CLINICAL CAPILLARY MICROSCOPY

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The pages of this volume mirror a vital science . . . pointing up the importance of capillary microscopy as part of the routine comprehensive medical examination. The authors have used human clinical biomicroscopy at several sites as an integral part of the full examination of 16,000 patients and in the systematic study of the small blood-vessels in health and disease.

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CLINICAL CAPILLARY MICROSCOPY

"Put it into our hearts to understand and to discern, to listen, learn and teach, to heed and to do . . ."

Acknowledgments

WE GRATEFULLY recognize the warm cooperation of our patients in London from 1941 to 45, and in Jerusalem from 1946 to the present.

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E. D.
J. L.

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PART I

Chapter 1

Introduction

WHAT is the place of capillary microscopy, a technique dependent on light microscopy, in these days of electron microscopy and television microphotometry? In human biomicroscopy, only rarely can we see vessels clearly at magnifications of 250 and usually the optimum magnifications are 100 at the nailfold, twenty-five in the conjunctiva and sixteen in the lip and tongue. Apparatus and techniques for human vital microscopy do exist for examining at magnifications of nearly 1000, but these methods are too elaborate for routine use or for examining large numbers of sick patients. With the more usual methods, only the capillary lumen with its column of blood is seen and the vessel wall is only occasionally visible. With special techniques, the wall can be seen at magnifications of about 200 to 300, but very little useful information is gleaned.

In these days of detailed examination of the ultrastructure of a minute area, it is believed to be more important than ever to get the "bird's eye view," to see a functional segment of tissue and to think in terms of the whole body and the whole patient. Otherwise, there is danger of not seeing the forest for the trees. On biomicroscopy, there is seen a natural view of undisturbed vasculature without anesthetics, without trauma. There is seen a functional unit of tissue and it is possible to make certain measurements without disturbing the patient, and without the method of taking the measurement altering the measurement. It is true that what is seen and measured is only rarely of diagnostic value and only on limited occasions characteristic of a particular disease. But the patient has been examined more fully and there is a better understanding of what is going on within him when the physician or medical scientist has become acquainted with the state of the small blood vessels at several sites in the body. After all, in the whole of medicine, few examinations are pathognomonic and only a small number are characteristic. There is no substitute for examining the patient as a whole. The shortcuts to diagnosis are strewn with pitfalls. But it is hoped that this book will show that it is worth while including biomicroscopy in the systematic examination of patients. Although information of special value is gleaned and valuable clues to diagnosis are elicited only occasionally, in many cases useful information is gathered and in all cases the findings, whether negative or positive are of interest.

In the nailfold, a group of capillaries or even a single capillary can be studied for years because they remain nearly always readily identifiable. In the conjunctiva, information is elicited about a network of vessels and this is a unique site for the study of micropools and intravascular red cell aggregation. In the lip, a mobile network of small vessels is open to study and the vessels of the tongue have special characteristics. Whether the results of the biomicroscopy examinations are negative (as is usual) or positive but nonspecific or characteristic, in every case, something has been learned about our patient as a whole. It is maintained that capillary microscopy should be part of a routine comprehensive medical examination.

A wealth of clinical information about the small vessels has accumulated from all over the world and some remarkable photographic studies are available. In this book, we have concentrated in the main on major common medical diseases and have stressed personal work using our own photographs. There is brief reference to the relevant literature, and many of the key papers opening up the whole field are documented. The book contains pictures of most of the usual findings and many of the rarer findings. The relevant pictures have been selected from over 5500 of our photographs. Special attention has been paid to the wide range of the normal — indeed, the greater one's experience the vaster the range of the normal. New workers in this field using this book will be able to avoid many of the pitfalls awaiting the beginner in microcirculation. Experienced workers might be glad to compare photographs and findings, and here and there may find a ray of light on some of their problems. The use of the book as a photographic atlas should prove useful and helpful. For example, an observer finding a particular phenomenon or a particular pattern will often be able to identify it here, find there is no need to photograph, and so contribute to the patient's convenience. Of course, investigators studying changes in particular patients will need to take a series of photographs, although a certain number of experiments on different patients can be identified by the use of the pictures here given. For example, in hypertension, various ganglion blocking drugs and the standard sympatholytic drugs have produced identical visible effects on the small blood vessels (Figs. 237-8).

The diligent worker should spend some time in one of the many microcirculatory laboratories and attach himself to an experienced teacher. Photography of the small vessels should be studied under an expert. One caution to the new worker in the field: The range of the human normal is very wide indeed. Considerable experience is needed before drawing conclusions that what is before us is abnormal or pathological, and controlled work is always necessary.

Many of the scientists cited in this work have aided us in the clarification of many problems in seminars and symposia and in discussion in their laboratories and in ours. For their cooperation we are grateful and it is hoped that the following pages will mirror a living vital science.

Chapter 2

Historical Note

ABOUT 300 years ago, Swammerdam and Leeuwenhoek discovered the erythrocytes, while Malpighi and Leeuwenhoek revealed the microcirculation. They identified the capillaries and the red cell blood cells within them. Boerhaave, around the beginning of the 18th century, made original studies on the conjunctival vessels and noted the intravascular aggregation of the erythrocytes in fever. Cowper, in London in 1704, followed the flow of the blood from arterioles to veins. Progress became rapid and gained momentum in many countries. Nasse (1836) found that increased blood sedimentation rate was caused by the increased aggregation of the erythrocytes. The early history of the microcirculation is scholarly recorded by Fåhraeus (1960) with an appropriate bibliography. For over a hundred years, the conjunctival capillaries have been studied systematically by biomicroscopy. An insight into the history of the microcirculation is given in the comprehensive papers of Illig (1961a), Bloch (1956), Knisely (1961) and Müller's (1922) book. Milestones in the progress of microcirculation were the founding of the American Microcirculation Conference (Bloch and Irwin in 1954) and the European Society for Microcirculation (Harders and Gelin in 1960).

Great impetus was given to the work on capillaries in recent decades by the studies, among others, of Krogh in Copenhagen, Lewis in London, Müller in Tübingen, Fåhraeus in Uppsala and Chambers and Zweifach, Clark and Knisely in the United States. Lombard (1912) initiated a new phase when he noted that the nailfold capillaries can be seen by putting a drop of immersion oil on the nailfold and viewing with an ordinary laboratory microscope with good lighting.

Basic work on the microcirculation with a predominantly experimental approach in animals is now pursued in many laboratories all over the world. Reference to some of these studies will be made.

BIORHEOLOGY

In the last forty years, the science of rheology has developed. Bingham in 1929 defined rheology as the "science of deformation and flow." Following the work of Bingham and also of Reiner, the specialties of biorheology and hemorheology became differentiated, as scientists worked on the mechanical behavior of the fluids, mainly blood, and the vessels and tissues involved in the various parts of the circulatory system. The journal *Biorheology* was founded by Copley and Scott Blair in 1963. Many are contributing to these vigorous disciplines. Key references will be given and Copley (1965) should be consulted. Weissenberg, and Wayland have helped integrate biorheology with microcirculation.

Chapter 3

Methods And Sites Of Examination

NAILFOLD

ANYONE possessing a standard microscope for use in routine medical laboratory work can begin a study of the capillaries of the nailfold. Good lighting is essential. Any good lamp will do. We use the American Optical Company lamp Model 370 which is tiltable and has an adjustable diaphragm in front of the bulb for modifying the amount of light. Observation is facilitated by the use of a strong table with a thin top with grooved finger rests to fit over the microscope stage. It is useful to fit the legs of this table into holes on a strong wooden base. The microscope is also placed over this base, and its stage under the table top. This arrangement allows for steadiness of the microscope and hand during observation and photography. A flask, containing water tinted with Loeffler's methylene blue reagent, placed between the lamp and the finger helps in focussing the light beam on the nailfold (which is covered with a drop of immersion oil). The flask prevents heating of the finger and aids in getting good contrast of the capillary against the tissue background. The lamp and flask are raised above the microscope base on a special platform. For ordinary observation of the nailfold vessels, the standard microscope is superior to the so-called capillary microscope and has the further advantage that it can be used for routine medical microscopy. With good lighting, the highest useful magnification with a regular microscope is x 60, usually.

However, for routine observation at x 100 and greater magnifications, and also to get good results with photography, a more elaborate microscope is necessary. The available leading research microscopes are excellent. But, since nailfold capillary photography has to be done with incident light, for photography, a special lamp is necessary, such as the high performance microscope lamp with a high-pressure mercury bulb. The relevant standard photographic accessories are all available. If this kind of microscope is acquired, the observer should use it routinely to benefit from the superior optics and the binocular vision. We have fitted a grooved finger rest on to the standard mechanical stage of the research microscope, and the screws on the mechanical stage can be used for fine adjustments of the position of the finger. This arrangement replaces the table over the microscope stage, but we put the table alongside the microscope on the side of the patient so that he has a convenient rest for his forearm when observing. The research microscope has a heavy base which obviates the need for the wooden base. When using the high performance lamp (with a cooling filter), the flask is not used. When using the research microscope for observation and not for photography, the simpler lamp is fully adequate.

The advantages of the nailfold site as a study area are the relatively simple equipment required, photographs are obtained with high magnification on the negative (up to x 100 but usually x 37.5 or x 62.5), and a group of readily identifiable capillaries and even a single identifiable capillary can be studied for months and