (Table 1). In two thirds of the cases appearing after initial examination, cancer was detected in the three-day pooled sputum specimen produced without aerosol induction. These results are consistent with our earlier findings on the initial examination (prevalence cases) and differ from those reported by Frost et al.

This apparent difference may result from the small size of the sample in both studies or from some other statistical artifact. For example, the results reported by these authors would be expected if the number of specimens obtained from the total population at annual examinations exceeded the number submitted by mail at four and eight months.

We remain unconvinced of the value of aerosol induction for collection of sputum cytology in a screening program for lung cancer.

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## PYROPHOSPHATE IMAGING FOR INFARCT SIZING

*To the Editor:* The timely overview of nuclear cardiology by Berger and Zaret (October 1 issue)[1] will surely assist physicians when they are considering the use of tracer techniques in cardiac disorders. I have recently written an editorial on scintigraphy for myocardial infarction, in which I expressed skepticism about the applicability of pyrophosphate imaging for the measurement of infarct size.[2]

First of all, pyrophosphate cannot be employed for assessment of interventions aimed at salvaging the heart from myocardial infarction. Although myocardial infarction is complete within three to six hours after cessation of the coronary blood supply,[3] radiophosphate scanning is not optimal until 36 hours after the onset of symptoms.[4]

Secondly, experimental data have established that cardiac uptake of pyrophosphate, because of a peculiar flow dependency, is maximal in the outer regions of the formed infarct, where histologic damage ranges from light to severe.[5] In fact, in both patients[4] and dogs,[6] infarct size computed from pyrophosphate scans is consistently larger than that derived from thallium images. Ideally, these two nuclear scintiscans should show concordant sizes of the infarct.

Finally, an acute infarct initially involves the subendocardial layer and subsequently spreads toward the subepicardial myocardium.[7] Nature spontaneously salvages 10 to 45 per cent of the transmural myocardial thickness, largely because of the availability of subepicardial collateral flow.[7] No current tomographic device has the resolution needed to differentiate infarcted from noninfarcted components of the myocardial region at risk.

My prediction is that infarct sizing with isotopes will require either development of newer radiopharmaceuticals or a quantum jump in single-photon tomographic instrumentation.

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1. Berger HJ, Zaret BL. Nuclear cardiology. N Engl J Med. 1981; 305:799-807, 855-65.
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## BIGUANIDES AND THE ERYTHROCYTE INSULIN RECEPTOR

*To the Editor:* Despite my reservations about the validity of using a labeled hormone with a high concentration and low specific activity in a radioreceptor assay, I found it remarkable that the dramatic increase in the numbers of insulin receptors reported by Holle et al. should have occurred when erythrocytes were incubated with metformin in vitro (September 3 issue).[1] Unlike other cells studied in vitro, peripheral erythrocytes have not been demonstrated to have a capacity for the complete synthesis of new proteins or receptors. Thus, the nature of the direct effect of biguanides on the red-cell insulin receptor is open to conjecture. Conceivably, such agents may alter the age distribution of red cells or in some way uncover insulin-binding sites that have become buried or nonfunctional as the cell has aged.[2] However, before any firm conclusions are drawn from the data presented by Holle et al., it should be emphasized that a major bioeffect of biguanides at the level of the insulin receptors on other cell types, particularly those of target tissues, has yet to be demonstrated.

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1. Holle A, Mangels W, Dreyer M, Kühnau J, Rüdiger HW. Biguanide treatment increases the number of insulin-receptor sites on human erythrocytes. N Engl J Med. 1981; 305:563-6.
2. Doms RF, Corash L, Gorden P. The insulin receptor is an age-dependent integral component of the human erythrocyte membrane. J Biol Chem. 1981; 256:2982-7.

The above letter was referred to the authors of the article in question, who offer the following reply:

*To the Editor:* We agree with Dr. Doms that studies with different cell types are needed before the phenomena occurring on erythrocytes can be generalized as a principal mode of biguanide action. However, we believe that our findings fit — better than any other mechanisms proposed so far — the clinically and pharmacologically observed effects of biguanides.

Biguanides are known to influence biologic membranes; their antidiabetic action is entirely extrapancreatic and depends on the presence of insulin. In particular, obese hyperinsulinemic diabetics seem to benefit from biguanide therapy.