



ANNUAL REVIEW OF IMMUNOLOGY

VOLUME 7, 1989





ANNUAL REVIEW OF IMMUNOLOGY

VOLUME 7, 1989



WILLIAM E. PAUL, *Editor*

National Institutes of Health, Bethesda, Maryland

C. GARRISON FATHMAN, *Associate Editor*

Stanford University, Stanford, California

HENRY METZGER, *Associate Editor*

National Institutes of Health, Bethesda, Maryland



ANNUAL REVIEWS INC.
Palo Alto, California, USA

COPYRIGHT © 1989 BY ANNUAL REVIEWS INC., PALO ALTO, CALIFORNIA, USA. ALL RIGHTS RESERVED. The appearance of the code at the bottom of the first page of an article in this serial indicates the copyright owner's consent that copies of the article may be made for personal or internal use, or for the personal or internal use of specific clients. This consent is given on the conditions, however, that the copier pay the stated per-copy fee of \$2.00 per article through the Copyright Clearance Center, Inc. (21 Congress Street, Salem, MA 01970) for copying beyond that permitted by Section 107 or 108 of the US Copyright Law. The per-copy fee of \$2.00 per article also applies to the copying, under the stated conditions, of articles published in any *Annual Review* series before January 1, 1978. Individual readers, and nonprofit libraries acting for them, are permitted to make a single copy of an article without charge for use in research or teaching. This consent does not extend to other kinds of copying, such as copying for general distribution, for advertising or promotional purposes, for creating new collective works, or for resale. For such uses, written permission is required. Write to Permissions Dept., Annual Reviews Inc., 4139 El Camino Way, P.O. Box 10139, Palo Alto, CA 94303-0897 USA.

International Standard Serial Number : 0732-0582

International Standard Book Number : 0-8243-3007-2

Annual Review and publication titles are registered trademarks of Annual Reviews Inc.

⊗ The paper used in this publication meets the minimum requirements of American National Standard for Information Sciences—Permanence of Paper for Printed Library Materials, ANSI Z39.48-1984.

Annual Reviews Inc. and the Editors of its publications assume no responsibility for the statements expressed by the contributors to this *Review*.

TYPESET BY AUP TYPESETTERS (GLASGOW) LTD., SCOTLAND
PRINTED AND BOUND IN THE UNITED STATES OF AMERICA

SOME RELATED ARTICLES IN OTHER ANNUAL REVIEWS

From the *Annual Review of Biochemistry*, Volume 57 (1988):

Cell-Surface Anchoring of Proteins via Glycosyl Phosphatidylinositol Structures, Michael A. J. Ferguson and Alan F. Williams

Molecular Organization and Function of the Complement System, Hans J. Müller-Eberhard

Tumor Necrosis, Cachexia, Shock, and Inflammation: A Common Mediator, B. Beutler and A. Cerami

Human Class II Major Histocompatibility Complex Genes and Proteins, Dietmar Kappes and Jack L. Strominger

From the *Annual Review of Cell Biology*, Volume 4 (1988):

Chemotaxis in Eukaryotic Cells, Peter Devreotes and Sally Zigmond

From the *Annual Review of Genetics*, Volume 22 (1988):

HLA Disease Associations: Models for Insulin Dependent Diabetes Mellitus and the Study of Complex Human Genetic Disorders, Glenys Thomson

Control of Antigen Gene Expression in African Trypanosomes, E. Pays and M. Steinert

From the *Annual Review of Medicine*, Volume 29 (1988):

Tumors of the Immunocompromised Patient, Israel Penn

Cachectin, Cachexia, and Shock, B. Beutler and A. Cerami

Immunology of Respiratory Viral Infections, Robert C. Welliver and Pearay L. Ogra

Selective Manipulation of the Immune Response In Vivo by Monoclonal Antibodies, W. E. Seaman and D. Wofsy

Applications of Antigen Receptor Gene Rearrangements to the Diagnosis and Characterization of Lymphoid Neoplasms, Jeffrey Sklar and Lawrence M. Weiss

From the *Annual Review of Public Health*, Volume 9 (1988):

Vaccines for Parasitic Diseases, Gene I. Higashi

The AIDS Epidemic: Six Years, June E. Osborn

From the *Annual Review of Pharmacology and Toxicology*, Volume 29 (1989):

Neurotransmitter Receptors and Phosphoinositide Turnover, De-Maw Chuang

Leukotriene Receptor Antagonists as Potential Therapeutic Agents, David W. Snyder and Jerome H. Fleisch

ANNUAL REVIEWS INC. is a nonprofit scientific publisher established to promote the advancement of the sciences. Beginning in 1932 with the *Annual Review of Biochemistry*, the Company has pursued as its principal function the publication of high quality, reasonably priced *Annual Review* volumes. The volumes are organized by Editors and Editorial Committees who invite qualified authors to contribute critical articles reviewing significant developments within each major discipline. The Editor-in-Chief invites those interested in serving as future Editorial Committee members to communicate directly with him. Annual Reviews Inc. is administered by a Board of Directors, whose members serve without compensation.

1989 Board of Directors, Annual Reviews Inc.

Dr. J. Murray Luck, Founder and Director Emeritus of Annual Reviews Inc.

Professor Emeritus of Chemistry, Stanford University

Dr. Joshua Lederberg, President of Annual Reviews Inc.

President, The Rockefeller University

Dr. James E. Howell, Vice President of Annual Reviews Inc.

Professor of Economics, Stanford University

Dr. Winslow R. Briggs, Director, Carnegie Institution of Washington, Stanford

Dr. Sidney D. Drell, Deputy Director, Stanford Linear Accelerator Center

Dr. Sandra M. Faber, Professor of Astronomy, University of California,

Santa Cruz

Dr. Eugene Garfield, President, Institute for Scientific Information

Mr. William Kaufmann, President, William Kaufmann, Inc.

Dr. D. E. Koshland, Jr., Professor of Biochemistry, University of California, Berkeley

Dr. Gardner Lindzey, Director, Center for Advanced Study in the Behavioral Sciences, Stanford

Dr. William F. Miller, President, SRI International

Dr. Charles Yanofsky, Professor of Biological Sciences, Stanford University

Dr. Richard N. Zare, Professor of Physical Chemistry, Stanford University

Dr. Harriet A. Zuckerman, Professor of Sociology, Columbia University

Management of Annual Reviews Inc.

John S. McNeil, Publisher and Secretary-Treasurer

William Kaufmann, Editor-in-Chief

Mickey G. Hamilton, Promotion Manager

Donald S. Svedeman, Business Manager

ANNUAL REVIEWS OF

Anthropology

Astronomy and Astrophysics

Biochemistry

Biophysics and Biophysical Chemistry

Cell Biology

Computer Science

Earth and Planetary Sciences

Ecology and Systematics

Energy

Entomology

Fluid Mechanics

Genetics

Immunology

Materials Science

Medicine

Microbiology

Neuroscience

Nuclear and Particle Science

Nutrition

Pharmacology and Toxicology

Physical Chemistry

Physiology

Phytopathology

Plant Physiology and

Plant Molecular Biology

Psychology

Public Health

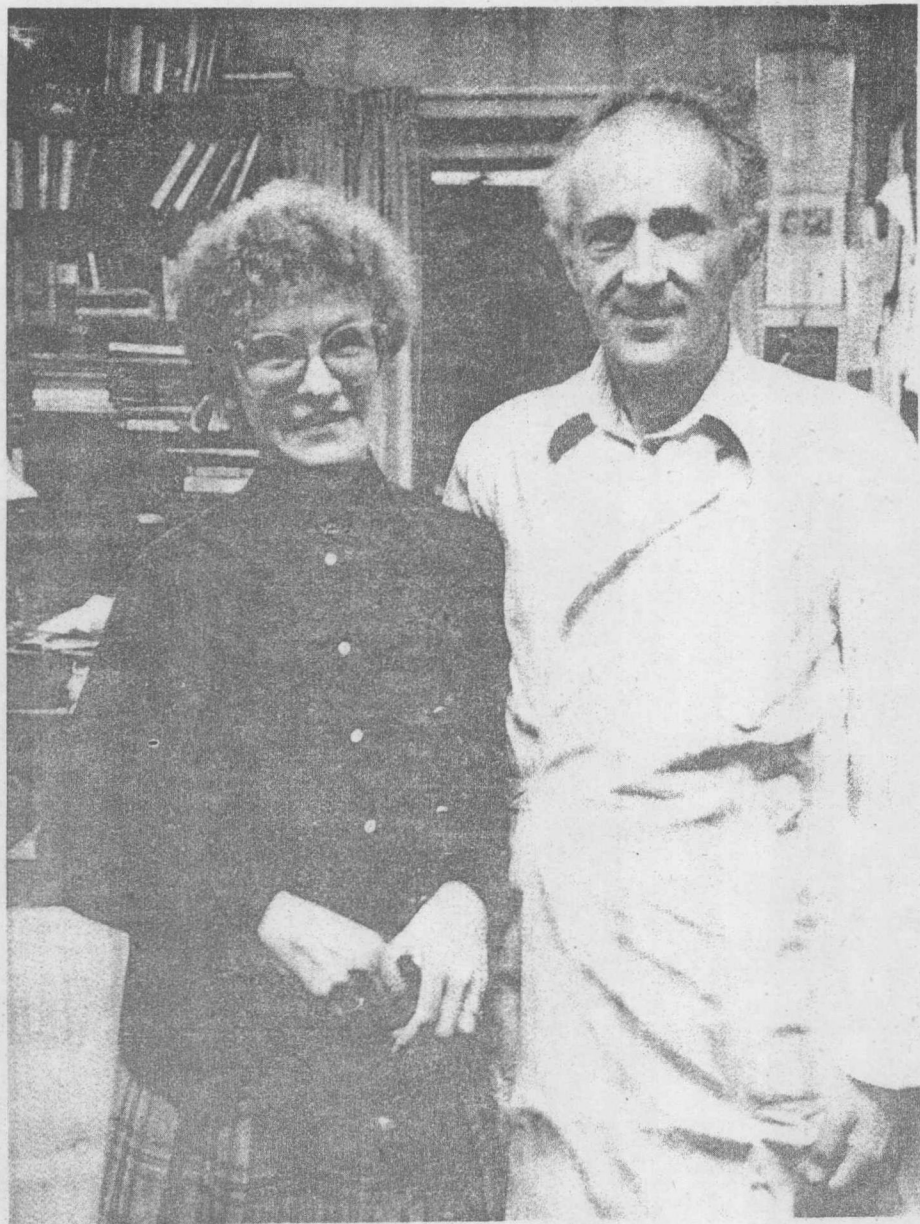
Sociology

SPECIAL PUBLICATIONS

Excitement and Fascination
of Science, Vols. 1, 2, and 3

Intelligence and Affectivity,
by Jean Piaget

A detachable order form/envelope is bound into the back of this volume.



Eva Wein

Levy Wein



CONTENTS

HOW ONE THING HAS LED TO ANOTHER, <i>George Klein and Eva Klein</i>	1
DECAY-ACCELERATING FACTOR: BIOCHEMISTRY, MOLECULAR BIOLOGY, AND FUNCTION, <i>Douglas M. Lublin and John P. Atkinson</i>	35
HETEROGENEITY OF MAST CELLS AND PHENOTYPIC CHANGE BETWEEN SUBPOPULATIONS, <i>Yukihiko Kitamura</i>	59
THE CELLULAR BASIS OF T-CELL MEMORY, <i>Jean-Charles Cerottini and H. Robson MacDonald</i>	77
MICROANATOMY OF LYMPHOID TISSUE DURING HUMORAL IMMUNE RESPONSES: STRUCTURE FUNCTION RELATIONSHIPS, <i>A. K. Szakal, M. H. Kosco, and J. G. Tew</i>	91
CELLS AND MOLECULES THAT REGULATE B LYMPHOPOIESIS IN BONE MARROW, <i>Paul W. Kincade, Grace Lee,Carolynn E. Pietrangeli, Shin-Ichi Hayashi, and Jeffrey M. Gimble</i>	111
TH1 AND TH2 CELLS: DIFFERENT PATTERNS OF LYMPHOKINE SECRETION LEAD TO DIFFERENT FUNCTIONAL PROPERTIES, <i>T. R. Mosmann and R. L. Coffman</i>	145
THE STRUCTURE, FUNCTION, AND MOLECULAR GENETICS OF THE γ/δ T CELL RECEPTOR, <i>David H. Raulet</i>	175
V-REGION CONNECTIVITY IN T-CELL REPERTOIRES, <i>P. Pereira, A. Bandeira, A. Coutinho, M. A. Marcos, M. Toribio, and C. Martinez-A</i>	209
THE IMMUNE SYSTEM OF XENOPUS, <i>Louis Du Pasquier, Joseph Schwager and Martin F. Flajnik</i>	251
MOLECULAR GENETICS OF CHRONIC GRANULOMATOUS DISEASE, <i>Stuart H. Orkin</i>	277
CELL BIOLOGY OF CYTOTOXIC AND HELPER T-CELL FUNCTIONS, <i>Abraham Kupfer and S. J. Singer</i>	309
THE LEUKOCYTE COMMON ANTIGEN FAMILY, <i>Matthew L. Thomas</i>	339
T CELL RECEPTORS IN MURINE AUTOIMMUNE DISEASES, <i>Hans Acha-Orbea, L. Steinman, and H. O. McDevitt</i>	371

(continued) v

MANIPULATION OF T-CELL RESPONSES WITH MONOCLONAL ANTIBODIES, <i>Herman Waldmann</i>	407
CLONAL EXPANSION VS FUNCTIONAL CLONAL INACTIVATION, <i>Daniel L. Mueller, Marc K. Jenkins, and Ronald H. Schwartz</i>	445
IMMUNOGENETICS OF HUMAN CELL SURFACE DIFFERENTIATION, <i>Wolfgang J. Rettig and Lloyd J. Old</i>	481
PROBING THE HUMAN B-CELL REPERTOIRE WITH EBV: POLYREACTIVE ANTIBODIES AND CD5+ B LYMPHOCYTES, <i>Paolo Casali and Abner Louis Notkins</i>	513
STABLE EXPRESSION AND SOMATIC HYPERMUTATION OF ANTIBODY V REGIONS IN B-CELL DIFFERENTIATION, <i>C. Kocks and K. Rajewsky</i>	537
T-CELL RESPONSES AND IMMUNITY TO EXPERIMENTAL INFECTION WITH LEISHMANIA MAJOR, <i>I. Muller, Thierry Pedrazzini, Jay P. Farrell, and Jacques Louis</i>	561
THE BIOLOGIC ROLES OF CD2, CD4, AND CD8 IN T-CELL ACTIVATION, <i>Barbara E. Bierer, Barry P. Sleckman, Sheldon E. Ratnofsky, and Steven J. Burakoff</i>	579
ANTIGEN RECOGNITION BY CLASS I-RESTRICTED T LYMPHOCYTES, <i>Alain Townsend and Helen Bodmer</i>	601
THE BIOLOGY OF CACHECTIN/TNF—A PRIMARY MEDIATOR OF THE HOST RESPONSE, <i>Bruce Beutler and Anthony Cerami</i>	625
T CELL RECEPTOR REPERTOIRE AND AUTOIMMUNE DISEASES, <i>Vipin Kumar, Dwight H. Kono, James L. Urban, and Leroy Hood</i>	657
T-CELL RECOGNITION OF MINOR LYMPHOCYTE STIMULATING (MLS) GENE PRODUCTS, <i>Ryo Abe and Richard J. Hodes</i>	683
INDEXES	
Subject Index	709
Cumulative Index of Contributing Authors, Volumes 1-7	720
Cumulative Index of Chapter Titles, Volumes 1-7	723

HOW ONE THING HAS LED TO ANOTHER

George Klein and Eva Klein

Department of Tumor Biology, Karolinska Institutet, S-104 01 Stockholm,
Sweden, and Lautenberg Center for General and Tumor Immunology,
Hadassah Medical School, Jerusalem, Israel

GEORGE KLEIN WRITES:

Dawn

This story starts on the 10th of January, 1945, when I emerged from a cellar on the outskirts of Budapest where I had been hiding, with false papers, during the last weeks of the German occupation. With a totally new feeling about the sunshine that was floating over the snow, the ruined houses, the dead and frozen soldiers, civilians, and horses, I suddenly realized, with a mixture of surprise, guilt, and delight, that I had survived in spite of an 80% chance that I would end my 19 years in the gas chambers or in a military slave labor camp. After a few quick walks in the newly liberated area of the still besieged capital, I decided that it was time to start my medical studies, already delayed by almost two years. During the first year after my graduation from middle school, it was impossible for a Jewish boy to enter medical school. After the German occupation nothing mattered except survival.

We were free at last, but it was a complicated freedom. After a few more days, the Eastern side of the city, Pest, was all in Russian hands. I moved around relatively freely but I was caught twice, like other young men who were automatically regarded as disguised soldiers. In comparison with my earlier escape from a Nazi labor camp, it was an easy matter to run away from the improvised, loosely organized Russian patrols. It was a wise move. Several friends of mine who went out to get a loaf of bread returned years later from Russia.

As soon as the streets were open, I walked to the University to see

whether it would open its doors for me now. I found deserted buildings, broken windows, and dead soldiers. Together with a friend we therefore decided that we should try to reach Szeged.

The journey of less than 300 km took more than five days. We walked long stretches, hitched on horsedrawn carriages and every other vehicle that we could get on, including a Russian military truck. We arrived in Szeged on February 4. It was a cold and beautiful morning. The city was intact, and we were admitted to the University on the same day. It was a strange place. All the professors had fled to the West. An assistant professor of forensic medicine with a Christlike head and very sad eyes was teaching anatomy, pathology, and forensic medicine all by himself. Students kept arriving from all former theaters of war, labor camps, and illegal hiding. Cadavers were abundant. The large dissection hall of the Anatomy Department was crowded. The smell of formalin, the half dissected or fully prepared body parts, and even the continually tipsy attendant appeared to me as parts of a magic, enchanting landscape, a previously forbidden paradise that was now all mine.

Two years passed as a single wave of febrile activity. I finished three terms during three months in Szeged and returned to Budapest when the university reopened there. I wanted to start research work, but the departments were still paralyzed. They had no resources and the routine work consumed the energy of all staff. Still, I got a first decisive inspiration from the professor of histology, Tivadar Huzella, one of the few internationally known scientists in Hungary and also one of the few true liberals among the medical professors of his generation. In spite of his consistent anti-Fascist stance, and his strong opposition to any form of discrimination during the war, he became a suspected person in the eyes of the new rulers. His uncompromising individualism and his democratic value system invited the enmity of the political opportunists who wanted to see a more compromising person in his position. His arch-enemy, the professor of anatomy, a political opportunist and a scientific nonentity who had resented Huzella's international fame for many years, delivered a list of accusations against him to the "people's court." The sympathies of all the students were on Huzella's side. The crucial trial, where all the absurd accusations—exemplified by the charge that Huzella ate eggs ordered for tissue culture—were readily dismissed, ended in tragedy when the presiding lay judge asked whether Huzella still believed a sentence he wrote during the war. Huzella had stated (an act of great courage at the time) that Hitler, Stalin, and Salazar were equally abominable dictators. If he would have been willing to exempt Stalin and admit his "mistake," he would have been cleared. But he stuck to his words and was summarily dismissed. He died a few years later. Today he has been "rehabilitated."

His home and laboratory are kept as a public memorial. They also house the leading immunological laboratory of Hungary.

Huzella had an exceptional ability to convey his own deep interest in biology to his students. He was convinced that the time had come when biology could be converted from "metaphysical speculation" into a natural science with precision and dignity similar to those of chemistry and physics. He believed that the biology of the interstitial space would turn into detailed biochemistry in a few decades but that the cell interior would remain a black box during the rest of the century. Before blaming him for a lack of foresight, we must realize that most biologists of the time were unwilling to accept his "optimistic" view even about the connective tissue.

I learned some tissue culture, but my practical experience remained rudimentary, and I compensated only slightly by avid reading in the still quite deficient library. After Huzella's removal, I realized that I could not learn more in the now largely nonfunctional department, and so I moved to Pathology. After a few weeks I found myself totally immersed in autopsies. There was a great abundance of cadavers here and very few pathologists. The large postwar classes of medical students had to be taught quickly. I greatly enjoyed the double task of teaching the little I knew and trying to explain to the rushed and often very nervous clinicians what their patients had died of.

In the early spring of 1947, one of "my" students approached me after an autopsy. He said something appreciative about my demonstration and asked whether I would be interested to visit Sweden with a student group. I was amused by his naiveté. Who would not like to visit Sweden? But were we not all aware of the fact that foreign travel was the exclusive privilege of important functionaries and people with much money and many good connections?

He replied that he was currently organizing a trip for students and that he would include me. Hungary still had an elected coalition government at this time. It was possible to get a passport, but this was not sufficient to leave the country. A special exit permit had to be issued by the "Allied" forces, i.e. the Soviet Army. It was very difficult to get this permit, and it was nearly impossible to obtain foreign currency.

I mailed my papers to my student who was interested in Sweden and totally forgot about our conversation.

Decisive Summer

In June 1947 my boss, Professor Baló, told me that I would be responsible for the autopsies during the coming month, virtually alone. I was happy, proud and frightened. I was not yet 22, far from being an MD, but the night's sleep of a professor in surgery could depend on what I was going

to find. The combined feeling of responsibility and awe turned every autopsy into an exciting detective story. During my minimal "spare hours" I also started my first attempts to do some experiments. I was sitting in a corner of the laboratory with a small water bath and a stalagmometer, trying to follow a lead that had been opened up by my chief.

The most important messengers of my future destiny appeared in the shape of two house painters in the middle of July. They had been ordered to repaint the laboratories. I was chased from room to room with my water bath, but I refused to give up. Finally, I was squeezed into a small corner in a tiny windowless alcove that I refused to leave. The painters complained to Professor Baló. With an irritated "you can take two weeks vacation for once" he ordered me to leave my paradise. A senior colleague was to take care of the autopsies. I was angry and disappointed. What was I to do during two whole weeks?

By coincidence I learned that some fellow students, two couples from the Pharmacology Department, were planning to spend the forthcoming week at the Lake Balaton. I was also told that they had invited some other friends and that I was welcome to join them. We were allowed to use the terrace of a bombed summer house and were going to sleep on mattresses, spread out on the terrace. It was quite warm during the first week in August, and we would have a roof over our head. After considerable hesitation, I decided to join them, but I felt ambivalent and uninterested.

The place was unexpectedly pleasant and my fellow students were much nicer in private life than at the University. On the second day, the two other boys went down to the train to meet another student from the Pharmacology Department, who was to join us. I did not know who it was, and since the Hungarian language does not distinguish between *he* and *she*, I did not even know whether we were expecting a boy or a girl. After a while I saw them walking up the hill with the new guest: a dark girl with a strange, breathtaking beauty. I perceived a most unusual combination of hilarity and sorrow, seriousness and play in her eyes. It was Eva, my future wife and colleague until this day.

I had seen her before at the university, but my obsessive preoccupation with work prevented me from giving her or any other girl much attention. Still, I could remember very well how I met her the first time. On the second day of my medical studies in Szeged, I was standing in the Dean's office, to get my papers. She entered, dressed in a skiing outfit, having arrived in the city after a long and adventurous trip from Budapest, like my own. She asked me how to get papers. I saw that she was very beautiful. Her direct way of talking to a strange boy—very unusual for a girl in Hungary at the time—struck me as original and sympathetic. During the forthcoming weeks I saw her at some lectures, but then she disappeared.

Later I saw her name on the posters of the city theater. She was playing small roles in Pirandello and Molière plays. Half a year later I saw her again in Budapest. She had returned to medical studies and came sometimes to my autopsy demonstrations. I knew that she belonged to the same group of students in the Pharmacology Department as my married friends and temporary hosts. Their "gang" treated me with friendly tolerance, and even with a trace of respect for my "knowledge"—in spite of their "objections" to the "dead morphology" that pathology represented in their eyes. I respected their intelligence and their dynamic experimentation and could therefore forgive their blatant ignorance of pathology and clinical medicine.

But this time everything was different. There was one table but only three intact chairs in the ruined villa, and we were six. We had to place a board on each chair to hold two. Eva and I were placed on the same board and had to coordinate our movements to prevent each other from falling down. This trivial problem initiated a contact that metamorphosed after only a few hours into a passion that conquered my entire consciousness with the force of an elementary power. All other interests and problems vanished as if they had never existed. I spent eight days at the lake, intoxicated, overwhelmed, cut-off from all earlier reality.

An unexpected telegram arrived on the seventh day. Everything was settled for the trip to Sweden! My former pathology student or, as we were soon to call him, Our Leader, had succeeded against all odds. He had pursued his plan with obstinate ingenuity and obtained all the exit permits for a group of seventeen students selected by himself with the arbitrariness of a sovereign. We came from different faculties and were to visit Stockholm and Gothenburg as the guests of the Jewish Student Club there, in order to see a country that was saved from the war.

Now I did not have the slightest wish to go. I felt very bitter about having to leave the person who had become more important than anything else in my life so far. The week at the Balaton appeared as an eternity; everything before was unreal. But vague feelings of responsibility and premonition commanded me to go. I left at dawn on a Sunday morning. Eva told me later that she heard the train whistle while half asleep and thought that a beautiful summer episode was now over. She did not believe that I would ever come back from Sweden or that she would see me again.

Cell Biology 1947

The first International Congress of Cell Biology had just terminated when I arrived in Stockholm. I was told that Torbjörn Caspersson was one of the most important figures at the Congress. His recent development of ultraviolet microspectrophotometry on fixed cells created much attention.

The method was based on his doctoral thesis, written in 1936 in German and largely unavailable to English speaking readers during the war years. It was the first major attempt to combine morphology and cytochemistry. Cells were photographed in monochromatic UV light under standardized conditions. A semiquantitative method was developed to map the localization of nucleic acids and proteins in different cell types. Jack Schultz, one of J. H. Morgan's last disciples, was the first American geneticist who saw the potentialities of the new approach. He traveled to Stockholm to work with Caspersson shortly before the outbreak of the war. He brought genetic thinking to the biophysically oriented group. His studies with Caspersson on the banding patterns of polytenic insect salivary gland chromosomes gave the first information about the distribution of nucleic acids and chromosomal proteins and set the conceptual basis for the development of the chromosome banding technique by Caspersson and Zech three decades later.

The chemistry of the genetic material was still unknown at the time of the Cell Biology Congress in Stockholm. Most biologists believed that only proteins could provide the necessary diversity. Nucleic acids were considered as repetitive, boring molecules. Levene and Bass pronounced the death sentence on the coding capacity of the nucleic acids already in the 1930s. The mistaken analogy between the "4-letter alphabet" of the nucleic acids and the phonetic alphabet served as a roadblock: how could one build a language from four letters? Caspersson's semiquantitative measurements of nucleic acids and proteins in different cell organelles led him to conclude that there was a definite relationship between nucleic acid and protein synthesis and that the former might actually govern the latter. This visionary insight was widely disbelieved, however. The idea that nucleic acids might carry genetic information that could be translated into proteins was totally foreign, even to Caspersson. The fundamental discovery of Avery, McLeod, and McCarthy on DNA-mediated transformation in *Pneumococcus*, published in 1944, was widely ignored or discarded as an artefact.

The Cell Research Department of Karolinska Institute had just moved to the newly built campus on the northern edge of the city; there I was to spend all my scientific years, up to the present day. I visited it first in the middle of August, 1947, the peak of the vacation season and soon after the Congress participants had left town. Members of the Department who happened to be in town were frantically trying to get settled in the new building. As I made my entry, tall, blond, 37-year-old Torbjorn Caspersson was lying under a large instrument in a blue overall, trying to fix the wires. I thought that he was an electrician or a technical assistant. His identity was not revealed to me and I was not introduced to him. After I had

learned the difficult art of protecting him from uninvited visitors a few years later, I could understand the reasons. In 1947, I was desolate when I had learned the next day that he had left for the USA. Only after a long series of complications did I get in touch with him, several weeks later. But my first conversation with him was decisive. Thanks to the rudimentary and largely theoretical knowledge of tissue culture, acquired in the Huzella laboratory two years earlier, I got the best-paid job of my life (if the importance of the salary is considered). I was employed as a junior research assistant, on 500 Sw Crs (about US \$100) per month.

I still remember the mixture of ecstatic happiness and enormous anxiety. My situation appeared totally hopeless. I knew virtually nothing. I was halfway through my medical studies, still far removed from an MD. I was desperately in love with a girl whom I had only known during a summer vacation of eight days and who was on the other side of an increasingly forbidding political barrier. I did not know a word of Swedish. Still, I was firmly decided to resist the more comfortable possibility of continuing my studies in Hungary.

My motivation was reinforced by a series of articles that kept appearing in the major Swedish daily, *Dagens Nyheter*, translated for me by my temporary host. The Prime Minister of Hungary, Ferenc Nagy (not to be confused with Imre Nagy) of the Smallholder's Party has just fled to the West, and he gave a series of interviews to the Swedish paper. In contrast to the rosy optimism that prevailed among my friends in Budapest who hoped that Hungary would become a democratic country, Nagy's statements had an ominous ring. He said that the influence of the Communist Party was increasing continuously behind the scenes. The Stalinist party leader, Rákosi, was acting under the protection of the Russian forces. The politicians of the other parties were frightened. Several of their leading representatives were arrested on false charges and deported to unknown destinations. Those who remained were increasingly inclined to give in. The police were infiltrated by party members. Nagy did not have the slightest doubt that a Communist takeover was imminent. Similar signals reached me indirectly from one of my teenage idols, Nobel Prize winning biochemist Albert Szent-Györgyi. He was still holding many high posts in Hungary at the time, but he had told his nephew, who was a friend of mine, that the days of freedom were numbered. If you were young and wanted to have a future in science, you should get your degree as soon as possible and leave the country.

Farewell, My Native Land

In mid-September, I decided to go back to Budapest and try to get out for good. My most important acquisition was safely tucked away in my breast

pocket: a re-entry visa to Sweden and a labor permit for continued work in Caspersson's department. My passport was still valid for a few months.

The reunion with Eva confirmed what we both knew already: we wanted to live and work together. The day after my arrival, some of our friends gathered at my home to hear the latest news from the "great world." I told them about Nagy's report and the iron curtain that was about to descend over Hungary. The reaction was mixed. Those who were already preparing to leave believed me. Others wanted to stay and hoped that my report was exaggerated. One of them—still a good friend today—declared that I was probably right, and for that reason, he was going to break all further contact with me. This was his country, Hungarian was his language, his historical roots were here. I should leave, if I felt so inclined, but he had to stay and do the best he could. Today he is the foremost medical historian of Hungary.

I had none of his historical perspectives. I had only one goal, to get married and leave the country.

But how to get married? It had to be in secret, because nobody would understand why two 22-year-old students who had known each other for only a short time and had no income would want to get married. And how could my future wife join me? She had no passport and the difficulties in getting one were now increasing day by day. We agreed that I would go back to Stockholm before my own passport expired and try to obtain letters of invitation for Eva that could help her to get a passport.

The last weekday before my trip was a Friday. Eva and I met outside the pharmacological institute to go to the day's lecture. I suggested that we should go to the prefecture instead and ask how one gets married. We got a list of the many documents you needed. It looked hopeless. It would take months to get them. I suggested that we ask for the first document, a certificate to show that we had no police records. We went to the police station. "It takes at least three weeks." Suddenly I acted on impulse. I had always heard others tell of such things but I myself had neither seen nor done it. I pulled a fairly modest bill out of my pocket and put it in the policeman's hand. "Pardon me, how much time was it, you said?" "I'll go and get it at once," he answered.

It was now 11 AM. We continued from office to office.

Everywhere the same answer: one week, four weeks, six weeks. A little bill in the hand—the certificate was completed within a few minutes. I was amazed to find that the shyness I usually exhibited before persons of authority vanished completely. I learned a lesson about the importance of motivation and the unsuspected possibilities it may open to surpass one's limitations.

By 3 PM only one document was missing: a medical certificate that neither of us had venereal disease. The tests would take several weeks. What to do now?

We went to a slightly older colleague who had recently finished his medical studies. He had just started his first assignment in the Children's Hospital. We told him, in the strictest confidence, about our situation. He had a good laugh and wrote the certificate on the hospital stationary. By 4 PM we were at the prefecture again. We had all the papers and wanted to get married that second. Two other friends, sworn to the highest secrecy, came along as witnesses to the wedding. The official had just finished the day's work and had taken off the broad Hungarian tricolor from his corpulent chest when we rushed in. We heard him telling his wife on the phone that he was on his way home for dinner. Marry us at this time of day? Not a chance! Come back on Monday!

I started to appeal to his human feelings. I had to leave the country on Sunday. How could I leave my young bride alone if we didn't get married? He was noticeably irritated and doubted that we had all the papers. While leafing through the documents, he caught sight of the doctor's certificate that had been drawn up at the Children's Hospital. He laughed until tears ran down his cheeks. This was the funniest thing he had seen during his whole time in service. Now he was in splendid spirits. The flag resumed its place on the large body. We promised to love one another til death us did part.

Afterwards we ate our wedding dinner on the hall bench together with our witnesses. There was only one dish: my mother's carefully packed goose liver sandwiches. In the evening we went back to our parents' homes where no one suspected anything.

That Sunday I returned alone to Stockholm. Eva joined me, after many complications, in March 1948, after the Iron Curtain had already descended over the country.

GEORGE AND EVA WRITE:

The Genetics Congress

In August 1948, several months after we were happily settled in our rented room and Eva had also started to work in Caspersson's department, the International Congress of Genetics took place in Stockholm. The presidential address of J. H. Muller was a scathing denunciation of the abuse of genetics in the Soviet Union. The scientific world was still largely unaware of the fact that the "theories" of a charlatan, Lysenko, had been declared "official" by the Central Committee of the Communist Party, meaning that it became essentially illegal to do any scientific work in