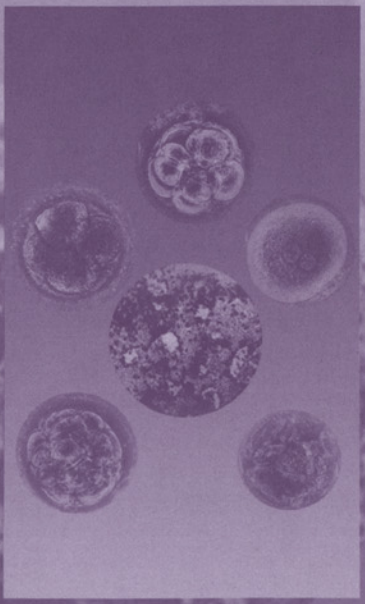
MOLECULARIZING BIOLOGY AND MEDICINE

NEW PRACTICES AND ALLIANCES 1910s – 1970s

edited by

Soraya de Chadarevian & Harmke Kamminga



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Molecularizing Biology and Medicine

New Practices and Alliances, 1910s–1970s

Edited by

Soraya de Chadarevian and Harmke Kamminga
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This edition published in the Taylor & Francis e-Library, 2005.

Amsteldijk 166
1st Floor
1079 LH Amsterdam
The Netherlands

British Library Cataloguing in Publication Data
Molecularizing biology and medicine: new practices and alliances, 1910s–1970s—(Studies in the history of science, technology and medicine; v. 6)
1. Molecular biology—History—20th century
I. Chadarevian, Soraya de II. Kamminga, Harmke
572.8′0904

ISBN 0-203-30423-3 Master e-book ISBN

ISBN 0-203-34414-6 (Adobe eReader Format)
ISBN 90-5702-293-1 (Print Edition)

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Preface

The project of this book is part of a collaboration between the Cambridge Wellcome Unit for the History of Medicine and the INSERM Unit 158, Paris. Jean-Paul Gaudillière and Ilana Löwy from the Paris Unit have been involved in all stages of this project. We are very grateful for their important input and continuous advice.

Most of the chapters were first presented at a conference on “Molecularizing Biology and Medicine”, held in Cambridge in July 1994. We thank all conference participants for their lively contributions to the discussions, and the speakers for their stimulating papers. We are also grateful to those authors in this volume who joined the project later, especially for their cooperation in meeting tighter deadlines.

We thank the British Council and the French Ministry of Education and Research for funding the collaboration between Cambridge and Paris. We are grateful for additional funding from the Wellcome Trust and for general support from our colleagues in the Cambridge Unit.

Soraya de Chadarevian
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Introduction

Soraya de Chadarevian and Harmke Kamminga

It is our aim in this volume to draw attention to the formation of particular strategic approaches in biology and medicine centred on molecules. These approaches became prominent in the interwar period and gained new momentum with the biomedical mobilization of World War II.[1] The identification, production, circulation and uses of molecules in biological research and in the explanation and treatment of diseases created new links between the laboratory, the clinic and industry. We introduce the term "molecularization" to describe the creation and transformation of these alliances. By following molecules through different biomedical contexts and networks, the contributors to this volume provide a novel historical perspective on innovation in the biological sciences and medical practice.

Nowadays a molecular vision of life, health and disease is linked specifically to the spectacular successes of molecular biology in the study of structure-function relationships of nucleic acids and proteins since the 1950s and 1960s, the development of recombinant DNA technologies in the 1970s, and the making of the Human Genome Project with its promises of a genetically based molecular medicine. Historians have used the terms "molecularization", "molecular vision", "molecular revolution", and "molecular politics" in this context (see Kay, 1993a and 1993b; Olby, 1990; Rheinberger, 1995; and Wright, 1994).[2]

The coupling between a molecular vision of life and molecular biology has been promoted vigorously by participant scientists and has been taken up in different forms by historians. Taking on board the molecular biologists' focus on nucleic acids and proteins, historians have tended to look for paths towards these ends in earlier work on macromolecules and in genetics (Judson, 1994; Kay, 1993a; Olby, 1990, 1995). Biochemists, on the other hand, have claimed their own place in this history by insisting that molecular approaches to life had been practised by biochemists all along, but that these encompassed a much broader range of molecules (Cohen, 1984; Fruton, 1992; Krebs, 1969).[3]

The notion of molecularization used in this volume opens up a new historio-graphie approach to the growth of a molecular culture in biomedicine, which differs from both these perspectives. Rather than treat work on macromolecules in historical isolation, we use molecularization to refer to small and large molecules alike. Yet we do not simply embrace the biochemists' outlook which places the accumulation of knowledge about the role of molecules in biological processes at centre-stage. It is neither our intention to trace the "origins" of molecular biology, nor to restrict molecularization to the growing understanding of molecules as biological and medical objects. Instead, we use molecularization to refer to practices centred on molecules, and focus on the interactions between different social groups in the creation and transformation of these practices.

Building on a variety of approaches, from network theory to social interactionism and interest theory, with a focus on laboratory practices and alliances, the authors make manifest the powerful role that molecules have played in forging links between the laboratory, the clinic, industry and wider social interests.[4]

The studies in this volume bring out particularly sharply that the relationships between these domains have been much more complex and varied than is suggested by the still common notion that "basic knowledge" is acquired in the research laboratory and is then "applied" in the clinic, with industry becoming involved in the large-scale production and commercialization of drugs. Particular alliances between research scientists, clinicians, industrialists and policy makers have confounded the distinction between "basic" and "applied" science. The very introduction of the terms "biomedical sciences" and "biomedical complex" in the 1960s made explicit the interconnections which, as the contributors show, had been formed and reformed in new configurations for many decades.

The studies presented in this volume cover the period from the 1910s to the 1970s. We have chosen to start in the 1910s, because strategies of molecularization were by then in the making in different fields of research and production, in several countries. In closing the volume in the 1970s, we consciously exclude the more recent developments linking molecular biology, biotechnology and genetic medicine, which are already receiving considerable attention in the literature (see especially Kevles and Hood, 1992; Krimsky, 1991). The studies collected here nevertheless offer tools for a historical re-evaluation of these more recent strategies of molecularization.

In the following sections, we provide, in outline, a historical framework for the chapters in this volume and then point to a number of common and intersecting themes running through them. In the epilogue to this volume, Steve Sturdy reflects on the history of molecularization, focussing on the central role of standardization in the creation of a "molecular economy" in biology and medicine.

MOBILIZING MOLECULES

The nineteenth century saw the "laboratory revolution in medicine" (Cunningham and Williams, 1993), with a large-scale move of medical men into the research laboratory, the creation of new sciences allied to medicine, such as experimental physiology, bacteriology, and physiological chemistry, and the beginnings of the pharmaceutical industry. Links were formed between the research laboratory, the clinic and industry, especially with the development and production of antisera and vaccines in the 1890s. The early successes of serum therapy for diphtheria created demands for new products on a massive and international scale, which could not be met by the few institutions devoted to research and production in this field, notably the Institut Pasteur in Paris and Robert Koch's Institute of Infectious Diseases in Berlin (Moulin, 1991; Weindling, 1992). Industry became involved in scaling up production of antisera against many bacterial diseases, simultaneously entering new medical markets for their products. In Germany, the state, too, became a significant player in this network, when the Ministry of Health assumed control over the standardization of antisera (Liebenau, 1990; Sturdy, this

volume).

Early forms of molecularization of medicine in the twentieth century built on these developments, but with two significant and interlinked innovations: a shift towards medical intervention at the level of specific molecules, and the active participation of industry, not only in the production, but in the identification of therapeutic molecules. Both features are exemplified by Paul Ehrlich's program of chemotherapy, which was initiated around the turn of the century in Frankfurt and was aimed at identifying synthetic dye stuff derivatives as therapeutic agents against parasitic diseases (see especially Lenoir, 1988; Liebenau, 1990).

Ehrlich tested hundreds of dye stuff derivatives, synthesized at his request by industrial chemists in the Hoechst Chemical Works, for specific therapeutic properties. Most of them turned out to be inactive, toxic, or both. Those showing promising activity in experimental animals were tested on patients with the cooperation of local hospitals and physicians. The active collaboration of the chemical industry, which made Ehrlich's research possible, was spurred by economic interests in finding uses for waste products of dye synthesis and in entering new markets opened up earlier by the vaccine and antiserum business. Their investment in this work, and Ehrlich's research strategy, was vindicated spectacularly by the most famous product of the chemotherapeutic program, "compound 606", the anti-syphilitic drug which was marketed by Hoechst under the name of Salvarsan in 1911. With the successful development of chemically well-defined synthetic products with therapeutic properties that were clinically tested, standardized and used widely for treatment, molecules in medicine became big business.

Ehrlich explained the action of dye stuff derivatives in terms of specific binding to (non-defined) chemical groups attached to the cellular protoplasm (Cambrosio *et al.*, 1993). His notion of protoplasmic receptors did not, however, provide molecular explanations and could not guide the design of drugs, nor could Ehrlich explain the etiology of the diseases in question in molecular terms. Nevertheless, Ehrlich's program of chemotherapy, together with its products and the new collaborations on which it relied, is an early example of molecularization in our sense. Furthermore, the success of the program in yielding therapeutically active products directed attention to molecular explanations in pathology and stimulated further searches for specific molecular drugs.

The chemotherapeutic tradition remained strong in Germany, as illustrated by the industrial development of sulphonamides in the 1930s. Chemotherapy was not, however, the only area in which molecularization was pursued. During the 1910s, chemical understanding was sought and clinical uses were explored in the case of other classes of substances, for example hormones and vitamins. In these instances, however, the active involvement of industry and treatment with well-defined molecules came at a later stage, after World War I (Bliss, 1982; Horrocks, 1995; Kamminga, this volume; Oudshoorn, 1993). Wartime pressures gave molecularization a new impetus, on a broader geographic canvas.

With the disruption of trade links during World War I, many overseas licences were revoked, and Salvarsan production and standardization, for instance, were taken up outside Germany. From quite different directions, vitamin research was intensified in the light of concerns about the nutritional value of army rations and civilian diets, under the threat of shortages in the food supply. Especially in Britain, scientists who were

investigating the detailed chemical composition of healthy diets became involved in the formulation of food policy at the highest levels (Teich, 1995).

The experience gained and the networks established during the war gave momentum to the search for means of medical intervention at the level of specific molecules more widely. The articulation of research strategies towards this end increasingly involved industry and the state as active partners, as well as clinicians and scientists. The involvement of industries, with their interest in finding cheaper synthetic ways of production, stimulated research on the structure of vitamins and hormones. The need for structural research on molecules was also stressed by biochemists, for their own purposes, in the promotion of their subject as the fundamental science of life and as the basis for a scientific medicine (Kamminga and Weatherall, 1996).

Much of this structural research was directed at vitamins and hormones, in view of their wide preventive and therapeutic use. In some instances, the structure determination of these molecules was not achieved until decades after their industrial production and clinical use began. A striking example is insulin, first produced and used therapeutically in the 1920s, whose three-dimensional molecular structure was determined only in the late 1960s.

In the interwar period, biochemical research was supported strongly by the policies of major funding agencies, such as the Medical Research Council (MRC) in Britain and the Rockefeller Foundation based in the United States (Abir-Am, 1987; Austoker and Bryder, 1989; Kohler, 1978, 1991). Both these bodies devoted a great deal of their funds to research on the structure and functions of biologically active molecules, from the 1920s onwards. The MRC also assumed a prominent role in setting international biological standards, especially in relation to vitamins and hormones (Liebenau, 1989).

By the late 1930s, multiple links between the research laboratory, the clinic, state and industry were in place, based on molecules of biological, medical and economic interest. Strategies of molecularization pursued in the interwar period were built upon and put to new uses during World War II, in which scientists were enlisted on an unprecedented scale.

The biomedical mobilization of World War II was in important ways centred on molecules, a point to which this book draws attention for the first time. Research scientists, clinicians, industry, workers, and the state machinery of the nations at war were mobilized for the investigation and large-scale production of a series of strategic molecules. These included above all antibacterial drugs, especially sulphonamides and the antibiotic penicillin, antimalarial drugs, and blood fractionation products for use in transfusion. The penicillin work in Britain and the United States provided the allied armies and physicians with a powerful weapon in the “war against disease,” spurring searches for other therapeutic molecules, or “magic bullets” (Bäumler, 1965; Neushul, 1993; Swann, 1983).[5]

In the postwar reconstruction, the penicillin project was made into a model, both to argue for state support of fundamental research and to set in place new managerial research strategies in the biomedical sciences (Swann, 1988). The mobilization model was also put to use in conducting large-scale clinical trials for drugs and in introducing screening programs for diseases defined in terms of abnormalities at the level of molecules.

Physical approaches to the study of biological materials promised fundamental knowledge of life processes and of disease causation, and attracted important funding in the postwar years. This support, together with the commercialization of a range of instruments for the analysis of large biological molecules and subcellular structures, encouraged many scientists to engage in this area of study (Elzen, 1986; Kay, 1988; Rasmussen, 1996). When a group of researchers at the California Institute of Technology, applying the new technologies, identified a new type of hemoglobin in the blood of sickle cell anemia patients, they announced their findings by heralding sickle cell anemia as the first "molecular disease". Sickle cell hemoglobin and its simple mechanism of inheritance stimulated hopes of finding molecular explanations for other genetic disorders. This focus on molecular causes of inherited diseases, however, was not necessarily followed by therapeutic breakthroughs.

More recently, new protein and nucleic acid technologies have opened up novel prospects of intervention at the molecular level. The biotechnology industry has been a major player in these developments since it was set in place in the late 1970s. The production of genetically engineered drugs such as insulin and growth hormone has been supplemented by the development of research tools and diagnostic technologies for use in the laboratory and the clinic. These new strategies and alliances have had, and continue to have, far-reaching and novel consequences. From the perspective of this book, however, they represent but one particular articulation of multiple practices centred on molecules.

FRAGILITIES AND POWERS OF MOLECULARIZATION

At the same time as drawing attention to processes of molecularization, the book shows up the contingencies and fragilities of these processes. As many contributors show, molecular strategies were frequently contested and often aborted. Both the powers and fragilities of molecularization become particularly clear when strategies of molecularization are followed over a long period, as is done, in different ways, in the opening and closing chapters of the volume.

Following the variegated career of one molecule, colchicine, Jordan Goodman shows that the successful use of colchicine as a molecular probe in cellular processes was bound to a particular context and could co-exist with, or be shelved in favour of, non-molecular uses of the same substance by other people in other places. Ilana Löwy shows that multiple efforts in the immunotherapy of cancer, from the 1910s onwards, did not lead to the development of effective anti-cancer drugs. Interferons, regulatory molecules of the cell which were hailed as "miracle drugs" in the 1980s, were no exception. According to Löwy, the ideal of molecularization nonetheless survived and found its articulation in a powerful network which linked scientists, industrialists and oncologists.

Molecularization has rarely converged successfully on etiology, diagnosis and therapy conjointly. Insight into the etiology of a disease in molecular terms, or its diagnosis at the molecular level, does not necessarily imply that a molecular cure is available, feasible, economic, or indeed desirable. On these grounds, and for reasons of professional autonomy, clinicians have often resisted the introduction of molecular diagnostics. In other cases, the therapeutic effect of chemically well-defined molecules is exploited

without their mode of action being well understood at the molecular level. Salicylic acid, sold under the brandname of Aspirin since 1899, is a striking example of a substance which is widely used for the prevention and treatment of a variety of symptoms, but whose molecular mechanism of action remains elusive. Even when the mechanism of molecular therapies is believed to be well understood, as in the case of insulin treatment of diabetes or a phenylalanine-free diet for phenylketonuria patients, unwanted "side-effects" and the varying susceptibility of patients to the same treatment indicate that the explanations are not complete (Paul and Edelson, this volume). Furthermore, the successful use of molecular drugs always depends on complex cultural set-ups and routines, as shown by Marks in this volume for the case of the contraceptive pill.

Especially in the clinic, molecular practices have existed side by side with physiological or organismic approaches, often developed in response to the obvious limitations of molecular or, more generally, reductionist practices. Holistic approaches do not necessarily negate the achievements of reductionist explanations, but are often integrated with the latter into more comprehensive frameworks of medical knowledge and practice (Lawrence and Weisz, in press).

Molecularization, then, has not been the only strategy pursued in biomedicine, nor has it been uniformly successful in its achievements. Even strong mate rial, technological and political support provided no guarantee for success defined in terms of criteria dictated by the molecular strategies themselves, at least in the short and medium term. For instance, Nixon's cancer campaign of the 1970s, which injected large sums of money into molecular strategies, did not produce a "cure for cancer", and gene therapy for molecular disorders such as sickle cell anemia continues to be a promissory note instead of clinical reality (Gaudillière; de Chadarevian, this volume). Furthermore, there have been trade-offs between successes of molecular approaches and losses on other levels. Funds and commitments channelled into screening for the inherited metabolic disorder phenylketonuria, for example, were at the same time channelled away from social programs for help with the practical problems faced daily by mental patients and their families (Paul and Edelson, this volume). The apparent power and success of molecular strategies today, then, depend on the criteria of evaluation which society has set for biomedical research and public health policies.

STRATEGIES OF MOLECULARIZATION

We now outline some major themes of molecularization, as they are presented in this volume. In treating these themes, it is our aim not only to highlight particular links between different chapters, but to delineate further the concept of molecularization as a historiographic tool. The manifold connections between the different themes are important: far from taking the laboratory, the clinic, industry, politics (or, indeed, molecules) as given, fixed entities, we want to indicate how they and their interrelations were created and transformed around molecular practices.

Instruments and Technologies

Technologies played a crucial role in the representation, definition, measurement, analysis, production and circulation of molecules, big and small. Not surprisingly, therefore, instruments and technologies form a pervasive theme of the chapters of this volume.

The development of technologies designed to measure and monitor molecules in the body became a central concern for those who reduced bodily functions to the interplay of molecules and understood diseases as disturbances of chemical processes. For Olga Amsterdamska the study of these technologies opens the way to investigating the interactions between biochemists and clinicians in a particular institution, the Rockefeller Hospital, created at the beginning of the century with the explicit aim of fostering a new scientific medicine, or a medicine based on physicochemical approaches to diseases. Van Slyke's apparatus for the measurement of bicarbonate concentration in the blood of diabetic patients, developed at this hospital, was based on a gasometric principle. Yet the choice of bicarbonate as an indicator of diabetes as well as the attempts to demonstrate the utility of the apparatus were based on and propagated a biochemical definition of the disease. While his name has been attached to the gasometric apparatus, Van Slyke, during his career at the Rockefeller Hospital, developed a whole series of instruments aimed at monitoring the concentration of metabolites in the blood and urine of patients. These same parameters were used as a means of classification for pathological conditions. A crucial requirement for these instruments was that they were simple and could be applied as routine diagnostic procedures.

Angela Creager stresses the importance of technologies in enhancing the authority of molecular approaches in the acrimonious debate between "molecularists" and "colloidalists" in the 1920s and 1930s. Where, as in the case of proteins, classical chemical methods for establishing molecular purity often failed, instruments such as ultracentrifuges provided important new criteria for classifying substances as molecules. Ironically, the ultracentrifuge and the Tiselius apparatus, which played a crucial role in shifting the balance of influence between the two groups of scientists involved in the debate, were designed by colloid chemists with the aim of studying the properties of colloidal substances. The same instruments were later employed to define quality control standards for therapeutic molecules.

In the interwar years only a few prototypes of these instruments existed, conferring a privileged status on those who had access to them and experience and skill in handling them. The production of simpler commercial models which set in after World War II made the technologies more generally available. With governments and foundations prepared to allocate funding for costly technologies, a large number of laboratories acquired these instruments. By the 1960s, they became part of the standard armamentarium of all biochemistry and molecular biology laboratories.

Jean-Paul Gaudillière emphasizes the impact of wartime biomedical mobilization on the establishment of certain research practices around big technologies. The ultracentrifuge and the electron microscope were deployed as instruments for purifying and visualizing viruses in the wartime project on influenza. The same instrumental practices, Gaudillière argues, were deployed in the construction of cancer viruses and

later in scaling up cancer virus research. The availability of commercial instruments was crucial for the standardization of such biomedical practices.

As in the case of viruses, so the construction of abnormal hemoglobins and the diseases associated with them was inextricably linked to the availability of technologies aimed at a molecular level of analysis. Soraya de Chadarevian follows the career of abnormal hemoglobins from Pauling's first representation of sickle cell hemoglobin in the Tiselius apparatus to the identification of new hemoglobin variants through chromatographic and electrophoretic fingerprinting techniques. Like Amsterdamska, she points to the importance of simple commercial instruments for the applicability of new diagnostic techniques in the clinic as well as in surveys in the field. She also discusses the role of molec ular models as a technology for the representation and analysis of molecular structure-function relationships.

De Chadarevian, like Goodman in his biography of colchicine, describes how molecules (or collections of molecules) themselves are turned into laboratory or diagnostic tools. In the course of its career, colchicine turned from a therapeutic agent to a tool for the study of mitosis and later into one for tracing microtubuli in the cell. Similarly, hemoglobin and its variants were used as tools for genetic analysis on a molecular level and more generally for structure determinations.

Finally, several authors deal with large-scale trials, surveys and screening programs as technologies aimed at tracing the presence of specific molecules in the body, or assessing the therapeutic efficacy of molecules. Gaudillière discusses the systematic screening for mammalian and human cancer viruses under the contract system established by the U.S. National Cancer Institute. Löwy explicitly links the cooperative organization of large-scale clinical trials, such as those for new cancer drugs organized by the Cancer Chemotherapy National Service Center in the U.S., to the experience of wartime research. In her chapter Löwy notes that "war research 'acclimatized' physicians with large-scale projects, coordinated actions and the need to suspend part of their expertise-based authority to achieve collective goals". This climate favored the development of cooperative enterprises such as the clinical trials of penicillin and streptomycin.

Also Lehmann's first experience with large-scale surveys dated, as de Chadarevian points out, from his service in the Royal Army Medical Corps in India during the war, where he studied the causes of anemia which commonly affected the troops. He acquired further experience in large-scale blood sampling as a colonial medical officer in Uganda, where he continued to study the causes of anemia and became interested in the distribution of sickle cell hemoglobin in African populations.

Phenylketonuria (PKU) screening marked a shift from social to biological, in this case biochemical, intervention in mental disorders. As Diane Paul and Paul Edelson show in their chapter, this shift was supported and welcomed by government agencies as well as by parents' associations. Despite many unassessed problems, such as the high incidence of false positive results, the unclear effects of dietetic treatment in healthy children and open questions relating to the prevention of the disease through phenylalanine-free diets, PKU screening was heralded as a model for the control of molecular diseases.

Lara Marks demonstrates the problems involved in applying a reductionistic model of women as hormonal bodies in the first clinical trials of the pill in Puerto Rico. Unlike experimental animals, the women participating in the trial could not be kept in a cage and

monitored for 24 hours per day. Instead, the organizers of the trials had to rely on the cooperation of women in following certain procedures. Despite the obvious limitations of the reductionistic approach, the trials did support the efficacy of the contraceptive pill in preventing pregnancy in women.

The Laboratory and the Clinic

Molecules created new alliances between the clinic and the laboratory. Several chapters in this volume take this as their central theme.

Laboratory techniques are not simply transferred or applied to the clinic. This point is made most forcefully by Amsterdamska, but also by other authors. Amsterdamska argues that the biochemists working at the Rockefeller Hospital did not merely take up "questions" posed by clinicians in their research. Clinical practices and concerns shaped all aspects of the biochemical work in this institution, as Amsterdamska illustrates in particular with respect to the development of monitoring techniques of bodily chemical functions. The construction as well as the meaning and the testing of these technologies relied on the close collaboration between clinicians and biochemists. Co-production rather than transfer of technology was therefore at work.

Focussing on hemoglobin as a model molecule for structural and genetic work, de Chadarevian takes up a similar point. She argues that, long before the advent of new therapies based on molecular genetic technologies, laboratory scientists derived material resources, functional knowledge and legitimation for their work from the clinic. Like Löwy in her chapter, she argues that molecular technologies (in protein research, genetics, or immunology) often failed to be translated into new therapeutic practices. Through the use of these technologies for diagnostic procedures or for monitoring patients, however, clinicians and laboratory scientists came to share a common molecular culture and provided mutual legitimation for their respective practices. Interferon or hemoglobin can thus be seen as "boundary objects" or molecules which, despite their different uses, link clinicians and laboratory scientists.

Following colchicine's life of multiple identities, Goodmann shows how molecules can move in and out of the clinic in a series of moves over time. Starting life as a therapeutic substance for the treatment of gout and rheumatic disorders, colchicine, after an uneven career as a research tool, came back to the clinic as a drug with a known, if disputed, molecular mechanism of action to which many disorders respond.

Together, these contributions render problematic the simplistic view of a oneway transfer of scientific advances from the laboratory to the clinic, and help to sharpen our view of how a molecular culture was constructed by interactions between both sites.

Molecules and Industry

Molecularization, in the laboratory and the clinic, also had important industrial dimensions. Industries were crucially involved in the production and circulation of standardized molecular reagents and drugs, as well as in the commercialization of instruments for the representation, measurement and analysis of molecules. Commercial interests often promoted molecular approaches. At the same time, industrial procedures

of production were also set in place in laboratories, and academic laboratories could keep a control function on industry through patenting procedures or monitoring industrial quality standards. The links between laboratory and industry were thus manifold and complex.

The chapters in this volume follow the industrial trail from the role of pharmaceutical industries in molecularization in the 1920s through the experiences of World War II to the rise of biotechnology industries in the 1970s. In her contribution focussing on early vitamin research, Harmke Kamminga shows how industrial interests in selling vitamin preparations and vitamin-enriched foods promoted structural investigations of vitamins in the interwar period. In this light, she discusses the transformation of a modest British food company, through its participation in vitamin research, into the well-known pharmaceutical company Glaxo.

Under the special conditions of World War II, the links between research laboratories and industries became tighter. This has been shown in the literature in relation to the production of penicillin. Angela Creager focusses on a much less well known military biomedical project, Edwin Cohn's Plasma Fractionation Project at Harvard. She emphasizes not only the close links between Cohn and the collaborating pharmaceutical industries, but the industrial style in which Cohn ran his own laboratory. The laboratory built a pilot plant for plasma fractionation which became the model for subsequent plants. The Harvard pilot plant served as the central production site for serum albumin as a substitute for full blood until commercial production was well underway in 1943. To cover the demands for serum albumin posed by the military, Harvard researchers had to operate the plant 24 hours per day. The management style Cohn imposed on the laboratory paralleled industrial as well as military structures. Following the fate of Cohn's empire after the war, Creager shows that Cohn chose to continue his close association with pharmaceutical industries, although professing his ideal of 'fundamental' research. Cohn exercised a control function over the industrial production of blood fractionation products by patenting his procedures and imposing biochemical quality standards which could only be met in his laboratory.

In his chapter on the virus cancer program in postwar America, Gaudillière stresses that the success of the virus theory of cancer causation relied on an extended network of contractors associated with the National Cancer Institute. These contract industries organized and guaranteed the production, circulation and control of biochemical and immunological tools for tracing viral cancer genes. They thus played a crucial role in the standardization of research practices, linking the laboratory as well as the clinic to industry. The contract system, Gaudillière argues, imposed a managerial style on scientific research which was modelled on industrial research practices.

Löwy traces new developments in the complex field of immunotherapy of cancer to the entrance of the biotechnology industry as a new player in the game. Mass-produced genetically engineered interferon could not fulfill the high-pitched promises of a cure for cancer, but was nevertheless integrated into routine treatment of cancer patients. A further point implicit in this and other chapters is that the industrial production of certain molecules rather than others both steers and limits choices of molecules for use in the clinic and the laboratory.

Policies and Politics

At important junctures, molecular approaches in research and to problems of health and disease were actively promoted by government agencies, foundations and associations representing patients. This support was often crucial in directing the course of molecular strategies, and in overturning resistances to them.

As discussed by Amsterdamska, in founding the Rockefeller Hospital in 1910, the American patrons intended to promote "scientific medicine" based on a chemical notion of the body and its malfunctions. Clinical practice of this kind required a closer interaction of biochemists and clinicians, which the Hospital was to foster. The Hospital remained a privileged place for the kind of collaborations envisaged by its founders, but it also provided the training ground for many future professors in the most important medical schools in the U.S. Training and educational policies more generally were obviously crucial in promoting molecular approaches in biomedicine.

Kamminga shows that the Royal Society Food (War) Committee set up in Britain during World War I and new government funds controlled by the Medical Research Council (MRC) were instrumental in boosting research on the structure and function of molecules. The role of the MRC in promoting new biophysical research after World War II is discussed by de Chadarevian.

As shown most explicitly by Creager, World War II, by means of government interventions and military interests, presented novel opportunities for the circulation of molecules. Cohn could build up his empire for blood products only through the special conditions of war. Once the war was over, he could maintain the central position of his laboratory in this field only by complying, at least in words if not in deeds, to the new government policy of "fundamental research".

Gaudillière and Paul and Edelson also stress the role of government programs and health policies in promoting molecular approaches in biomedicine in postwar America. Nixon launched a large cancer virus program rather than supporting other approaches to the cancer problem or to public health more generally. Behind the decision of the program stood a "policy-making community" which encompassed the American Cancer Society, the National Cancer Institute, big pharmaceutical companies and the U.S. Congress, linked together by experts circulating between these institutions. The molecularization of cancer etiology, Gaudillière concludes, had important political content and was carried by large biomedical networks formed in the aftermath of World War II.

Government organizations, together with parents' associations, were also instrumental in the shift from social to biochemical approaches to mental disorders. Paul and Edelson remind us that, before reliable tests for PKU or other metabolic disorders were available, a government report stressed the importance of metabolic screening. When Guthrie developed his bacteriological test to measure blood phenylalanine levels in newborn babies, he negotiated directly with the National Association for Retarded Children and with the Children's Bureau of the Department of Health, Education, and Welfare. Before the first field trials ended, and notwithstanding existing doubts concerning the diagnosis and treatment of PKU, the Bureau was already committed to a national screening program.

As the chapters collected in this volume indicate, molecularization had many meanings and involved many actors. Van Slyke's attempt to design instruments to measure and monitor chemical functions in the body was not the same as Pauling's or Lehmann's search for molecular causes of diseases. The isolation, purification and analysis of molecules in the laboratory was not the same as the mass-production and commercialization of molecular drugs. Molecularization involved research laboratories, industries, the clinic and the policy arena. Molecular strategies created new links, or radically changed existing links, between these domains, affecting society at large. The concept of molecularization allows us to link these changes together and to emphasize that the molecular-genetic culture in biomedicine known today rests on more than advances in molecular biology and biotechnology: it was preceded by, and embedded in, technically and socially much more diverse biomedical practices and links centred on strategic molecules.

NOTES

1The term "biomedical sciences" was introduced in the 1960s to justify the National Institutes of Health's diversion of funds, allocated for the study of human health and disease, into basic molecular biology (Feinstein, 1995, p. 289). For convenience, we occasionally use the term with reference to earlier periods.

2 The authors differ in the connotations they give to these terms, either implicitly or explicitly. Lily Kay (1993b) has used "molecularization" to refer to practices centred on macromolecules, especially proteins, from the 1930s. Robert Olby (1990) locates the beginnings of the "molecular revolution" in biology around the same period, also restricting this to studies of macromolecules. Susan Wright's (1994) term "molecular politics" refers to the recombinant DNA debates of the 1970s. Hans-Jörg Rheinberger (1995) has used "molecularization" specifically in relation to the new genetic medicine.

3 On the dispute between molecular biologists and biochemists, see Abir-Am (1992) and de Chadarevian and Gaudillière (1996).

4 The pioneering study of laboratory practices in the biomedical field is Latour and Woolgar (1979); see further especially Clarke and Fujimura (1992). Alliances between laboratory science and medicine are examined in Pickstone (1992) and Löwy (1993), while industrial connections are at centre-stage in Gaudillière and Löwy (1997), Liebenau (1987) and Swann (1988). Studies of science policy in relation to the life sciences and medicine are presented in Abir-Am (1982), Austoker and Bryder (1989) and Kohler (1991).

5 The term "magic bullet" was first used by Ehrlich in the context of serum therapy. He assumed that the protective substances, being produced by the human body itself, were both highly specific and non-toxic. Synthetic molecules as used in chemotherapy, however, would not have perfect affinity for the cellular protoplasm and would inevitably be toxic to some degree (Marquardt, Chapter 12). The term "magic bullet" was revived in relation to penicillin, even if it did not conform strictly to Ehrlich's criteria. It was later used more loosely for "wonder drugs" in