evidence points to formation of reticulum fibers in tubercles between 1 week and 14 days following infection (*3, 5*). As far as can be determined from a careful survey of the literature, such early occurrence in human infection has not been reported. This is not surprising since most autopsied cases from which material is obtained are relatively late cases and have evidence of caseation necrosis.

Recently we were able to study (*6*) the spread of early tuberculosis in a 4-year-old child, who had died as a result of poisoning. In this case, the primary tubercle lay just beneath the mucosa of a small bronchus and induced a bronchial spread of the infection, with extremely minute and early tubercle formations ranging from a few lymphocytes and monocytes in the smaller alveolar ducts to early tubercle formations, quite like the early experimental infections produced by Opie (*7*). The photomicrographs of these new structures show well-formed reticulum being laid down as soon as a few monocytes and lymphocytes have gathered into a knot (Figs. 1 and 2).

Fig. 1 (Top). An accumulation of large mononuclear cells and lymphocytes in an early tubercle. The reticulum is spread both over the surface of the mononuclear cells and between the cells. Note that some of the lymphocytes are meshed in the reticulum. Fig. 2 (Middle). Note abundance of reticulum surrounding and interlaced among the mononuclear cells. This is a pre-giant cell stage. Fig. 3 (Bottom). This section from an area of normal lung shows an arrangement of reticulum fibrils about a bronchiole continuous with fine fibrils in the alveolar walls. The reticulin stain used in these sections was that of Wilder (*9*).

Preparation of reticulum stains from normal lung areas in sites where the earliest tubercles are found show modest amounts of reticulum to be peribronchiolar and perivascular, and continuous in fine meshwork in alveolar walls (Fig. 3).

In the sections with tubercles, although reticulum is occasionally seen surrounding lymphocytes, our findings are similar to others in that the lymphocyte seems incapable of forming reticulum; however, once argyrophile fibers are laid down, lymphocytes may be found in their mesh. The reticulum fibers in our sections were around and among monocytes. Reticulum is found in the seven- to nine-cell accumulation stages of earliest identifiable tubercles and here appears at the earliest monocyte exudative phase. Observations of older tubercles are similar to others previously reported in that the fibers were most dense around the edge of the primary tubercle and where there are giant cells. In comparison of the reticulin stain with hematoxylin and eosin stains of the same lesion, we believe the reticulum fibers to be interjacent to but distinct from the fibrin. It was also interesting that under lower-power magnification, the distribution of the lesions in this case showed an intimate connection of the early tubercle lesions to small terminal bronchioles and alveolar duct walls. Acidfast stains on the lesions were positive for tubercle bacilli.

Miller (*1, 5*) reports the occurrence of reticulum in tubercles prior to formation of giant cells, but these tubercles are obviously in a more advanced stage than those reported here. Fresen (*2*), in 1950, in early human cases studied with silver stains, reported observations leading to the belief that epithelioid cells originated from reticuloendothelial cells and that epithelioid cells formed reticulum. Although reticulum formation has been extensively studied, most authors have not considered that reticulum occurs at the stage exhibited here.

Tuberculosis still remains an important infectious disease with a high mortality. Current work, such as that of Lurie (*8*) on the spreading effects of ACTH and cortisone, and also studies on chemotherapeutic agents in tuberculosis, should include investigation of the effects of these agents on early reticulum formation.

ANDERSON NETTLESHIP
MAE NETTLESHIP
Department of Pathology, University of Arkansas Medical School, Little Rock

References and Notes

1. W. S. Miller, *Am. Rev. Tuberc.* 7, 141 (1923).
2. O. Fresen, *Klin. Wochschr.* 28, 194 (1950); *Beitr. Klin. Tuberk.* 104, 104 (1950).
3. N. C. Foot, *Am. J. Pathol.* 1, 341 (1925).
4. A. R. Rich, *The Pathogenesis of Tuberculosis* (Thomas, Springfield, Ill., 1953).
5. W. S. Miller, *Am. J. Pathol.* 3, 217 (1927).
6. This report is a partial summary of work reported before the Southwestern Section of the Society for Experimental Biology and Medicine at Oklahoma City, Okla., 18 Nov. 1955.
7. E. L. Opie and B. J. Barker, *J. Exptl. Med.* 10, 645 (1908).
8. M. B. Lurie *et al.*, *Ann. N.Y. Acad. Sci.* 56, 779 (1953).
9. H. C. Wilder, *Am. J. Pathol.* 11, 817 (1935).

21 September 1955

Sweetpotato Internal Cork Virosis Indexed on Scarlett O'Hara Morning Glory

The internal cork disease of the sweetpotato (*Ipomoea batatas* L. Lam.) was discovered in the 1944 South Carolina crop and diagnosed as a virus disease by Nusbaum (*1*). Transmission of the necrotic spot root symptoms was demonstrated by root-plug grafting with an attending long incubation period of approximately 1 year. Since 1944 the disease has spread throughout most of the states growing the crop.

This situation posed the need for an indexing host with a shorter incubation period than sweetpotato. The prime essential was to find an indicator host better suited for studying the nature of the causal virus in order that more rapid progress could be made in studies designed for control of the disease.

By manipulation of the growth status and physiological behavior of peach seedlings, the incubation period of yellow-red virosis was shortened to 3 weeks from 1 to 3 years (*2*). Like the woody plant viruses (*3, 4*) for which grafting is often the only feasible means of transmission, internal cork virus has thus far been transmitted only by grafting. Ideally, an indexing host should be one

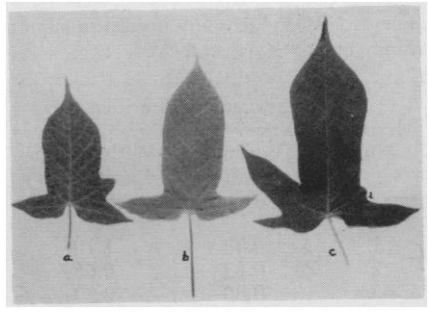

Fig. 1. Internal cork virus symptoms induced on Scarlett O'Hara morning glory by modified Yarwood technique (*7*): *a* leaf No. 4, 9 days after inoculation; *b* chlorotic condition that usually follows about 2 weeks later; *c* leaf No. 3 from base of stem and immediately below *a*, only leaf No. 1 having been inoculated.

that can be infected by mechanical inoculation and that has a short incubation period. When such an indexing plant is used, both growth status and environment control (*5*, *6*) are very important.

In late 1954 at the Plant Industry Station, Beltsville, Md., a systematic procedure was developed for finding an indexing host employing several methods of transmission including dodder, grafting, insect and mechanical methods and involving the sweetpotato and its relatives.

This report gives the results obtained by using a modification of the Yarwood (*7*) method of mechanical transmission, employing the freshly cut edges of leaf and necrotic root tissue. It singles out Scarlett O'Hara morning glory (*Ipomoea* sp., *8*) as a remarkably good indicator or indexing host.

The pot-label techniques of mechanical inoculation—of rubbing infected tissue between two pot labels and involving an exposure of 3 to 5 seconds—failed. However, the squeezing action of a flat-tipped tweezers forces virus extract out onto the wounded, buffer-carborundum-coated leaf surface, exposing the virus but a fraction of a second before it can enter leaf tissue. This morning glory is a rapid grower and may unfold as many as one leaf each day. Symptoms begin to show on the younger leaves, usually well above the point of inoculation. The incubation period is extremely short, ranging from 7 to 15 days, 8 to 11 days being most common. Among the numerous varieties and species under test, the only clearcut symptom picture was obtained on Scarlett O'Hara morning glory when the inoculum source was sweetpotato leaves with purple rings (induced by scion grafting) and roots containing necrotic tissue. The first symptom is a vein-banding mottle, and often the leaves are reduced in size and take on a variable chlorotic aspect (Fig. 1). Most infected plants are dwarfed somewhat but produce blossoms and apparently virus-free seed. During the past 7 months many experiments have been conducted successfully using this technique.

E. M. Hildebrand

Plant Industry Station
U.S. Department of Agriculture
Beltsville, Maryland

References and Notes

1. C. J. Nusbaum, *S. Carolina Agr. Expt. Sta. Bull. 381* (1950).
2. E. M. Hildebrand, *Contribs. Boyce Thompson Inst.* 11, 485 (1941).
3. ———, *Science* 95, 52 (1942).
4. ———, *Proc. Am. Soc. Hort. Sci.* 43, 124 (1943).
5. ———, *Cornell Univ. Agr. Expt. Sta. Mem. No. 323* (1953), p. 1.
6. ———, *Plant Disease Reptr. Suppl. 222* (1953), p. 185.
7. C. E. Yarwood, *Plant Disease Reptr.* 37, 501 (1953).
8. Scarlett O'Hara morning glory is an *Ipomoea* hybrid (*I. bona-nox* L. × *I. hederacea* Jacq.) with two distinctive leaf shapes: (i) hastate or long shield shaped and (ii) 3-lobed or maple leaf shaped. The leaf shapes come true from seed but are usually mixed when common seed sources are used. Taxonomists now commonly employ *Calonyction aculeatum* L. House for *I. bona-nox*.

14 September 1955

Microfoundations

I would like to suggest the term *microfoundation* to complete the spectrum whose other end is occupied by the Ford Foundation. According to a recent editorial [*Science* **122**, 1253 (1955)] the small foundation is typified by an endowment of $2 million and so really belongs toward the middle of the spectrum. The Holter Research Foundation is a microfoundation operating on the income of an endowment of well under $50,000. It is an operating microfoundation with one full-time physicist, one full-time unpaid biophysicist, and one part-time unpaid technician.

The small foundation undoubtedly produces more per dollar per man-hour than the large foundations, because of greater ease of administration and simpler public relations problems. I do not know whether this condition can be extrapolated to the microfoundation.

The microfoundation is not blessed with any committees whatever, and every man-hour, outside of janitoring, can be used for the drawing board or the soldering iron. We at Holter stick the invoices in a drawer, and if the funds get low we wait until the next month's budget before purchasing anything more. Our results, although not spectacular, have adequately justified our existence through various original contributions in the fields of physics, medicine, and education. We may or may not be typical of microfoundations. The productivity unit is, of course, hard to define, particularly when quality is involved. Using publications by professional journals, for lack of any better criterion, as an index of at least passable quality, it might be interesting to find which size foundation produces the most results per dollar, per man, per year.

Edmond G. Toomey

Board of Trustees, Holter Research Foundation, Helena, Montana

13 January 1956

Mean Rate of Change and a Graphic Method for Its Evaluation

Given a set of data represented by n points P_i (x_i, y_i) on ordinary rectangular graph paper, with the x_i not necessarily regularly spaced, the determination of the mean rate of change of the dependent variable y is often a problem of practical importance (*1*). Merely taking an arithmetical average of the $n-1$ slopes $m_i = \left(\frac{y_{i+1}-y_i}{x_{i+1}-x_i}\right)$ of the segments joining successive points is not very satisfactory, since the presence of two points with almost equal abscissas but widely separated ordinates would lead to a numerically large slope (for example, P_1P_3, Fig. 1) and excessively distort the final average. This difficulty can be eliminated by using a weighted average, taking the difference in x-coordinates $x_{i+1}-x_i$ as the weight w_i to multiply each slope m_i. However, this results in telescoping sums, and the final formula would depend on only the first and last of the observed data (which are generally more subject to experimental errors than intermediate determinations):

$$\frac{\Sigma wimi}{\Sigma wi} = \frac{\Sigma(y_{i+1}-y_i)}{\Sigma(x_{i+1}-x_i)} = \frac{y_n-y_1}{x_n-x_1}$$

In an effort to develop a formula more representative of the entire series of values, the following plan proved to be the most effective. Consider joining on the graph pairs of points P_i and P_j in all possible ways and assigning to each slope

$$m_{ij}\left(=\frac{y_j-y_i}{x_j-x_i}\right),$$ the weight w_{ij} equal

to the difference x_j-x_i between the corresponding abscissas. The weighted average

$$\frac{\Sigma w_{ij}m_{ij}}{\Sigma w_{ij}} \quad (1 \leqq i < j \leqq n)$$

of the slopes of *all* of these segments provides the following formula, which is easily derived algebraically (*2*).

Mean rate of change (m.r.c.) =

$$\frac{\Sigma(2i-n-1)y_i}{\Sigma(2i-n-1)x_i} \quad (i = 1, 2, \ldots, n) \qquad (1)$$

For example, with $n = 6$, m.r.c. =

$$\frac{-5y_1-3y_2-y_3+y_4+3y_5+5y_6}{-5x_1-3x_2-x_3+x_4+3x_5+5x_6}$$

It has been found advantageous to renumber the subscripts so that they will be centered about zero. Thus, for $n = 5$, the points may be thought of as P_{-2} (x_{-2}, y_{-2}), P_{-1}, P_0, P_1, P_2; for $n = 6$, the subscripts may be relabeled to read P_{-5} (x_{-5}, y_{-5}), P_{-3}, P_{-1}, P_1, P_3, P_5. In general, when n is odd, let $n = 2m+1$, and then $h = -m, -m+1, \ldots, -1, 0, 1, \ldots, m$. When n is even, let $h = -n+1, -n+3, \ldots, -1, 1, 3, \ldots, n-1$.

With this change made, formula 1 takes the following more convenient form:

$$\text{m.r.c.} = \frac{\Sigma hy_h}{\Sigma hx_h} \qquad (2)$$

For example, with five points, desig-