the area becomes fully vascularized from below with a plexiform pattern of small vessels (Fig. 1*h*, the same burn at day 56). Gradually the appearance of the area returns toward normal, but although the vascular pattern is less distinct it is still abnormal at day 99 (Fig. 1*i*). On gross examination after 9 months the area appears as a faint white atrophic scar, yet an abnormality in the microcirculation is evident: the subpapillary vessels are somewhat enlarged and more prominent than in normal skin. Examination of scars from superficial trauma or burns more than 2 years old does not reveal any of these changes which apparently are completely reversible.

In abrasions the same developments were seen (Fig. 2) 21 days after a thin strip of epidermis was removed with a razor. Many small capillary loops "bud" from large deeper vessels within the injured area.

In accidental lesions horizontal orientation of surrounding capillaries was clearly apparent. Figure 3 shows a burn, infected, and now healing at 19 days, and Fig. 4 shows a cat scratch, which, though very narrow, illustrates the typical pattern of the capillaries surrounding the lesion. The same changes were also seen around actively developing keloids.

Histologically, the changes that occur are those to be expected from the in vivo pattern. The edge of the healing burn at 10 days (Fig. 5*a*, *b*) shows small dermal papillary vessels pointing horizontally toward the burned area. The vessels show evidence of active growth, with some proliferation of the endothelium, and are abnormal when compared with the normal vessels in a nearby area (Fig. 5*c*).

Blood vessels grow into and revascularize all healing tissues. In our study, this is seen in the response of the deeper dermal vessels as they grow into the lesions from below. However, the striking reaction of the papillary capillaries surrounding the injured area, particularly those several millimeters from the wound, was unexpected. Since only the vessels immediately adjacent to the wound revascularize its edges and since the vessels farther away do not provide significant revascularization, even though they are inwardly oriented, the possibility of a potent attracting factor was suggested. Such a factor, conceivably a chemical produced by the injured tissue, apparently attracts the capillaries and causes a progressively more horizontal orientation and growth toward the wound. The potency of this hypothetical factor can be estimated by its ability to influence capillaries even several millimeters away from the lesion. In general, the size of the wound is related to the distance at which capillary changes occur and suggests a diffusible attracting substance (see Figs. 3 and 4).

In burns the surrounding skin may suffer some thermal injury, however, the possibility of such a direct effect can hardly explain the occurrence of the same phenomenon around the more sharply circumscribed lacerations and abrasions. Furthermore, the surrounding pattern of horizontally oriented capillaries pointing toward the lesion does not appear to be a mechanical result of contraction of the wounds, for these clearly widen during the first few days after experimental injury (see Fig. 1*b* and subsequent figures). Sliding of the epidermis over an injured area to provide re-epithelialization is a well-known occurrence; however it cannot be responsible for the capillary changes observed. The epidermis is avascular and the capillaries that are involved are located in the upper corium; hence the epidermis could not pull the vessels mechanically with it. Movement of the corium *en bloc* toward an area of superficial trauma does not seem likely.

This pattern of horizontal orientation of the cutaneous capillaries occurs around lesions in several skin diseases, for example, erythema multiforme and dermatitis herpetiformis (*3*); psoriasis and lichen planus (*4*); dermatomyositis, milium, lichen ruber planus, and erythema induratum (*5*); and also around healing leg ulcers due to venous insufficiency (*6*). However, the general nature of these changes has gone unrecognized, the pattern apparently having been attributed to the characteristic pathology of the lesions. Our studies suggest that the horizontal orientation of these capillaries is actually part of a normal general response to injury and an attempt to heal the lesion.

JAMES G. ZIMMER
D. JOSEPH DEMIS
Department of Dermatology, Walter Reed Army Institute of Research, Washington 12, D.C.

References

1. M. J. Davis and A. L. Lorincz, *J. Invest. Dermatol.* **28**, 283 (1957).
2. J. G. Zimmer and D. J. Demis, *ibid.* **39**, 501 (1962).
3. J. C. Michael, *Arch. Dermatol.* **8**, 603 (1923).
4. O. Gilje, P. A. O'Leary, E. J. Baldes, *A.M.A. Arch. Dermatol.* **68**, 136 (1953).
5. O. Gilje and E. Mylius, *Excerpta Med. Intern. Congr. Ser.* **52**, 130 (1962).
6. O. Gilje, *Acta Dermato-Venereol. Suppl. 22*, **29**, 1 (1949).

14 January 1963

Reovirus and Wound-Tumor Virus: Serological Cross Reactivity

Abstract: *Reovirus and wound-tumor virus share a common antigen capable of fixing complement. This suggests a relationship between these animal-pathogenic and plant-pathogenic viruses.*

The human-pathogenic reoviruses formerly known under the name of ECHO type 10 (*1*) are very widely distributed throughout the world and have been found among numerous representatives of the animal kingdom, either directly, or through the presence of specific antibodies (*1*). The plant-pathogenic wound-tumor virus can infect several species of plants in dozens of families (*2*) and, in addition, can infect at least three related species of agallian leafhoppers that act as biological insect vectors (*3*). The wound-tumor virus also infects transovarially a low percentage of the offspring of its insect carrier (*4*).

Reoviruses and wound-tumor virus are very similar morphologically (*5*). The structure of the wound-tumor capsid is closely similar to that of the reoviruses capsid, as shown in separate descriptions in the literature (*6*). The similarity is emphasized by the appearance of the capsid into which phosphotungstate has penetrated. Both viruses contain ribonucleic acid. According to Black and Markham (*7*), the wound-tumor ribonucleic acid is double-stranded.

In view of the morphologic similarity, it was of interest to study the possible serologic relationship between reoviruses and wound-tumor virus (*8*). This problem was informally discussed in Montreal in 1962, during a session of the Virus Subcommittee, eighth International Congress of Microbiology. The discussion centered around similarities in virus morphology, serology, and other characteristics as criteria for groups of related viruses. It then be-

came apparent that reoviruses and wound-tumor virus might belong to the same group, provided they are serologically related.

Serologic tests were facilitated by the availability of wound-tumor antiserum (*9*) prepared against highly purified wound-tumor virus extracts of plant tumors. The reovirus titers were $10^{-5.5}$ tissue culture infective dose (50/ml) for each strain (*10*). Because there is a common complement-fixing antigen in the three reoviruses (*1*), it was decided to use complement fixation for the tests. The reovirus antigens were the respective three strains of virus, grown in monkey kidney cells with Earle's basic salt solution, 10 percent lactalbumin hydrolyzate, and fetal calf serum, diluted 1 to 4 in veronal buffer at *p*H 7.2.

For preliminary experiments, a constant concentration of antigen and antiserum was used with complement at various dilutions. The results indicated that more complement was used with reovirus I, II, and III and wound-tumor antiserum than in the controls with either normal antigen plus wound-tumor antiserum, or reoviruses I, II, and III and normal serum. The normal serum was obtained from untreated healthy rabbits. The normal antigen consisted of monkey kidney cells in Earle's basic salt solution, 10 percent lactalbumin hydrolyzate, and fetal calf serum, diluted 1 to 4 in veronal buffer at *p*H 7.2.

The positive results of preliminary tests were followed by a quantitative assay with the technique described for wound-tumor complement fixation by Windsor (*11*) and by Ellen M. Ball (*12*). Twofold serial dilutions of antigen and antiserum were made up to a dilution of 1:128 and tested against each other in a grid titration. Complement fixation took place up to and including a dilution of wound-tumor antiserum of 1:128, and of reovirus antigen dilution of 1:64, while the controls remained negative at 1:64 and 1:128.

There seems little likelihood that any normal plant antigens may have contributed to the reaction since the control tests were negative at the higher dilutions. As pointed out by Sabin (*1*), the presence of small amounts of reovirus antibodies can always be expected in normal sera. The results indicate the presence in the normal serum of a component that reacted at a dilution of 1:32 with reovirus antigen.

Serological relationship between a human (animal)-pathogenic virus and a plant-pathogenic virus has thus been indicated. It is recognized that this evidence is only strongly suggestive but not conclusive. Before these results can be accepted as final, further tests will be required, including antiserum end-point titration, reciprocal reactions between reovirus antiserum and wound-tumor antigen, and controls in which serum from animals injected with healthy plant material are employed. Attempts will also be made to obtain normal serum from animals that lack reovirus antibodies.

Ordinarily, relationships would not be evident between seemingly widely separated viruses. The significance of such observations has been discussed recently by Macleod and Markham (*13*). Certainly, similarities in host range can hardly continue to be considered as criteria for relationships among viruses (*14*).

This reported serological relationship between reoviruses and wound-tumor virus is, to our knowledge, the first known instance of a common complement-fixing antigen between a human-pathogenic and a plant-pathogenic virus. The wound-tumor virus causes tumors in several plant species and it has been shown to multiply not only in plants but also in insect vectors (*15*). It can be transmitted easily to its insect host by needle inoculation (*16*), but only in a low percentage of cases can it be introduced mechanically into susceptible plants (*2*). The similarity in morphological structure and serological relationship indicates that wound-tumor and reoviruses should be classified as belonging to the same group. An effort is being made to establish whether agallian leafhoppers can be rendered "plant infective" by the three reovirus strains. If so, will the reoviruses cause a plant disease distinguishable from the wound-tumor disease?

The finding of a complement-fixing antigen common to both reoviruses and wound-tumor virus would have far-reaching implications in the study of virus reservoirs, virus survival in nature, fundamental aspects of virus-host interactions, and in public-health problems. It might also influence ideas concerning the origin of viruses (*17*).

GERT STREISSLE*
KARL MARAMOROSCH
Boyce Thompson Institute for Plant Research, Yonkers, New York

References and Notes

1. A. B. Sabin, *Science* **130**, 1387 (1959).
2. L. M. Black, *Handbuch der Pflanzenphysiologie*, vol. 15 (Springer, Berlin, in press).
3. ———, *Proc. Am. Phil. Soc.* **88**, 132 (1944).
4. ———, *Phytopathology* **43**, 9 (1953).
5. K. Maramorosch, *Ann. Rev. Entomol.* **8**, 369 (1963).
6. C. Vasquez and P. Tournier, *Virology* **17**, 503 (1962); R. F. Bils and C. E. Hall, *ibid.* **17**, 123 (1963).
7. L. M. Black and R. Markham, *Neth. J. Plant Pathol.*, in press.
8. The impetus for beginning this investigation was provided by Dr. Albert B. Sabin, who first suggested this problem to us.
9. Kindly supplied by Dr. L. M. Black, University of Illinois, Urbana.
10. Made available through the courtesy of Dr. Maurice R. Hilleman, Merck Research Institute, West Point, Pa. Additional reovirus was purchased from the American Type Culture Collection.
11. I. G. Windsor, M.S. thesis, University of Illinois (1956).
12. University of Nebraska, personal communication.
13. R. Macleod and R. Markham, *Virology* **19**, 190 (1963).
14. K. Maramorosch, *Trans. N.Y. Acad. Sci.*, in press.
15. L. M. Black and M. K. Brakke, *Phytopathology* **42**, 269 (1952).
16. K. Maramorosch, M. K. Brakke, L. M. Black, *Science* **110**, 162 (1949).
17. Supported in part by U.S. Public Health Service grant AI-04290.
* On leave from the German Federal Research Institute for Animal Virus Diseases, Tuebingen. Present address: BFA, Viruskrankheiten der Tiere, Waldhaeuser Hoehe, Tuebingen, Germany.

18 April 1963

Base Composition of the RNA of a Reovirus Variant

Abstract. *A variant of reovirus 3, Dearing strain, isolated after repeated passage of the original Dearing virus in L cells, is similar to the parent virus in many ways. It is, however, less sensitive to specific antibodies and metabolic inhibitors, and is released from L cells to a lesser extent than the original virus. Calculated as moles per 100 moles of total base in RNA, the percentage of guanine is 20.2, adenine, 29.8, cytosine, 21.0, and uracil 29.1. These values closely approximate those reported previously for the parent virus.*

Reovirus type 3 contains a minimum complement of 10.2×10^6 molecular weight units of RNA per particle (*1*), an amount larger than that present in any other RNA-containing virus thus far examined. Furthermore, reovirus RNA appears to have a secondary structure similar to that of DNA (*1*). The ratios of its bases are complementary. Reovirus RNA melts sharply in a narrow