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IN MEMORY OF SYOTEN OKA - BIORHEOLOGIST AND PERSON

OKA'S THEORIES BEARING ON THE VESSEL-BLOOD ORGAN AND ITS EEFL INTERFACE

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It was in 1960 when I first met Professor Syoten Oka in Tokyo, after a Special Lecture I gave on 'Hemorheology - An Introduction', with George W. Scott Blair as co-author, before the 8. Congress of the International Society on Blood Transfusion (1). I was surprised to see Professor Bun'ichi Tamamushi, the colloid and surface chemist, whom I had met a few years earlier in England and thereafter at the 3. International Congress on Rheology, held in 1958 at Bad Oeynhausen, Germany. He introduced me to the physicist Syoten Oka and two of his associates immediately following the lecture. One of them was the physicist Professor Eiichi Fukada.

Key Words: Apparent viscosity, atherogenesis, atheroma, biorheology, blood flow, Copley-Scott Blair phenomenon, EEFL, endoendothelial fibrin(ogenin) lining, erythrocyte sedimentation, fibrin-coated capillaries, hematocrit, hemorheology, LDL, LDL desorption, low density lipoprotein, mathematical interpretation, negatively charged tube, Oka's electrostatic theory, red blood cells, shear stress, vascular permeability, vessel-blood organ.

During this first visit to Japan, I met several times with Syoten Oka and Bun'ichi Tamamushi. At that time we discussed many problems regarding the new science of biorheology and hemorheology, its most active branch. Recently I redefined hemorheology as the biorheology of the vessel-blood organ. The interface between its two portions is the endoendothelial fibrin(ogenin) lining (EEFL).

At one of my meetings in 1960 with Syoten and Bun'ichi I mentioned that Mr. Robert Maxwell, Publisher of Pergamon Press, initiated in 1959 the journal BIORHEOLOGY and invited me and George W. Scott Blair to act as its Editors-in-Chief. The journal started publication in 1962 with Syoten Oka as one of its Editors and with the cell biologist Professor Noburo Kamiya of Osaka as well as the pathologist Professor Satimaru Seno of Okayama as Members of the Honorary Advisory Editorial Board.

Syoten Oka and I met on each of my subsequent five visits to Japan as well as during international congresses in USA, European countries, Israel and Japan. We became friends. I regretted very much that due to Syoten Oka's illness we could not meet in 1989 during my visit to Japan.

The science of rheology was first introduced in Japan by Bun'ichi Tamamushi. Noburo Kamiya was already well known internationally for his outstanding research on the biorheology of cytoplasm. In my Plenary Lecture on 'Rheological Problems in Biology' at the 1. International Congress on Rheology, held in Holland in 1948, I referred in some detail to Kamiya's work (2). Neither Bun'ichi Tamamushi nor Syoten Oka were aware of Kamiya's studies when I met with them in Tokyo in 1960. It gave me special pleasure to learn that I had to come from New York to make this known to them. When I visited Noburo Kamiya in his laboratory at the University of Osaka after the Congress on Blood Transfusion in 1960, I told him about my acquainting Syoten Oka and Bun'ishi Tamamushi with his biorheological studies. Two years later I was very pleased to hear that my friends Syoten and

Noburo had met and were engaged in certain biorheological inquiries.

Prior to 1960 no work in hemorheology was done in Japan. In a communication 'Hemorheology in Japan: A Brief History' (3) I mentioned that my Special Lecture referred to above played a role, although a minor one, in hemorheological studies in Japan. These studies were started by Syoten Oka.

I was elated to secure funds from the Office of Naval Research, United States Department of the Navy for travel and subsistence to invite some thirty participants from many parts of the globe to the Symposium on Biorheology. I was asked to organize such a Symposium by the two Presidents R.S. Rivlin and R.S. Marvin of the IV. International Congress on Rheology, held in 1963 at Brown University, Providence, Rhode Island, USA. I was glad that Syoten Oka could be one of these participants with his communication 'Theoretical Considerations on the Flow of Blood Through a Capillary' (4). I also succeeded to have Noburo Kamiya as a Special Lecturer on 'Rheology of Cytoplasmic Streaming' (5), before the entire Congress.

In 1966 Syoten Oka participated in the 1. International Conference on Hemorheology, held at the University of Iceland, where he presented his communication 'Theoretical Approach to the Effect of Wall Surface Condition in Hemorheology' (6). It was in Reykjavik at this Conference, when Syoten Oka became Vice President of the newly founded International Society of Hemorheology, which three years later during the Society's 2. International Conference, held at the University of Heidelberg, Germany was renamed The International Society of Biorheology. It had its First International Congress in 1972 in Lyon, France. At all these and future congresses of the Society and other international scientific congresses and conferences Syoten Oka was highly active. I recall with great pleasure my co-chairing with him a Session on Biorheology at the XVI. International Congress of Hematology, held in Kyoto, Japan in 1968.

In 1975 the highly successful United States-Japan Cooperative *Seminar on Hemorheology* and Thrombosis was held in Kobe, Japan. It was organized by the United States-Japan Cooperative Science Program with Professor Shosuke Okamoto as Japan Coordinator, representing the Japan Society for the Promotion of Science, and me as the United States Coordinator, representing the National Science Foundation. Syoten Oka presented in this Seminar his important contribution 'A Theoretical Approach to the Effect of Shear Stress on the Development of Atheroma' (7). It was in this communication in which he stated that the development of atheroma was influenced by the transport of matter between blood and the vessel wall due to diffusion of cholesterol and proteins.

Syoten Oka developed a new physical theory, based on polymer physics and the theory of rate processes. He proposed that the principal vascular component is protein, the macromolecular chains of which are "held together by electrostatic forces and hydrogen bonds in addition to van der Waals forces". He stated further that "the chains are executing thermal segmental motion, by virtue of which cholesterol, or other accumulating material, is transported through protein system as a result of an elementary diffusion jump from one equilibrium position to the next over a potential-energy barrier. When the wall is sheared, weak van der Waals bonds may be broken down to some extent depending upon the magnitude and duration of the shear stress, which results in lowering the potential energy barrier for diffusing molecules, that is, in increasing its diffusion coefficient".

Oka's above mentioned theoretical approach was further developed in his paper 'Physical Theory of Permeability of Vascular Walls in Relation to Atherogenesis' (8). My theory of atherogenesis, first proposed in 1978, is associated in part with Oka's theoretical approach to atherogenesis. It relates to our surface hemorheological studies on fibrinogen systems with highly purified β-lipoprotein or low density lipoprotein (LDL), as well as on desorption of LDL (9,10). LDL desorption was found to occur in surface chemical studies by Miller et al (11). What is particularly important in Oka's theory is his postulation that the

structure of the polymeric system will change with the applied shear stress or stretch due to the energy supply. He considered that the originally tight structure of the macromolecular system changes into a loose structure which permits an easier transport of the diffusing molecules.

Birger Blombäck referred to recent epidemiological studies by Hamsten and coworkers. Their findings provide some evidence for the validity of my theory of atherogenesis, based on our surface hemorheological findings of interaction between low density lipoprotein and fibrinogen (12).

As I knew that Syoten Oka was interested in problems regarding erythrocyte sedimentation, I sent him a manuscript on our findings after it was accepted for publication (13). He responded with a theoretical treatment 'A Mathematical Interpretation of the Parameters Affecting Erythrocyte Sedimentation' (14), which was published as an Appendix to our paper (13). I appreciated greatly Syoten Oka's scientific cooperation in contributing his theoretical treatment to our experimental findings.

I am especially indebted to Syoten Oka for his keen interest in my theory of the EEFL. He was particularly concerned with my findings, first published in 1958, of decrease of apparent viscosity when the blood systems were in contact with fibrin as compared with glass and other surfaces, such as silicone. This phenomenon, which Copley, Scott Blair and our associates studied in more detail, was referred to by Oka as the 'Copley-Scott Blair Phenomenon'. In many publications Oka attempted to explain it. His first communication regarding this phenomenon was presented in Reykjavik in 1966 (6). Oka followed up this study with several other publications on the EEFL (15-17).

Syoten Oka's new electrostatic theory is of particular significance in relation to the EEFL. He presented it in September 1984 in Kurashiki, Japan at the Satellite Symposium of the Third International Congress on Cell Biology held in Tokyo (18). Oka's theory gives an explanation of the decrease in the apparent vis-

cosity of blood in negatively charged capillaries. He referred to the Copley-Scott Blair phenomenon of lowering of apparent viscosity in fibrin-coated glass capillaries. Oka stated that "the red blood cells bearing negative charge receive a repulsive electrostatic force at the entrance of the capillary from the negative charge of the capillary. The repulsive force causes a reduction in the hematocrit in the capillary, resulting in a decrease in the apparent viscosity of blood flowing in the capillary. This electrostatic effect becomes the more remarkable, the smaller the capillary becomes". Oka suggested "to measure the hematocrit in the negatively charged tube" to test his new electrostatic theory.

Oka referred also to our findings of significant decrease in the viscosity of plasma and serum in fibrin-coated capillaries. He contended that this phenomenon can likewise be explained by his new theory. Oka pointed out that "protein molecules in plasma and serum are negatively charged so that they receive an electrostatic repulsive force from the charge on the inner surface of the tube".

In his conclusions Oka stressed that the cells and tissues in biological systems are generally charged, so that his electrostatic theory "may well be applied to microvessels and to the permeability of charged substances into tissues".

Oka referred to the EEFL in many personal communications. His last four communications concerning it were in letters to me, dated from 14 September to 24 November 1987 (19), to which I referred in my last survey on the EEFL, published in 'Perspectives in Biorheology II, Festschrift for Syoten Oka' (20).

I was delighted when at the II. International Congress of Biorheology, held at Rehovot, Israel in 1975, I gave the Presentation Address at the Poiseuille Gold Medal Award Ceremony for Syoten Oka (21). It was published in a Special Issue of Biorheology dedicated to Syoten Oka (22).

From my above mentioned Presentation Address in 1975 I should like to quote the following: "Recently I wrote to Professor Eiichi Fukada of Japan and asked him to let me know something about Syoten Oka's interests outside of his pursuit of science. From a letter which I received in New York last week, a few days before my departure, I cite the following: "I think that he likes animals, since his character is so gentle and warm. He is loved by everyone who knows him" (21).

I also like to quote from the Presentation Address: "Those among us who, like me, have had the privilege and pleasure to meet Syoten Oka, either in his country, in a European country, such as Iceland, Germany, France, or in the United States will have been charmed by his warmth, his natural modesty, and, above all, by his feeling of wonder about the world. As any research scientist deeply feels, it is this wonder which is the source for any scientific inquiry into nature" (21).

As I expressed sixteen years ago, my relationship to my dear friend Syoten and my memories of this wonderful person are everlasting.

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ADDENDUM

Below is an excerpt from Syoten Oka's letter of 23 March 1990 to me. It was the last letter received from a very dear friend.

A. L. Copley

At the end of next June the annual meeting of Japanese Society of Biorheology will be held in Nara, an ancient city near Kyoto. I was invited to give a special lecture. I shall talk on some problems concerning the flow rate of blood in man under zero gravity. As you know, there are unknown factors at present. I want to point out two subjects: 1) Physiological adaptation of living things to the environment of weightlessness, and 2) The effect of plasma layer, or the slippage of blood flow at the vessel wall.

The Poiseuille's law had been derived under the assumption that blood flow shows no slippage at the vessel wall just as water does not slip at the glass wall.

I have read your manuscript: FLUID MECHANICS AND BIORHEOLOGY with great interest. The existence of slippage at glass surface coated with fibrin had been shown experimentally by you and Scott Blair. Morrison, Tordella, Benhow etc. have shown also slippage on other wall surfaces. The slippage of blood flow at the vessel