USSR PROGRESS IN THE FIELDS OF HEMATOLOGY AND BLOOD TRANSFUSION

Numbers in parentheses refer to appended sources.

Twenty-five years ago, the first institute of blood transfusion in the world was organized in Moscow. At present, this institute is called the Central Order of Lenin Institute of Hematology and Blood Transfusion (TsNOIFK, Department of Clinical Medicine, Academy of Medical Sciences USSR).

Being continually concerned with questions of public health and military-military defense, the institute expanded its activities and became the central organization directing all aspects of blood transfusion and hematology in the USSR. In the process of this expansion, a network of republican, rayon, oblast, and municipal affiliates (blood transfusion stations) was opened throughout the country by the institute. The municipal stations have the task of organizing blood-transfusion units at city district hospitals (rayonnye stantii). Among the affiliates of the Central Order of Lenin Institute, there are prominent scientific institutions like the Leningrad, Tbilisi, Kharkov, and Minsk institutes, to which special hematological clinics are attached.

The fundamental problem of blood transfusion, that of preserving blood, was successfully solved by the USSR scientists. Originally, in 1930, the blood could be preserved in a completely fresh (physiologically unchanged) state for only 2 weeks. This period has been extended to 30-40 days and is being extended still further at present. Considerable work has been done on the development of effective preservation media and antiseptics to be used in preservation. Both the Central Order of Lenin Institute and the peripheral stations participated in work which attempted to establish whether preserved blood is therapeutically equivalent to fresh blood. This question has been decided in the affirmative. One of the most recent achievements is development of the dextran-saccharose-citrate solution TsNOIFK No 6, which permits preservation of erythrocytic mass for 30 days without hemolysis. The erythrocytic mass can be thus transported to other cities.
In this connection, one may also mention the special ampules TsIPK (Central Institute for Blood Transfusion) No 1 and TsOLIPK No 2.

The antitoxic and antibacterial properties of blood are well known from clinical experience. This applies particularly to transfusions of immune blood for the treatment of infectious diseases. Work in this field has been done by N. N. Burdenko, V. V. Akkerman, S. P. Zayeva, K. M. Dvolyatskaya-Barysheva, and B. N. Babushkin. As far as the stimulating effect of blood transfusion is concerned, A. A. Bogomolova's hypothesis of colloidostatic shock is no longer adequate.

In the field of hemotherapy, extensive work on the effect of blood transfusions after heavy blood losses and shock has been carried out by the Central Order of Lenin Institute. The results of this work were of particular benefit during World War II. No less important is the problem of hemotherapeutic treatment of suppurative and septic processes. The therapeutic effect of blood transfusion, particularly in the treatment of blood of another group, in this class of diseases was already recognized 20 years ago by S. I. Sponsulkovsky, et al. The Central Order of Lenin Institute is working on the differentiation of indications for this type of treatment. The impression prevails at the Institute that hemotherapy of suppurative and septic conditions is the best method of treatment, particularly in combination with the application of antibiotics.

The work of A. N. Fyukov, Kh. V. Vladis, F. P. Vinograd-Finkel', I. I. Yurovskaya, and Ye. V. Shashina in the field of erythrocytotherapy has opened up new ways for the treatment of leukoses as well as other diseases. The combination of transfusions of erythrocytic mass with penicillin therapy, which has been proposed by them, is being applied extensively in the treatment of acute leukoses, hypoplastic anemias, and adverse agranulocytic reactions.

Particularly noteworthy is the beneficial effect of serum transfusions, especially of concentrated solutions of dry serum, in the treatment of protein insufficiency. The best results in nutritive dystrophy were obtained when massive quantities of serum were injected daily or within short intervals (1-2 days).

Extensive work on blood transfusions, carried out after operations for cancer, indicates a beneficial effect, although there are no definite indications that metastases are prevented. In the field of hemotherapy of infectious diseases, work on the transfusion of immune blood was expanded considerably during recent years. This method was found particularly effective in acute and chronic dysentery. Investigations on the transfusion of blood and its components for the treatment of liver and kidney diseases have yielded promising results as far as kidney diseases are concerned. Work carried out at the Central Order of Lenin Institute and its affiliates on the Rh factor clarified the significance of this factor in posttransfusion complications and the etiology of congenital hemolytic disease.

The USSR blood-transfusion service was able to supply a sufficient quantity of preserved blood and blood substitutes during World War II. The work on blood substitutes was stimulated by the war. In this connection, development of salt solutions used alone or in combination with blood or serum may be mentioned. Practical experience has shown that human plasma or serum are the best blood substitutes and that the use of whole blood often may be dispensed with entirely. One of the most significant achievements in connection with the use of these natural blood substitutes was solution of the problem of drying plasma and serum. Work on this subject was done at the Central and Leningrad Institutes of Blood Transfusion. The convenience of transportation and practically unlimited storage qualities of dry serum resulted in the very successful application of this preparation during World War II. An important phase of activity was concerned with the fractionation of human plasma in order
to obtain therapeutic agents. In the course of this work, new and original methods for the preparation of gamma-globulin, serum, fibrin, and thrombin were proposed. These products are now being tested clinically on an extensive scale.

Of considerable significance is the work of Soviet scientists on the production of preparations from heterogenous blood. At the Leiden Institute of Blood Transfusion, A. M. Pilato developed methods producing fibrin preparation from the blood of cattle. L. G. Bogomolova proposed a new preparation, a hemastatic sponge which produces a good therapeutic effect and which is prepared from human and animal plasma. During World War II, the problem of preparing substitute for human serum in the form of colloidal protein solution was solved by the Central Institute for Lenin Institute. This was referred to as "colloidal infusion," the term "N. G. Seleniky's and D. A. Arapov's species nonspecific serum and V. A. Burtsev's heterogenous serum. B. L. Sherskiy, et al., proposed a method of preparing a hydrolyzate of animal proteins for the treatment of hypoproteinemia. B. L. Rubinshtein, M. M. Gorskoy, and N. R. Rutberg developed a new method for maintaining plasma with retention of fibrin.

In the field of hematology, important results were also achieved by Soviet workers. After the completion of extensive experimental and clinical observations, a detailed theory of blood formation was developed. Work in this connection was done by A. A. Zavaret, A. N. Timofeyevsky, M. A. Kryukov, M. I. Arinkin, Kh. Kh. Vlasov, and G. A. Krushchew. At the Central Institute of Lenin Institute, original ideas concerning the etiology, pathogenesis, and therapy of the most important diseases of the blood-forming system (pernicious anemia, chlorosis, erythroblast, Weil's disease, and leukoses) were developed. Valuable contributions were made by S. F. Langel and his collaborators, who initiated the physiological school of hematology. By developing a practical method for the study of the bone marrow during life, M. I. Arinkin, Stalin Prize Laureate, opened up a new perspective for solving complicated problems related to normal and pathological conditions in the blood-forming system. A. A. Kastenkov, P. K. Korshunov, and N. S. Rakhmanov developed a method of puncturing the spleen and lymphatic nodes for diagnostic purposes.

Of fundamental importance were data proving that leukocytes are closely related to malignant tumors from the pathogenic standpoint, as can be shown by producing experimental leukosis in animals with the aid of endogenous and exogenous carcinogens (A. A. Bogomolova and E. N. Chavchenko). An ingenious method of determining homoplastic substances in various liquids of the organism was developed. This replaced Singer's method, which was completely unsatisfactory. Clinical and experimental investigation of the role played by the stomach, liver, and hemoplastic potential of the spleen were carried out by Kh. Kh. Vlasov, N. A. Yefidov, N. S. Dullstein, P. M. Alperin, and A. A. Bubnov. The introduction of various diagnostic methods into hematology represented a considerable advance. In this connection, the work of A. A. Timofeyevsky, P. I. Bovensolov, and G. K. Khruoshchev on the biology of cells and their capacity to undergo tissue differentiation in vitro may be mentioned.

Of theoretical importance was the study of the restorative, adaptive, and regulatory role of the nervous system in hemoplasia, carried out in recent years (Chavchenko), when the parotid or upper cervical ganglia of dogs are removed or damaged, or the vagus is cut, the anemia develops anemia, which is a result of corticosubcortical disturbances, is spontaneously checked for a while. According to A. A. Bogomolova, this phenomenon indicates mobilization by the organism of compensatory mechanisms under the regulatory action of the central nervous system. According to Chavchenko, excessive straining of the nervous system of mice by M. K. Petrov's method expedites the appearance of spontaneous or induced leukemia.
The Central Order of Lenin Institute of Hematology and Blood Transfusion is studying problems related to hemolysis (endogenous hemolytic substances have been isolated by Rubinstein and Ginsburg), the biology of erythrocytes (S. Ye. Severin), and the mechanism of enzymatic systems participating in the oxidative processes which take place in tissues and organs in anemia and leukemias (Berviz and Bulanova). Metabolism of blood pigments (hemoglobin, porphyrins, and iron) was investigated in cases of anemia and during the period of blood regeneration by donors (Belousov). Shifts in protein fractions by the electrophoretic method (G. Ya. Rozenberg and Astrakhian), as well as the structural viscosity of blood (I. S. S. V. Vasilevsky Kozyra) under dynamic conditions in leukemia and cancer, were investigated. In this manner, extensive data were accumulated for use in establishing general relationships in the field of hematology.

According to results obtained in the Cytological Laboratory (Terent'yeva), lymphocytes of normal blood develop polyphenotypical under condition of tissue culture in the sense that they have a capacity toward differentiation in various directions. The investigator established in this work that the capacity towards differentiation in leukemia patients varies depending on the severity of the course of the disease.

The achievements of the Hematological Clinic of the Central Order of Lenin Institute deserve particular attention. In regard to pernicious anemia, workers at that clinic published the first known description of some pernicious anemia and defined more precisely the pathogenesis of this disease. They also developed methods of treatment, among which blood transfusion is the most effective. Chronic hypoplastic pernicious anemia was differentiated (Kh. Kh. Vladov). This disease was later described by foreign authors under the name of achromic anemia. Methods of treating relatives of pernicious anemia and of so-called macrocytic anemias were developed (Shamsheba). Komshenkov and M. S. Bulatdinov differentiated advanced chlorosis and described the clinical aspects of this disease.

An original and effective method of treating hemolytic anemias with plasma, followed by transfusion of erythrocytic mass, was proposed (Kh. Kh. Vladov, A. P. Belousov, and Osmenshina). The effectiveness of erythrocytotherapy in combination with administration of antibiotics in anemic conditions was established. This method of treatment is also effective in hypoplastic anemias and agranulocytosis.

Hemorrhagic diseases, particularly Weil's complex of symptoms, were studied in combination with surgical-clinical aspects (S. I. Spachokhotsky, N. A. Bakulev, and L. I. Kazansky). Indications for splenectomy in this disease are determined on the basis of a clinicohematological differentiation of the condition, while the role of the vascular factor in its genesis was confirmed by clinical and experimental observations. A special form of hemorrhagic disease was differentiated in schizsphrenics (Kh. Kh. Vladov and Goldemberg), a finding which is of great theoretical as well as practical importance.

M. I. Arlinkin's school of hematology, in the persons of V. A. Beyer and N. K. Heslop, is continuing to develop in its work the concept of the nervous regulation of hemopoiesis. One may mention in this connection Beyer's observations that the modification of hemopoiesis in wounded persons, as well as his original hypothesis to the effect that the functional condition of the brain marrow forms a reflection of the reactive state of the organism, and, therefore, may serve as an indication of the qualitative peculiarities of this state. Arlinkin's method of investigating the bone marrow of living subjects has already been mentioned. The results of investigations of this type, on correlation with data on peripheral blood, led to new relationships which aid in the clinical evaluation of the hemogram. Arlinkin's work stimulated application of cytological methods of diagnosis in clinical practice. I. Kassirskii's and
G. Alexeyev's work is concentrated on the investigation by Arking's method of the dynamics of blood formation in the bone marrow when various pathological conditions are present. Shulev, Kastirsky, and Abramov developed methods of cytological diagnosis by the puncture of lymphatic nodes, the spleen, the liver, and other organs.

Of interest is the work of Makarevich, Krayevsky, and Lazovsky, who established the fundal part of the stomach is of importance in developing the internal factor in cases of pernicious anemia. This finding was confirmed by experimental and pathological studies of Fox and Castle. Experimental investigations carried out on dogs by Kh. Kh. Vlados, A. A. Bogdasarov, M. S. Duilein, and N. A. Pysedorov showed that on removal of one of the parts of the stomach (the fundal or pyloric), the remaining part contributes to compensation and elimination of the temporary anemia resulting from the experiment. Lazovsky demonstrated that the histological structure of the mucous membrane of the stomach's remaining part is modified in the course of this compensatory adaptation. The group of investigators headed by Vlados has also studied the role of the liver in hemopoesis (see above).

One of the most important achievements of USSR hematology is the work by L. F. Larionov, Stalin Prize Laureate (according to Spravochnik Akademii Meditsinskikh Nauk USSR, Moscow, 1946), Larionov is director of the Laboratory of Experimental Cancer Therapy, Institute of Oncology, Academy of Medical Sciences of the USSR. On the application of a new chemotherapeutic method of treating leukemia and lymphosarcomatosis with embikhin, a substance of the nitrophen mustard class. (2) The compound embikhin was synthesized by Prof. V. J. Nemen and the Leningrad Oncological Institute. Larionov's investigations were started in 1947 before publication by foreign authors on the therapeutic application of compounds of this class appeared in print, so that the method developed and applied in the USSR is entirely different. Its distinguishing characteristics, as compared with the US method of applying a brief shock treatment with standardized maximum doses and repeating this treatment on recurrence, are mild and gradual treatment, individual dosage, and prevention of recurrences by the treatment. By histological examination of samples taken from the bone marrow, spleen and lymph organs of experimental animals (rabbits), it could be established that embikhin curbs its strongest inhibiting effect on granulocytopenia, followed by that on lymphopoesis, and, finally the weakest effect, on erythropoesis.

While experimental results obtained by L. L. Malysheva indicate that embikhin probably will not find extensive application in the treatment of carcinomas, its effect on the metabolisms of nucleoproteins and some clinical results give rise to the hope that this drug will be of help in the therapy of malignant tumors other than lymphosarcomatosis. In fact, instance, treatment in combination with X-ray therapy of metastases which cannot be operated on, etc.

A thorough toxicological investigation of embikhin was carried out, using rats and rabbits as experimental animals. The qualitative results roughly corresponded to those obtained by Graef et al. (American Journal of Pathology, Vol. XXIV, No. 4, 1946). The "therapeutic" dose of embikhin for rats (i.e., a dose which affects the blood-forming system only) was found to be 0.2 mg/kg of body weight and amounted to one-tenth of the lethal dose. (3)

The 50th anniversary of the Central Order of Lenin Institute of Hematology and Blood Transfusion was commemorated by the 29th Expanded Plenary Session of the Scientific Council of the Institute, which was held at Moscow in May 1951. In his introductory speech, Prof. A. A. Bogdasarov, director of the Institute, presented some of the information outlined in the general progress report given above. (27) Prof. N. A. Bakulev, in a paper entitled "Some Problems of Surgery in the Light of L. P. Pavlov's Teaching," recommended hemotherapy in

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Combination with narcotics for the treatment of shock. Prof. V. I. Kazanskiy, Head, Division of Surgery, and Member of Scientific Council, Tbilisi Medical Academy, reported on an original method of chemical anesthesia of the chest cavity behind the chest wall, to be used as a measure for preventing shock in extensive thoracic operations. In connection with their reflexogenic zones in combination with blood transfusion and application of drugs as a method of treating shock.

A report presented by A. A. Bagdasar'yan dealt with the application of hemotherapy in hypoproteinemic conditions. In this report, a basis was laid from various conditions. Electrophoretic investigations showed that in septic component's blood, while the globulin content rises, the plasma's albumin content lowers in connection. The method was found to be of advantage in the treatment of inflammatory infiltrates, as well as of trophic and various ulcers (S. S. Ivakhnenko, B. I. Minayerova, V. F. Bogdanovskiy, et al.).

Of great interest was the pioneering proposal to use the whole blood or blood preparations as a means of tissue therapy in a number of diseases (Pr. Ye. N. Klyukinova, Prof. Filatov). The beneficial effect of transfusion of preserved blood in cases of bronchial asthma and ulcers was noted of inflammatory infiltrates, as well as of trophic and various ulcers (S. S. Ivakhnenko, B. I. Minayerova, V. F. Bogdanovskiy, et al.).

Mention is to be made of a new method of applying serum in septal forms of scarlet fever. In cases of hemolytic anemia, the effectiveness of therapy with plasma, followed by transfusion of whole blood, as well as clinical use of the iron salt of ascorbic acid, may be noted (Prof. Kh. Kh. Vladov and A. F. Belousov).

Prof. P. R. Vinograd-Finkel' presented a report on problems of blood preservation. In the course of this report, he made efforts to prove USSR priority in work in this field.

Prof. S. Ye. Severin summarized the characteristics of the metabolism of erythrocytes, calling attention to progress in the study of carbohydrate-glucose as a nutritive substrate for erythrocytes and that of glycolysis, stating that both favor the preservation of erythrocytes. Prof. P. S. Vasil'ev, on the basis of work on blood proteins, brought out the important function of proteins during blood preservation. He emphasized the role of the fixation of lipid-protein complexes in the process of hemolysis and in blood conservation.

It was further mentioned in the discussion which took place during the meeting that the theory of blood conservation based on biochemical and physicochemical investigations carried out at the institute permits a rational approach to the search for preservatives that are capable of prolonging the period during which blood can be stored to 60-90 days. In the course of this work, new substances for preserving blood were proposed: polyalcohols (P. G. Jinsburg), the stabilizer synantrhopol (V. D. Yan'kovskii, A. G. Polyakyanina), the antibiotic styrmycin (G. A. Krotova and M. Ye. Zepp) and other substances which can be added to preserved blood, was developed (Prof. I. I. Fyodorov). It was brought out during the discussion that further work on directions: (1) preservation of metabolic processes and of the structure of erythrocytes during the whole period of storage; and (2) reversible suppression of anaerobic metabolism of erythrocytes so that a state of

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A paper by D. N. Gruzdev outlined achievements in the field of blood substitutes and blood preparations. This author explained the advantages of USSR methods of producing blood substitutes and antishock liquids, the preparation of which is based on I. P. Pavlov's physiological teaching (the liquids of Prof E. A. Arazyan, Prof M. A. Fyedorov, D. N. Gruzdev, and others). He mentioned in particular work on methods for the production of dry plasma and dry serum which has been carried out at the institute, stating that ten different preparations are at present being produced from human blood and several from animal blood.

In a report dealing with the production of blood preparations from human plasma, G. Ya. Rosenberg told about the work done by USSR scientists in that field. He stated that the Central Order of Lenin Institute of Hematology and Blood Transfusion, in cooperation with the Moscow Institute I. M. Mechnikov, has carried out an investigation on methods for the fractionation of blood proteins. As a result of this work, in which Prof A. A. Bogdassarov, G. Ya. Rosenberg, and L. S. Pohzharyskaya participated, five therapeutic preparations (gamma-globulin, albumin, fibrin films, thrombin, and erythrocyte mass) are being produced simultaneously in the course of the same process. The majority of these preparations have been tested clinically and are being introduced into medical practice. As a result of this work, the whole approach to the treatment and utilization of blood destined for the production of antimeasles serum has been modified. The use of this serum has been abandoned; a concentrated gamma-globulin preparation which contains measles antibodies is being used instead.

On the basis of material presented at the meeting and statements made during discussions which took place there, a lot of ground remains to be covered in research on the production and preservation of plasma preparations. Thus, the question of prolonged conservation of the protein composition of blood plasma has yet been completely solved. Furthermore, the question of enrichment of plasma with biological and pharmacologically active substances such as hemoglobin, vitamins, narcotic agents, etc., requires additional thorough investigation. Also, further research on the application of preparations from heterogeneous blood is necessary.

The plenary session passed a resolution to the effect that the most important and pressing task is study of the mechanism of the regulation of hemopoiesis, this being the basis of the whole field of both theoretical and practical hematology. In this study, the effect of the nervous system under both normal and abnormal conditions must be emphasized. Another task, according to the resolution, is clinical investigation of the effect of chemotherapeutic agents in combination with new methods of treatment of hematological disturbances such as sleep therapy, the novocain block according to A. V. Vishnevsky and A. D. Speranskly, and application of cytotoxic serum prepared according to the principles laid down by I. I. Mechnikov and A. A. Bogomolets.

In the concluding phase of the meeting, Kh. Kh. Vindos summarized the present state of hematology in a report entitled "Results and Perspectives of the Development of USSR Hematology" [Ed. 2].

In view of its scope, this meeting must be regarded as an all-Union conference on questions of hematology and blood transfusion.
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1. "Progress of Blood Transfusion and Hematology During the Past 25 Years," Prof. A.A. Bagdasarov, Corresponding Member, Academy of Sciences USSR, Sovetskaya Meditsina, Vol. XV, No. 9, September 1951, pp. 1-5

2. "Results and Perspectives of the Development of USSR Hematology," Prof. Kh. Vladis, Corresponding Member, Academy of Sciences USSR, Sovetskaya Meditsina, Vol. XV, No. 9, September 1951, pp. 5-8
