Thorax, 1978, **33**, 545–546

Editorial

Sputum elasticity: A frog in the throat?

The change in the consistency of mucus that is produced during chest diseases has often been considered to contribute to difficulty in its removal. This has stimulated interest in the flow properties (properly referred to as rheological properties) of sputum in different diseases. To this end many studies have been carried out using sputum from patients with a variety of conditions, although in most cases workers have limited themselves to the use of techniques and instruments that are more suitable for the evaluation of simple fluids. These techniques have included the use of standard instruments, such as capillary and efflux viscometers, and also empirical techniques, such as measurement of pourability index (Keal, 1970). The information provided by such methods is limited because sputum is not a simple (viscous) fluid, such as water or glycerin. It is a complex material exhibiting viscoelastic behaviour (Davis and Dippy, 1969; Sturgess *et al*, 1971; Litt *et al*, 1977), which is a combination of liquid and solid behaviour. The typical rotational viscometer, where the experimental fluid is sheared in the gap between one stationary and one rotating surface of either two concentric cylinders or a cone and plate, provides an assessment of the liquid-like component but is incapable of evaluating the solid-like component. This explains some of the experimental difficulties and anomalous results that have been reported. A good example is the phenomenon of "rolling-up" of the sample in the gap between the measuring surfaces, which can eventually result in the expulsion of the experimental sample from the gap! This produces results that are very difficult to interpret (Tekeres and Geddes, 1971). Consequently the use of such techniques can be very misleading and therefore should be used with great caution for the evaluation of the progress of a chest condition or the in-vitro action of drugs.

Materials that are viscoelastic can be evaluated properly by using techniques that impose a very small displacement on the test sample. Suitable methods include the creep test, where the sample is subjected to a small force (stress) that results in an infinitessimal displacement, and the dynamic oscillatory test in which the sample is exposed to a stress that is varied sinusoidally and is transmitted by the sample to a suitable recording device (Davis, 1973). In both methods the material is examined in a non-destructive manner. By "stretching" the material and then allowing it to recover one can obtain information about primary (cross-linking), secondary (entanglement), and tertiary (hydrogen bonding) interactions. The dynamic test is to be preferred since by varying the frequency of oscillation a complete spectrum of behaviour can be obtained. This in turn provides information on the nature of the gel network with respect to the degree of cross-linking or entanglement and the molecular weight of the constituent glycoproteins.

Although these techniques are essentially straight-forward in operation, however, it is imperative that any technique is properly evaluated with materials of known properties, such as perfectly viscous liquids and viscoelastic gels. Only by regular calibration with such materials is it possible to appreciate instrumental artefacts and structural changes. The extensive use that has been made of these techniques in polymer science provides a useful basis for comparison, since mucus exhibits similar behaviour to that of a high molecular weight, uncross-linked polymeric gel. Such comparisons in behaviour should also stimulate further investigation of inexplicable results. An example is the so-called "notched-plateau" that has been reported in the frequency response curves of fresh sputum (Mitchell-Heggs, 1977). This effect should be investigated further since it has not been observed with non-biological polymeric systems.

Other methods have been used to evaluate the physical properties of mucus. A novel and intriguing approach is the use of the excised frog palate to evaluate mucociliary clearance. This technique has been described by Sadé *et al* (1970). The upper palate of the bullfrog or toad is placed in an environmental chamber so that a saturated atmosphere can be maintained. The palate will cease to secrete mucus after 24–36 hours, although the cilia will continue to beat. Samples of exogenous mucus can then be placed on the palate and will be transported by the beating cilia.

Using such a model it has been possible to show that materials that are purely viscous will not be transported. It has been noted that if the elasticity of a mucus sample is plotted against transport rate there is a sharp increase in transport with increase in elasticity up to an optimum value. At higher values of elasticity there is a slow decrease in transport with increasing elasticity (Shih *et al,* 1977). This effect has been observed not only with human bronchitic sputa but also with mucus from the canine trachea and human ear mucus from patients suffering from secretary otitis media. Significantly, Giordano *et al* (1977) have shown excellent correlation between mucus transport on the frog palate and clearance from the lung of the dog. Variation in elasticity of mucus samples can result either from different solid contents of the samples (Shih *et al,* 1977) or, from unreported experiments, the presence of divalent cations such as calcium, magnesium or copper.

The observed optimal elasticity for mucus transport could possibly be of clinical significance. For instance, the mucus obtained from patients with chest diseases has an elasticity in excess of the optimum for clearance (Davis and Dippy, 1968; Hwang *et al,* 1969). However, a large decrease in mucus elasticity would have to be induced before any significant improvement in mucus clearance would be produced. Also, if such reduction was produced by the action of drugs upon mucus itself, then overdosing could result in over-thinning of the secretion and the possibility of watery mucus draining back to the lower regions of the lung.

Such studies, where proper physical methods of measurement are combined with a convenient and suitable biological model, could well explain the apparent lack of success that has been experienced with the so-called mucolytic drugs. During treatment with such drugs it is often observed that either no effect is produced or that the drug is so effective that the patient virtually drowns in his own secretion.

The combination of theses two techniques should therefore enable the evaluation of drugs that affect mucus structure in a more rational manner, particularly with respect to the route of administration, potency, and dosage range. Also, it is hoped that future studies will lead to a better understanding of the nature of the mucus gel network and the role played by serum proteins during disease.

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