The Heineken Lectures were presented during a special session of the Royal Netherlands Academy of Arts and Sciences on 25 September 1998 in Amsterdam.

Royal Netherlands Academy of Arts and Sciences

KNAW / Heineken Lectures

1998

Amsterdam, 1999

ISBN 90-6984-251-3

© Royal Netherlands Academy of Arts and Sciences, P.O. Box 19121, 1000 GC Amsterdam, the Netherlands.
No part of this publication may be reproduced, stored in a retrieval system or transmitted in any form or by any means, electronic, mechanical, photocopying, recording or otherwise, without the prior written permission of the publisher.

CONTENTS

It was the fifth time that the Heineken Lectures were organized by the Royal Netherlands Academy of Arts and Sciences as part of the festive programme of the presentation of the bi-annual Heineken Prizes for Sciences and the Arts. In an open meeting the winners of the Heineken Prizes gave a lecture about their work for an audience of scholars and scientists, general public and the media. This publication of the Heineken Lectures 1998, gives us insight into the work for which the laureates have been honoured: Heineken Prize for Biochemistry and Biophysics – Tony J. Pawson, Heineken Prize for Medicine – Barry J. Marshall, Heineken Prize for History – Mona Ozouf and Heineken Prize for Environmental Sciences – Paul R. Ehrlich. This year the particular artistic field chosen for the Heineken Prize for Art was sculpture and the prize was awarded to Jan van de Pavert.

A 'dramatic' development has taken place since the presentation of the Heineken Prizes in 1996. The End of Science has been proclaimed. But, science is in good company, because the end of history, the end of art and the end of nature have also been proclaimed. The closing stages of the second millennium seem to attract prophets of doom like a magnet. Nonetheless, John Horgan, author of the book *The End of Science; facing the limits in the twilight of the Scientific Age*, has conducted interviews with highly reputed scientists and scholars and unveiled a number of interesting questions. The main thrust of his book is of course that after the contributions of Newton, Einstein and Darwin, and quantum physics, we can expect no more new discoveries of a truly fundamental nature. Horgan's interviewees generally agreed that paradigms on a par with these could no longer be expected. The book is an indictment against the degeneration of research into so-called *ironic science*: the free postulation of speculative assumptions which are no longer falsifiable by experiment. Horgan attacks especially the superstring theory, which is supposed to bridge the gap between the general relativity theory and quantum mechanics. Infinite little strings are supposed to form the raw material for the known particles; hypothetical strings that exist in inconceivable ten-dimensional hyperspace; it is a mathematical model in line with current ideas, which cannot be verified by experiment.

I think that our colleagues from the field of physics would have plenty to say about this. It does however touch the sensitive area where science falls victim to its own success. We see the meteoric costs of mega- not to mention giga-science and

learn that the government is no longer prepared to pay the price for new fundamental knowledge and deeper insight. Even more dangerous is that society is so preoccupied with the pressing problems of environment, health and crime that it is investing less time and money in scientific research which does not meet short-term needs.

This is not the place for exploring these questions in depth. But I would like to point out that we must invest more in the public understanding of science. Unfortunately, this is highlighted all the more by the recently formed Dutch coalition cabinet, which decided to reduce the science budget. The new Minister of Education, Culture and Science policy is not to be envied. He has to cut expenditure on higher education and scientific research by hundreds of millions of guilders. Relatively speaking, these economies are far more trenchant than those earmarked for defence. But this does not stop the defence cuts from getting immeasurably more political attention. It is clear that there is a need for a collective attempt to convince the public and the politicians of the need to halt the downward spiral in the science budget.

The Heineken Prizes play an important role in our efforts to enhance public awareness and understanding of science and its impact upon society. Every two years we are able to present to the general public a group of the world's most prominent scientists and scholars. Fortunately, the national press displays a great interest in the personality and work of the prize winners.

I am grateful to the Heineken Foundation and the Alfred Heineken Funds Foundation for so generously financing the five prizes, in recognition of scholarly, scientific and artistic excellence. The service they render to the arts and sciences cannot be praised highly enough.

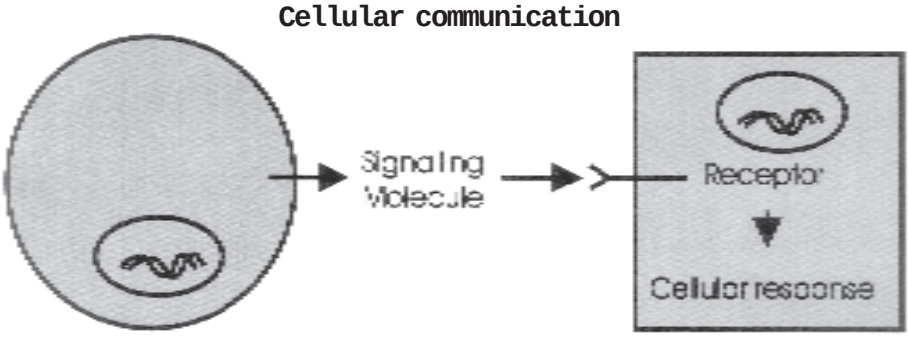
Pieter J. Zandbergen
President of the Royal Netherlands Academy of Arts and Sciences

Tony J. Pawson

Protein modules in signal transduction

Dr. Anthony J. Pawson received the Dr. H.P. Heineken Prize 1998 for his important discovery of the 'SH2 Domain' in proteins involved in signal transduction in living cells. His work has yielded a better insight in the way in which cells communicate with neighbouring cells.

The development and maintenance of complex organisms, such as ourselves, requires a constant process of cell-to-cell communication. This is necessary for the proper differentiation of cells in the embryo and their organization into distinct tissues, and for the ongoing supply of new cells in the adult. In addition, after birth the body must fight infection and respond to its environment through a continuous flow of molecular information between cells. This communication is achieved through the release by one cell of a signalling molecule, frequently a protein hormone, which exerts a specific biological effect on a separate, target cell.



One cell releases a signalling molecule, often a protein, that binds to a receptor displayed on the surface of a target cell. The activated receptor then intiates a response in the target call by stimulating intracellular biochemical pathways

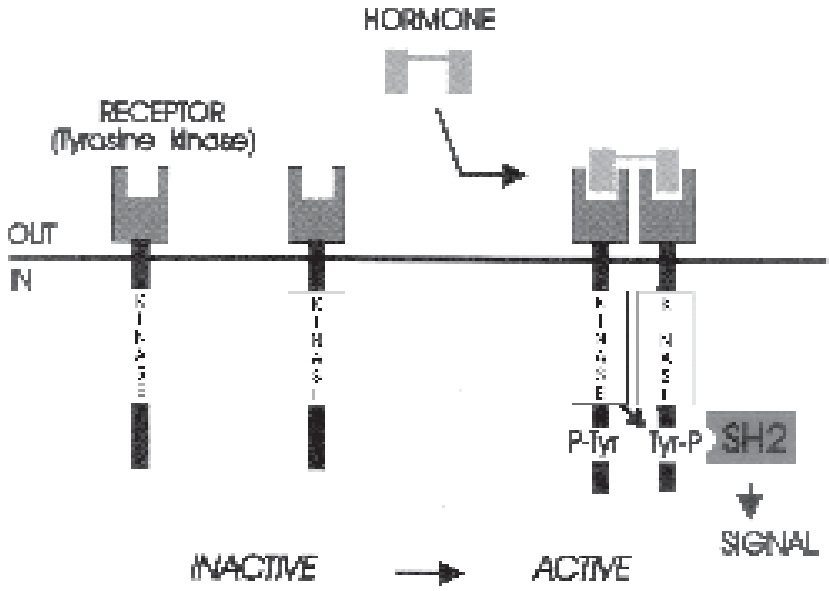
For the target cell to respond, it must express a receptor (also a protein) which binds tightly to the hormone. Receptors frequently have a region that protrudes from the surface of the cell to engage the hormone, a segment that spans the cell's outer membrane, and a component located in the interior of the cell. Thus the receptor serves as an antenna, that senses conditions outside the cell and can transmit this information to the inside.

Binding of a hormone to its receptor modifies the properties of the receptor's cytoplasmic region, which consequently activates biochemical pathways within the cell. These pathways can potentially lead to numerous internal targets and thereby influence essentially every aspect of cell behaviour, including gene expression, cytoskeletal architecture, progression through the cell division cycle, survival, migration and metabolism. A well-known example of this process involves insulin signaling. Cells within the pancreas release the hormone insulin; target cells display an insulinreceptor on their surface which is absolutely

necessary for the insulin response. Binding of insulin to its receptor induces receptor activation, and numerous changes in the receptor-expressing cell.

While this molecular conversation is absolutely essential for cells to achieve and sustain a viable body, breakdowns in this cellular communication underlie a broad range of diseases, including cancer, developmental abnormalities, immune and cardiovascular disorders and neurological diseases, amongst others. In the example given above, a failure to make or respond to insulin results in diabetes. Conversely, an inappropriate activation of a growth-promoting receptor, caused for example by a mutation in the gene encoding the receptor protein, can result in abnormal and ultimately malignant cell growth. I have been primarily interested in understanding the mechanisms through which cells respond to activated receptors, and in learning whether there are general rules which govern the flow of biochemical information within animal and human cells. My work was originally prompted by the observation that numerous receptors possess cytoplasmic

Receptors signal through SH2 proteins



A hormone such as platelet-derived growth factor binds to a receptor that spans the membrane, and has a cytoplasmic tyrosine kinase domain. The activated receptor self-phosphorylates on tyrosine (Tyr), and the resulting phosphtyrosine (P-Tyr) motif on the receptor is recognized by the SH2 domain of a cytoplasmic signalling protein.

protein-tyrosine kinase domains, whose activity is normally dependent on binding of the appropriate hormone to the extracellular region (the insulinreceptor being one example). A protein-tyrosine kinase transfers a phosphate group from ATP to the amino acid tyrosine, within the context of a protein (which is composed of numerous amino acids linked in a linear chain), yielding a protein that now contains phosphotyrosine. A number of cancer-causing (onco-) genes encode mutant versions of such receptors, which are constitutively active in phosphorylating substrate proteins on tyrosine even in the absence of any external signalling molecule. A single activated tyrosine kinase at the membrane can change many properties of the affected cell, and the questions we set out to answer were how this happens, and whether this might provide general clues about what was effectively a black box, namely the internal signalling pathways through which receptors are linked to their targets. At the time in the early 1980s, a reasonable hypothesis was that tyrosine kinases and their substrates would associate in a typical enzyme-substrate interaction, resulting in phosphorylation of the protein substrates. These substrates, which were envisioned to be enzymes, would then undergo a conformational change resulting in their activation. Such a scheme involving the consecutive activation of soluble enzymes would be consistent with the known pathways that mediate intermediary metabolism. However, one puzzling property of activated tyrosine kinases was that they appeared to be their own best substrates. In other words, a tyrosine kinase will prominently (auto)phosphorylate in what we and others found to involve an intermolecular reaction. That is to say one tyrosine kinase chain adds phosphate groups to tyrosine residues on a neighbouring chain. Using an oncogenic tyrosine kinase called v-Fps, we found in 1984 that one autophosphorylation site is located within the catalytic domain itself and stimulates enzymatic activity. However, the means by which activated tyrosine kinases might interact with their downstream targets, and indeed the identities of these targets remained mysterious.

To digress for a moment, it is important to point out that tyrosine kinases can be divided into two classes – cell surface receptors of the sort discussed above, and proteins that are confined to the cytoplasm. These cytoplasmic tyrosine kinases tend to associate with the internal face of the plasma membrane, and frequently serve as signalling subunits of complex, multi-chain receptors such as those for antigens in lymphoid cells, as well as cytokine receptors. The venerable Src tyrosine kinase, as well as Fps, are cytoplasmic proteins that belong in this second class. In analyzing the regions of the Fps tyrosine kinase that are required for its oncogenic activity we identified a region that precedes the kinase domain, and despite the fact that it is not required for kinase activity plays an important part in

its biological function. Our early work, published in 1986, suggested that this non-catalytic region can modify enzymatic activity and has a role in substrate recognition. A comparison of the family of cytoplasmic tyrosine kinases indicated that they share this sequence of approximately 100 amino acids, which we therefore termed the Src homology (SH) 2 domain, with the kinase domain itself being the SH1 region. We proposed that the SH2 domain might form an independently folding module, or cassette, that directs interaction of the tyrosine kinase with components of the host cell.

Subsequent work identified a growing number of cytoplasmic signalling proteins that possess SH2 domains. SH2-containing proteins have been found that regulate phospholipid metabolism, Ras-like GTPases, protein phosphorylation and dephosphorylation, gene expression and cytoskeletal architecture. We proposed that these proteins might all be involved in tyrosine kinase signalling, by virtue of the fact that they possess the SH2 domain. Support for this idea came from our finding that the Ras GTPase activating protein (GAP), an enzyme that downregulates the Ras protein, is itself phosphorylated on tyrosine in response to growth factor stimulation and associates with two other phosphotyrosine-containing proteins. The issue, however, remained as to the precise function of the SH2 domain in signalling from receptor tyrosine kinases (which themselves do not have SH2 sequences, unlike the cytoplasmic tyrosine kinases), and the reason for the strong propensity of growth factor receptors to autophosphorylate at numerous tyrosine residues, including sites located outside the kinase domain proper. In 1989 we undertook a series of experiments using recombinant DNA techniques in which SH2 domains from a variety of quite distinct cytoplasmic proteins were expressed in isolation in bacteria, and asayed for their ability to bind activated receptors. Using extracts of cells stimulated with platelet-derived growth factor (PDGF) or epidermal growth factor (EGF), we found that a variety of isolated SH2 domains would bind directly to the activated PDGF- and EGF-receptors provided that the receptor had undergone autophosphorylation on tyrosine. Particular SH2 domains would also bind to specific phosphotyrosine-containing proteins other than activated receptors. These data led to a simple suggestion for the mechanism by which receptor tyrosine kinases might interact with their targets (published in 1990).Binding of a hormone to its receptor induces receptor autophosphorylation, which serves two functions. Tyrosine phosphorylation in the kinase domain stimulates kinase activity, while the phosphorylation of tyrosine residues outside the kinase domain providedocking sites for SH2 domains. This results in a physical association of activated receptors with downstream targets. We showed that there is specificity in the interaction of SH2

domains with different receptors, although at the outset we did not understand the molecular basis for this discrimination. We also indicated that proteins with two SH2 domains might bind co-operatively to activated receptors.

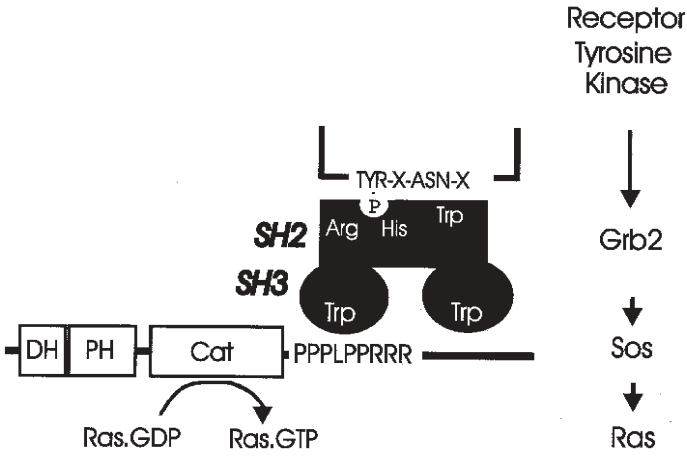
This model had several interesting implications. First, it suggested that rather than having a simple enzyme-substrate interaction with their targets, activated receptor tyrosine kinases inducibly bind their targets in an SH2 domain-mediated interaction. Second, it implied that the common presence of an SH2 domain allows an otherwise biochemically diverse group of proteins to couple directly to activated receptors. Thus rather than tailoring every target to undergo a unique allosteric change upon tyrosine phosphorylation, the SH2 domain functions as a portable module or cassette that can be plugged into virtually any host protein, and endow that protein with an ability to associate with activated receptors or other phosphotyrosine-containing proteins. What might be the consequences for a cytoplasmic signalling protein that associates through its SH2 domain with an activated receptor? Such a protein might become a preferred substrate for phosphorylation, once physically tethered to the receptor tyrosine kinase. However, it was also possible that re-localization within the cell, caused by binding to the receptor at the membrane, might contribute to stimulating a signalling enzyme by bringing it into the vicinity of its substrates. Even more intriguing was the possibility that the SH2-containing protein might not be activated by its own phosphorylation at all, but simply through its recruitment to the phosphorylated receptor. We now know of several cases where this seemingly heretical notion, that tyrosine kinase targets are not necessarily activated through tyrosine phosphorylation but rather by their docking onto receptors, holds true. Although entirely incomplete, the broad mechanism through which signalling proceeds was starting to emerge.

Signal transduction is controlled through regulated protein-protein interactions, mediated by modules such as SH2 domains. A critical function of these modules is to direct the localization of signalling proteins and thus their association with activators, targets and regulators. Through the repeated use of such modular domains, a network of interactions can be established that stretches throughout the cell, and provides the molecular framework through which signals are transmitted. Several findings both from our laboratory and from an increasing number of investigators pursuing this area started to fill in many of the missing pieces in the signal transduction puzzle. SH2 domains serve as the proto-type for a growing family of protein modules that mediate specific protein-protein and protein-phospholipid interactions. These include SH3 domains, that recognize proline-rich motifs and PTB domains that like SH2 domains can bind selectively to

phosphotyrosine-containing motifs, amongst many others. In several cases, proteins with SH2 domains were found to lack any obvious catalytic elements, but to contain other protein interaction modules such as SH3 domains. In principle, we proposed, such a protein might serve as an adaptor to physically link an activated phosphotyrosine-containing receptor to a target with proline-rich motifs.

In 1992, R. Horvitz and colleagues identified such an adaptor in the nematode worm *Caenorhabditis elegans*, that on genetic grounds appeared to link a receptor tyrosine kinase to activation of the Ras pathway. This protein, called Se-5, has the organization SH3-SH2-SH3, This finding was very important for a number of reasons – it was the first genetic confirmation for an important physiological function for SH2 and SH3 domains, and it began to unlock the critical question as to how tyrosine kinases communicate with the Ras protein. At the time, I proposed that the SH3 domains of a protein such as Sem-5 might physically bind a guanine nucleotide exchange factor, that activates Ras by causing the release of GDP and consequent binding of GTP. We turned to another invertebrate system, the fruit fly Drosophila melanogaster, to pursue this idea. We isolated a Drosophila homologue of Sem-5 (termed Drk), and in a serendipitous series of experiments with E. Hafen, were able to show not only that Drk is critical for linking tyrosine kinases to Ras in the intact organism, but also that the SH3 domains of Drk bind an enzyme called Sos, that was known to activate Ras. Mutations that interfere with the ability of the Drk SH2 domain to bind activated receptors, or with the binding of the SH3 domains to Sos, blocked signalling in vivo to the Ras pathway. Subsequently, several laboratories, including ours (in collaboration with D. Bowtell), J. Schlessinger's, D. Bar-Sagi's and J. Downards's, all showed that the mammalian homologue of Sem-5 (Grb2) physically associates with mammalian Sos proteins, which are thereby recruited to activated receptors. Interestingly, Grb2 is not significantly phosphorylated on tyrosine during his process, and the enzymatic activity of Sos does not seem to change.

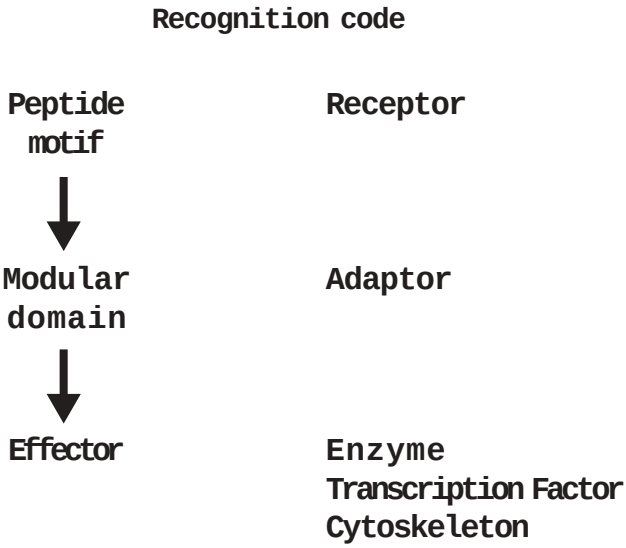
Thus the activation of the critical Ras pathway by receptor tyrosine kinases is apparently accomplished solely through combined SH2- and SH3-mediated interactions and relocalization of the downstream target Sos in the plasma membrane. Specificity in signal transduction is of particular importance. We now understand that SH2 domains recognize not only phosphotyrosine, but also 3-6 amino acids immediately following the phosphorylated tyrosine residue. Each SH2 domain shows a unique preference for amino acids at these C-terminal positions, and this confers specificity in the recognition of individual



An activated receptor tyrosine kinase binds to the SH2 domain of an adaptor protein. The SH3 domains of the adaptor bind proline-rich motifs in the tail of another protein Sos, that acts to activate the Ras GTPase. Thus, activation of Ras requires a series of modular protein interactions

phosphotyrosine sites by distinct SH2-containing proteins. Indeed, we have been able to engineer SH2 domains with modified binding specificity, and have shown that their biological activity matches their biochemical binding properties.

These results have suggested that the amino acid sequence surrounding a receptor's autophosphorylation sites will dictate which SH2-containing proteins that receptor can bind, which in turn will determine which biochemical signalling pathways the receptor can activate. Therefore, in signal transduction there appears to be a recognition code in which peptide motifs on activated receptors are read by modules, such as SH2 domains, which in turn are linked to enzymes, to transcription factors or to cytoskeletal components. While this view of signalling was originally established using receptor tyrosine kinases, the same general principle seems to hold for a remarkably broad range of signalling systems. Receptors of the Fas/TNF-receptor family possess a cytoplasmic module called a death domain, which interacts with an adaptor that itself has a death domain and a related module through which it couples to downstream targets. Thus although the details are quite different, the overall concept of regulated modular protein-protein interactions and the use of adaptor proteins is the same. Ion channels in the nervous system and elsewhere are organized, and likely exert a large part of their signalling activity, through modular interactions involving elements known as PDZ domains.



We propose a recognition code in signal transduction in which peptide motifs in receptors are recognized by modular domains, frequently found in adaptor proteins. These interaction domains are coupled either directly or non-covalently to effectors, which can be enzymes, transcription factors or cytoskeletal components.

Furthermore, there is growing evidence that a major role of serine phosphorylation, as with tyrosine phosphorylation, is to directly control specific protein-protein interactions. Indeed, the networks of protein-serine kinases and phosphatases that function within the cytoplasm and nucleus to regulate many features of cell behaviour are increasingly seen to be controlled by adaptors and docking proteins, that direct their subcellular location and activation. Similarly, the cell cycle is regulated through a series of modular protein complexes that target individual proteins for serine phosphorylation, and frequently degradation, in a fashion that gives directionality to progression through cell division. Events such as endocytosis and protein trafficking also involve protein modules that mediate specific interactions, some of which were originally detected in the context of tyrosine kinase signalling. One can also argue that events in the nucleus that control gene expression involve a regulated series of protein-protein and protein-DNA interactions that are reminiscent of those occurring at the membrane and the cytoplasm.

These modular protein complexes are not only of academic interest. Aberrant signalling involving modular proteins is associated with cancer, with diabetes, with immunodeficiencies, and with several inherited developmental defects. The work described above has started to reveal the molecular language through which cells process information and regulate their behaviour. The basis for this information flow is a network of modular protein domains that control the function of signaling proteins by modifying their site of action and their associations with other proteins. Using this relatively simple device, the human cell has built up a complex web of interactions through which cellular activity is controlled. As we learn more of these interactions it may prove possible to design drugs that will manipulate their formation, and thus be useful in the treatment of human disease.

The ideas outlined above summarize the work of a large number of scientists with whom I have had the pleasure of working. In particular, Ivan Sadowski, Jim Stone and Gerry Weinmaster played essential roles in the early analysis of phosphotyrosine signalling and in the discovery of the SH2 domain. Michael Moran and Deborah Anderson identifed the association of SH2 domains with activated receptors. Paul Olivier, Luc Marengere, Jane McGlade and Maria Rozakis-Adocock were instrumental in establishing the connection between tyrosine kinases and Ras. In addition, I have benefited greatly from numerous discoveries made in other laboratories, and from a marvellous series of collaborations, some of which are noted above. In particular, Tony Hunter's discovery of tyrosine phosphorylation, Hidesaburo Hanafusa's identification of the Crk adaptor, and Lewis Cantley's work on the recognition motifs for SH2 domains stand out as being of great importance. I am particularly indebted to my colleagues in Vancouver and Toronto, where our work has been undertaken. We were fortunate to be close to Michael Smith when he was doing his pioneering work on site-directed mutagenesis, a technique which was critical for our early research. I have benefited enormously from my close connection with Janet Rossant, Alan Bernstein, Joseph Culotti, Julie Forman-Kay, Lewis Kay in Toronto.

Biomedical research is a communal enterprise, and I am indebted to these and many other colleagues for their insights and wisdom.

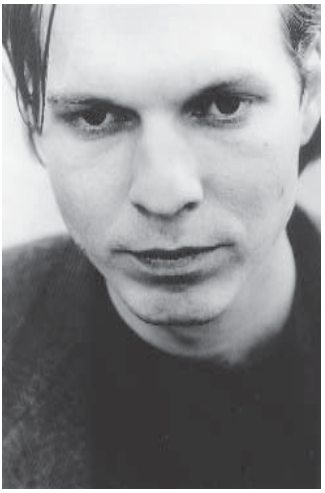
Review articles

Pawson, T. and J.D. Scott. 1997. Signaling through scaffold, anchoring and adaptor proteins. *Science.* 278:2075-2080.

Pawson, T. 1995. Protein modules and signalling networks. *Nature.* 373:573-580.

Jan van de Pavert

The formal in art and its acceptance



The Dr. A.H. Heineken Prize for Art 1998 was awarded in the category of sculpture to Jan van de Pavert for his recognizable and personal oeuvre. In fourteen years the young artist Van de Pavert developed into a strong personality with a rich and diverse palette.

I do not believe that there exists a clear definition of the term 'formal art'. I do understand, however, that there are plenty of artists who are determined that they do not want their work to be regarded as formal. Someone will sometimes drop the word 'formal' in a studio, within earshot of an artist, who then looks upset and reacts with denials, as if it was an insult. But I am certain that a large part of the artist's problem concerns the formal, and that defining the problem of the formal leads to an unproblematic acceptance of art. 'James Welling's work is not only photography. It is also *about* photography.' 'The signs which appear in Lasker's paintings *are about* the appearance of signs in painting.' 'My sculptures are about the viewer's stance towards them. Hence the shiny surfaces in which the audience can see themselves; the relationship between the work and the viewer is thus made visible.' Such definitions of signs, of technique and of the work of art in relation to the viewer all concern the formal side of the artwork.

However many ideas are invested in a work of art and whatever direction it takes, the decisions which result in its creation are partially dependent upon its relationship to other works of art. However, speakers and writers seldom acknowledge that they are addressing this formal side. In fact, they often explicitly deny it.

During the 1950s the word 'formal' primarily referred to something like a balance within the framework of the canvas. During the same period, though, the idea of a formal art was turned inside out: artistic production became regarded as an attempt to exclude these formal aspects. Hence the rise of the term '*in*formal' art. Art with a style like that of a child, for example; action painting; COBRA and various works of abstract expressionism – these were all examples of informal art.

In those days a work of art was regarded as the expression of a personal subject. The artist was a subconscious medium. He brought his paint onto the canvas with gestures. These gestures then had to be explained to the public by the critic and the art historian (at least, that was the case for European art in particular). A booklet from 1965, about the acquisitions made by the Boijmans Van Beuningen Museum, is still redolent of that spirit. It contains this wonderful sentence about the paintings of Asger Jorn: 'These Nordic images lead a slumbering existence in the painter's subconscious, *and are brought to the surface of consciousness by the very act of painting itself*' (my italics). Behold, the artist is the medium: the subconscious is spread onto the canvas through his gestures, with the art historian interpreting the results for us.

That 1965 booklet not only discusses the subconscious: the artist is 'more emotional than intellectual', full of 'dreams, anguishes, nightmares'. The 'informal', of course, fitted well into this irrationality. So too did a view of society

as being tragic. (Discussing the painter Francis Bacon, the world was described as 'condemned to disintegration', while Horst Antes prompts mention of 'a Europe intoxicated by the "economic miracle" of the 1960s'). An art which expounds so much tragedy and which is so full of angst and messages from the subconscious cannot, of course, embrace any programme which contributes to the creation of a forward-looking society, as was the case with Bauhaus or De Stijl. It is also clear that the struggle for balance as part of such a programme had to be absent from it. And that the notion of the *in*formal was an expression of this.

It is striking that since that time art critic and historians have virtually only ever mentioned the word 'formal' in order to repudiate it. Never has there been any question of a discourse in which a work of art's formal aspects are acknowledged as such.

Between 1955 and 1969 an enormous change took place in art. Monochrome paintings appeared; composition and colour were rejected. 'Happenings', photography, films (and later videos), and space-filling installations appeared. And the artist changed from being a seething paint-thrower into an active decision-maker. Or a theoretician.

An entire catalogue could be compiled containing hundreds of illustrations which would show – like an evolutionary family tree – the various forms of transition from uncontrolled brushwork to the late 1960s.

However, the arguments and justifications put forward by art historians and critics did not exhibit the same gradual change. From about 1965 you suddenly find a different type of text, containing different arguments which legitimize different works of art. An evolutionary family tree, showing the step-by-step transition from one concept to the next, no longer exists. At a stroke, a new generation of art historians took over. The older ones were left speechless. Take, for instance, a rather didactic book from 1965 by Haftmann (an important figure in the Documenta exhibitions), which accepts the 'old' explanation of *belle peinture* and abstract expressionism: here again we have painters who subconsciously depict their inner impressions. But Haftmann devotes just a single column of text to the new Pop Art and *nouveau réalisme*. He first talks about the freedom of the artist, saying that we should accept such freedom, but then says that that very liberty 'has in recent years given rise to a rebellious, unrestrained grasp on reality, obsessed with sarcasm and black humour.' Haftmann has evidently been caught unawares. He mumbles on a little about the legacy of Dadaism and then abruptly ends his text.

What occurred next, from about 1965, was a new debate about the work of art on an entirely different, formal basis: the painting was discussed as an object – an

object on the white wall of the museum or gallery. From that point on, the work of art became something to be analysed or interrogated. The artist's mark or signature was understood as traditional and affirmative – and as such, rejected. The canvas suddenly became a framework or a carrier, neither of which notion had previously been considered. The white wall upon which the work of art hung was no longer neutral but, as a wall in a gallery, became the field within which the object became a commodity – and adopted a critical or an affirmative stance.

It is particularly striking that the notion of the painting as an object which became so specific from the 1960s onwards is nowhere to be found in the 1950s. Not even, in fact, where we might expect to find it: for example, in association with Yves Klein's monochrome canvases. At that time, nobody's work was more eligible for the interpretation of the painting as that of Yves Klein (apart, I suppose, from the German/Central American Goerritz). But the Pompidou Centre's 1983 catalogue contains summaries of articles written about Klein's work – and prior to his death in 1962, these do not include a single text which mentions the canvas as an 'object' or a 'carrier'. They do not even suggest such a notion. Later, in 1967, it becomes clear from statements by Robert Ryman – an artist and producer of white canvases (quoted in Lucy R. Lippard's *Six Years*, 1973) – that not only has the notion of the painting as an object become generally accepted, but also that Ryman is apparently apologetic for the fact that his works are objects. Granted, Ryman is an American. And the new formal notions – of which I find that of the 'canvas as object' a prime example – would probably not have had such an edge if American ideas about art had not penetrated European ones so deeply.

There still remains the impression that no texts exist which mark the transition from the 1950s to the 1960s. I therefore think that there must have been a clean break: European art historians had mastered the language with which they had legitimized the action painters and the abstract expressionists. In the meantime, a few artists and art critics, in particular, began to formulate a new context. The number of artists and critics who associated themselves with this new context grew. After a while, a new crop of historians appeared who no longer accepted the language by which abstract expressionism had once been given a justificatory cachet. The 'old' group of historians dwindled in size, and as they retired, a new language established itself – a new justification of art.

This turnaround would not have been so powerful and so lasting if it had not been coupled with the new affluence and cash injections of the 1960s and early 1970s. Those who research art history see that the greatest and most lasting influence is always accompanied by the greatest flow of money.

It is important here to point out again the critical connotation which the new

ideas had from the 1960s – the work of art as an object on a white wall, and the object on the white wall as a commodity. Despite these connotations, which tied formal art to society and politics during the 1960s and later, the art of that period was clearly distinct from the avant-garde movements of the early 20th century. After all, the idea of auguring the promises of a forthcoming era was specific to the latter – and was a prevailing idea not only in art, but also in the politics of that period. In my opinion, that is the reason why it is problematic to apply the term 'avant-garde' to the art of the 1960s: in these years it was critique which dominated. Critique distances; anticipation does not. Anticipation existed perhaps only in terms of power (just as a student occupation of a university administration block is a reference to power. In art, I am reminded of Jan Dibbets, for example, who as a young man stood outside the Stedelijk Museum digging at its cornerstones and told an interviewer that he wanted to expose its foundations. In any case, one should remember that we are now almost as far removed from the 1960s as 1900 was from Courbet and Manet's major works).

But then, at some later point after the 1960s, ideas changed again. This is the last change in the arguments used to justify art which I shall describe. This turnaround originated during the 1970s. Perhaps by then it was already evident amongst those artists who associated themselves with performance and video: there, revulsion prevailed over critique, sex and suffering over analysis (Ben d'Armagnac). A change also came about through the new interest in Europe from Kounellis and Fuchs. It could be seen in the work of many artists who became well-known between 1965 and 1978. The specific characteristics of their work had for the most part developed during the period 1965-1972, and later in the 1970s they simply repeated their inventions. Consider, for example, Kounellis' steel plates and coal sacks, Richard Long's stone gardens, Carl André's steel tiles or Mario Merz' number sequences and igloos. The works themselves became heavier, their impact lighter. Once again, the work of art became a representative object: the specific characteristic of the work (coal sacks, steel tiles, etc.) acquired the same role as the artist's style had once had in abstract expressionism. This change also suddenly made it possible to appreciate expressionists like Lüpertz or Baselitz and the so-called trans-avantgarde.

It appeared that attention to the formal aspects of art could simply be extended a few decades after all. Certainly, during the 1980s and early 1990s such notions as the work of art as object, the canvas as carrier, the gallery as white cube and the artist's style as signature remained intact. Photography, for example, could still (or again) be presented as an alternative, so that the artist did not have to use a brush; no personal 'signature', no inner emotion, no composition – just registration.

But the context for those formal aspects was now an entirely different one. It was no longer that of criticism. The new context primarily referred back to the art itself. References were made to the end of the modern, to cracks and fissures in meanings, or to the absence of values in meanings. Within the course of a text, it was proposed that even what the text itself was proposing could be deconstructed. In the place of criticism, art became the extension of a 'meta-language': language about language, images dealing with images, art about art.

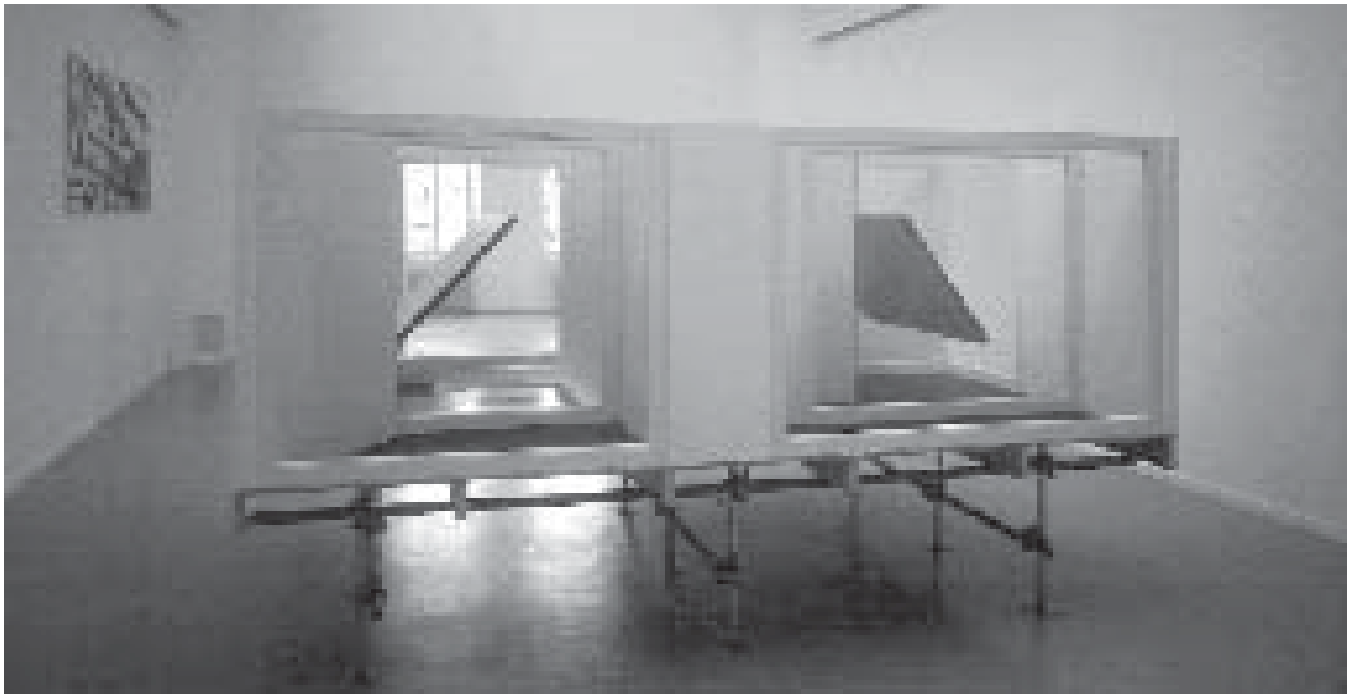
This was the time when painter Jonathan Lasker claimed that the signs which appear in his paintings were about the appearance of signs in paintings. And when it was said about James Welling's photographs that they were not just photographs, but that they were about photography. And when an artist stated that her work was about the viewer's position in relation to the work. Purely formal exercises, every one.

Ultimately, one can say that the art of the 1980s has become a purely formal art: art which deals with the operation of art, and which does so on a theoretical (or quasi-theoretical) foundation which continually undermined the possibility of finding other relationships beyond art.

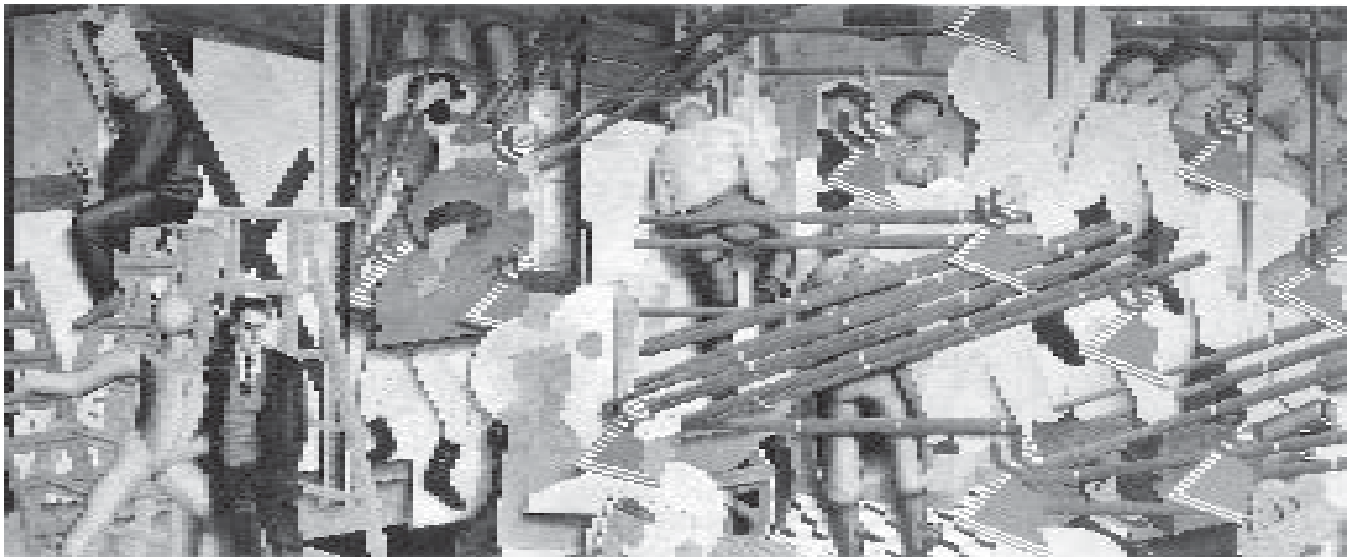
At Documenta 9 in 1992, a work by Heimo Zobernig was shown, *Ohne Titel*. It consisted of a long, whitewashed wall standing in front – and blocking the view – of a set of cabinets. In these were hung 18th and 19th century paintings. You could still just see the tops of their frames. I think that that work marked the end of a road. In it, the depiction of the relationship between art and seeing, between the audience and the object, found its dullest expression. It ended in boredom and the shrugging of shoulders.

Today, in the second half of the 1990s, art can once again be legitimized using such terms as 'process'. The artist as author is back. But I do not want to go into that any further here.

There are notions from the 1980s that have stuck between the teeth of art historians and critics alike. Thus, any depiction in a painting is still often called a 'reference'. And everything which has anything to do with ideology, politics and the future is 'utopian'. Augury, too, is utopian – and with it all the struggles of the avant-gardes. Such notions are an obstacle to better understanding. Amongst other things, confused ideas about depiction and anticipation-oriented art (ideology, politics, the future) are obstructing any pronouncements in that direction. What we need is a formula by which these hangovers of the thinking which dominated the 1980s can be remedied. It is high time that critics and curators acknowledged the formal aspects which lead to their acceptance or appreciation of a work of art. And perhaps it is time that artists freed themselves from critics and historians.



Showcase, 1998, aluminium frame, wood, plywood, glass, varnish, ironwork, 246 × 400 × 280 cm



Diego Rivera in the Soviet Union, 1998, mural, silicate paint on mineral stucco, 659 × 273 cm

Barry J. Marshall

Peptic ulcers, stomach cancer and the bacteria which are responsible

The Dr. A.H. Heineken Prize for Medicine 1998 was awarded to Dr. Barry J. Marshall for his insight to associate gastric spiral bacteria (helicobacter pylori) with gastritis and ulcer diseases, which has subsequently revolutionized the treatment of peptic ulcer disease: a cure can be reached with simple medical treatment.

The discovery of *Helicobacter pylori* and proof that it causes peptic ulcers cannot be properly understood without placing it within the historical context of gastric and duodenal disease developed over the past hundred years.

A – duodenal ulcer location
(70% of peptic ulcers)
B – gastric ulcer location (30% of peptic ulcers)

Fig. 1. Location of peptic ulcers.

The historical origin of peptic ulcers (ulcers in the lining of the acid-secreting part of the gut i.e. the stomach and duodenum, see Figure 1) is not well described. This is because immediate post-mortems on patients who died from intestinal bleeding were not common before the 19th century. In addition, the stomach digests itself soon after death, making it impossible to find relics of peptic ulcer disease. Nevertheless, gastrointestinal bleeding and the vomiting of blood was described by Hippocrates who used pulverised oyster shells to treat the illness, an antacid treatment which is still in use in indigestion remedies today (calcium carbonate $CaCO_3$).

After the turn of the century investigators measured the amount of gastric acid produced in ulcer patients and could document that people with duodenal ulcers had increased levels of acid secretion. Since psychosomatic causes of disease prevailed before 1950, 'stress' was blamed for peptic ulcer.[1] This was based on the earlier observation that middle and upper class professional men were more likely to develop severe ulcer problems. After the 1930s however this no longer held true, with working men becoming more likely to develop an ulcer than managers.[2,3] Nevertheless, psychosomatic theories were entrenched in folklore and, as a result, ulcer treatment took the wrong path with patients being given weeks of bed rest, nasogastric milk drips and the very bland soft 'Sippy' diet of boiled creamy food.[4,5,6] This had very marginal effects on ulcer disease, and most patients with severe symptoms eventually had surgery, where the lower half of the stomach was

removed to reduce acid secretion. As well as surgical complications, many patients developed cardiovascular disease because of the very fatty 'ulcer diets'.

An advance came in the 1970s when it was proven that proper administration of antacids could heal almost all ulcers, indicating that acid was the primary cause.[7] Unfortunately for the patients however, several gallons of antacids such as Mylanta had to be consumed over a month or so to ensure healing. In addition, maintenance antacid treatment was necessary to keep the ulcer problem at bay, indicating that acid-lowering treatments could only perform a holding action and could not cure patients with peptic ulcer.

Two other major breakthroughs occurred around 1970. When it was found that the stomach could easily be examined using fibre-optic endoscopy, gastroenterologists were suddenly able to accurately diagnose either gastric or duodenal ulcers, identify risky or bleeding ulcers, and could be more selective in their recommendations for medical treatment or surgery. In addition, they were able to study the underlying pathophysiology of ulcer disease i.e. they were able to take small biopsies from the lining of the stomach. Thus, they could sample parts of the stomach and look for bacterial infections.

These possibilities both aided and hampered progress. Histologic examination of the gastric mucosa (stomach lining) showed that most patients with ulcers had gastritis i.e. infiltration with various white cells including neutrophils. Thus, gastritis seemed to be an accompanying disorder in patients with both gastric and duodenal ulcers. The cause of gastritis was unknown, but it was very common, more likely to be present in older persons and very common in alcoholics. This supported the idea that gastritis was a natural ageing process or was caused by the ingestion of toxic drinks such as alcohol. Although the cause of gastritis was unknown, cultures were taken from the gastric juice of patients with gastritis, but no bacteria could be isolated. This was because acidic gastric juice kills bacteria, and methods were not available for specialised culture of organisms such as *H.pylori* (which require slightly reduced levels of oxygen).

In the 1970s, through the discoveries of Sir John Black,[8] the H2 receptor antagonists were discovered, which enabled patients to heal their ulcers by simply taking a pill which reduced their acid secretion. This was a marvellous advance. It no longer seemed necessary to keep patients in hospital, they did not need to take massive doses of antacids, and surgery could be saved as the treatment of last resort. Between 1975 and 1980 Tagamet, the first H2 receptor antagonist, became the most widely used and most profitable drug in history.[9]

In 1979 at Royal Perth Hospital, Dr. Robin Warren reported that spiral bacteria were present on the gastric biopsies of patients undergoing endoscopy in Perth,

Western Australia. He was interested because these bacteria were not reported in the medical books and they seemed to be associated with inflammation of the stomach (gastritis). Dr. Warren continued to make his observations and report these findings, but since gastritis was not recognised as a clinical entity of any importance, most doctors ignored the bacteria reported by Dr. Warren.

In July 1981 I began a collaboration with Dr. Warren as part of my physician training at Royal Perth Hospital. I examined the clinical records of 25 of the infected patients to see if there was any obvious correlation between gastro-intestinal diseases and the presence of the bacterium. This initial survey was unsuccessful – there were no obvious links between the bacteria and disease. At the end of 1981 therefore, Dr. Warren and I decided to study a large group of consecutive patients having endoscopy to see if the bacteria were present. We coded the biopsy material so that it could be reviewed in a blinded fashion, cultured biopsies from all patients and entered the results of their endoscopy into a database. The outcome of that study was that the bacteria could be correlated with the presence of gastritis – so closely that it was almost impossible to have gastritis without the bacteria – therefore the bacteria were probably the cause of this puzzling disorder. Secondly, the bacteria were cultured and we could prove that they were a new species somewhat related to *Campylobacter* (the curved bacteria present on fresh chickens which can cause gastroenteritis), but the new organism was similar in some ways to vibrios such as the cholera organism. Thirdly, we noted that all patients with duodenal ulcer, most patients with gastric ulcer, and about half the patients with gastric cancer were infected with the bacterium.[10]

We could not find any food, medication, or lifestyle habits that correlated with the presence of the bacteria. It seemed that anybody could be infected with them, but that only people with the bacteria could develop an ulcer. At the end of 1982 I hypothesised that, by causing an initial episode of gastritis, these bacteria could lead to peptic ulcer.

I found that there was good historical evidence linking gastritis to peptic ulcer[11] and there were even references to these bacteria in the literature.[12,13] I obtained histology specimens from the United States and Holland, and was able to identify the new bacterium (then called *Campylobacter Like Organism*, CLO). Thus, the bacteria were not uniquely Australian and apparently were present in persons all over the world.

At the time CLO were first cultured, gastroenterologists including myself were becoming disillusioned with the H2 blocker acid-lowering ulcer therapy. Many patients had been taking the medications continuously for five years or so and

were still having recurrences of peptic ulcer whenever they stopped the drug. Thus, we were certain that acid-lowering therapies, even strong ones such as H2 blockers, had no effect on the underlying ulcer problem. When we looked for CLO in patients taking ulcer treatment, we could easily see that the bacteria were still present, and that the patients still had gastritis even when their ulcers were completely healed.

As well as acid reduction, there was one other ulcer drug commonly prescribed in Europe and Australia. This was DeNol (bismuth subcitrate), which was known to heal ulcers, and apparently had a lower recurrence rate i.e. some patients were actually cured by a brief course of this treatment. This suggested to me that the drug might actually be an antibacterial agent and could kill the CLO. *In vitro* studies confirmed that bismuth was highly toxic to CLO and clinical studies confirmed that suppression of CLO in patients could actually heal gastritis.[14] Thus, there was at least suggestive evidence that treatments which suppressed or cured the bacterial infection could cure ulcers. I then observed that the new bacteria could be completely eradicated by combining bismuth with antibiotics. Thus, by 1984, I was able to commence a prospective double blind study testing the hypothesis that eradication of the CLO could result in permanent cure of peptic ulcer.

In spite of suggestive data in preliminary trials, most physicians still believed that gastritis was a harmless condition, unrelated to CLO. Instead, they preferred the hypothesis that CLO were mere commensal organisms colonising the damaged mucosa of patients with gastritis. To convince the skeptics that the CLO were actually the cause of gastritis it was necessary to infect an animal with the new bacterium and demonstrate that gastritis would develop. Since my experiments on small animals were unsuccessful, I decided to infect myself with the organism and did this by drinking a petri-dish full of CLO in June 1984. A week after the infection I began vomiting. Sure enough, biopsies showed that I had developed both CLO infection of the gastric mucosa and severe acute gastritis as was seen in patients with peptic ulcer (see Figure 2). In my case the disease was self-limiting, and biopsies returned to normal when the CLO disappeared two weeks later.[15]

Thus, in 1985 I was able to present a global hypothesis for peptic ulcer disease as caused by the new bacterium. I proposed that CLO bacteria were very common and very likely to infect humans in childhood. The infection would be initially associated with an acute vomiting illness or abdominal pain but after a few days symptoms would subside, although in most persons the bacteria would remain to cause chronic gastritis. Many years later, in adulthood, persons with chronic gastritis had sufficient damage to the gastric mucosa to allow even normal levels of

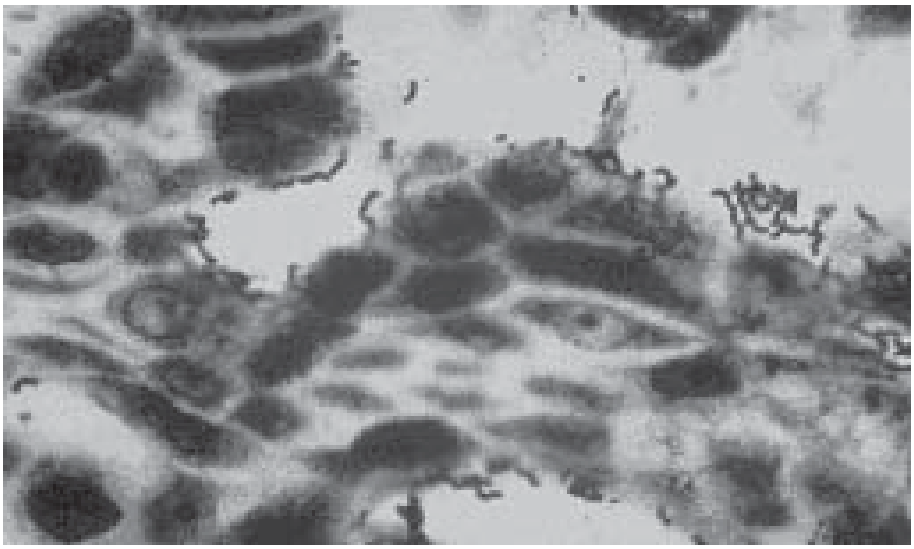
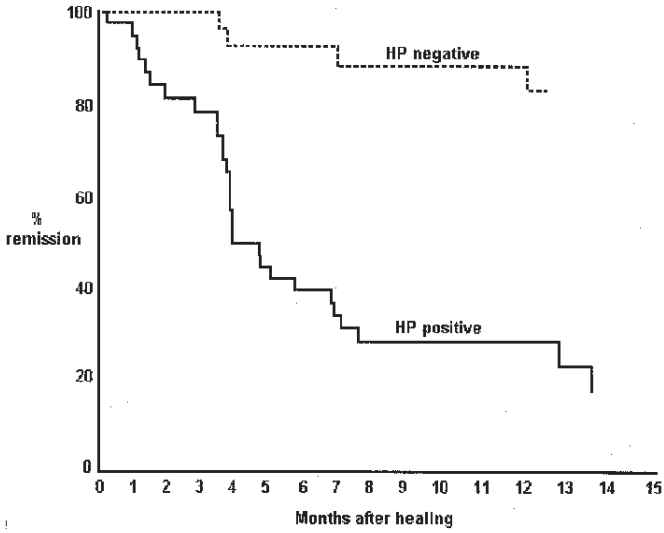


Fig. 2. Eight days after a healthy volunteer ingested a culture of *H.pylori*, silver stain shows *H.pylori* (deep black curved structures) attached to epithelial cells (brown).

acid to break through and cause a peptic ulcer. Extrapolating from this hypothesis I could predict that eradication of the bacterium would permanently cure peptic ulcer by returning the gastric mucosa to a healthy state.

From 1985 to 1987, again in collaboration with Dr. Warren, I conducted a double blind study of antibiotic usage in the treatment of peptic ulcer. I found that 80% of patients were permanently cured of their ulcer if the CLO was eradicated with a two week course of antibiotics. Although the healing rate was no greater than the healing rate of acid-lowering treatments, patients with cure of the CLO infection no longer needed maintenance acid-reduction therapy. In fact, most were usually completely well and required no further treatment. Conversely, when patients were merely treated with acid reduction, all but 20% of them had a recurrence of their ulcer within 12 months (see Figure 3 and Table 1).

For several years the CLO continued to baffle scientists by their ability to live in the stomach. In 1987 I discovered that CLO could survive in acid by means of its urease enzyme. This enzyme allows it to break down urea present in the gastric juice to form an ammonia- and bicarbonate-laden layer around itself. This alkaline 'micro-environment' protected it from the killing effect of the acidic gastric juice (see Figure 4). Other bacteria such as salmonella, *E.coli* etc tended to be killed far more easily than CLO.



The upper line (HP negative) shows the relapse rate for patients given antibiotic treatment for duodenal ulcer. Only 10-20% required antacid treatment again in the subsequent 12 months. The lower line (HP positive) shows a randomised prospective control group, 90% of whom had recurrence of ulcer. This high recurrence reflects the natural history of duodenal ulcer – a chronic recurring disease.

Adapted from: B.J. Marshall, C.S. Goodwin, J.R. Warren, R. Murray, E.D. Blincow, S.J. Blackbourn, M. Phillips, T.E. Waters, C.R. Sanderson. A prospective double-blind trial of duodenal ulcer relapse after eradication of Campylobacter pylori. Lancet 1988;2:1437-1442.

Fig. 3. Differences between HP+ and HP- groups on relapse

Fig. 4. *H.pylori* at home beneath the gastric mucus. The bacterium protects itself from acid by generating ammonia and bicarbonate by the breakdown of urea.

Table 1. Antibiotic treatments currently used for *H.pylori*

GENERIC NAME	DOSING	DURATION	CURE RATE (%)
omeprazole	20 mg BID	7 days	85-95
or			
lansoprazole	30 mg BID	7 days	
and			
clarithromycin	500 mg BID	7 days	
and			
amoxycillin	1,000 mg BID	7 days	
bismuth subsalicylate	Two tablets (525 mg) QID	7 days	85-95
or			
bismuth subcitrate	One tablet (120 mg) QID	7 days	
and			
metronidazole	250 mg QID	7 days	
and			
tetracycline	500 mg QID	7 days	
and			
omeprazole	20 mg BID	7 days	
or			
lansoprazole	30 mg BID	7 days	

At the same time, I was able to develop rapid detection methods for CLO based on its urease enzyme. I observed that a small gastric biopsy placed into a gel could cause a colour change as the ammonia was generated. Thus, patients were able to have diagnosis of CLO in just a few minutes after their endoscopy procedure, and could therefore immediately commence curative antibiotic therapy.[16] Later, I developed a non-invasive breath test whereby patients simply swalled a trace of urea labelled with a carbon isotope. If CLO were present, the urea was broken down to release isotopically labelled CO_2 in the patients' breath. This 'Urea Breath Test' (UBT) has become a very popular and accurate way of diagnosing CLO in patients who do not need endoscopy (see Figure 5). Other diagnostic tests such as antibody detection in blood are also now widely used.

For the 10% of persons in Western populations who would normally have developed peptic ulcer in their lifetime, the spectres of chronic upper abdominal pain, haemorrhage, and gastric surgery are no longer present. Almost all 'idiopathic' peptic ulcers can be tracked to a defined cause such as CLO or, in about

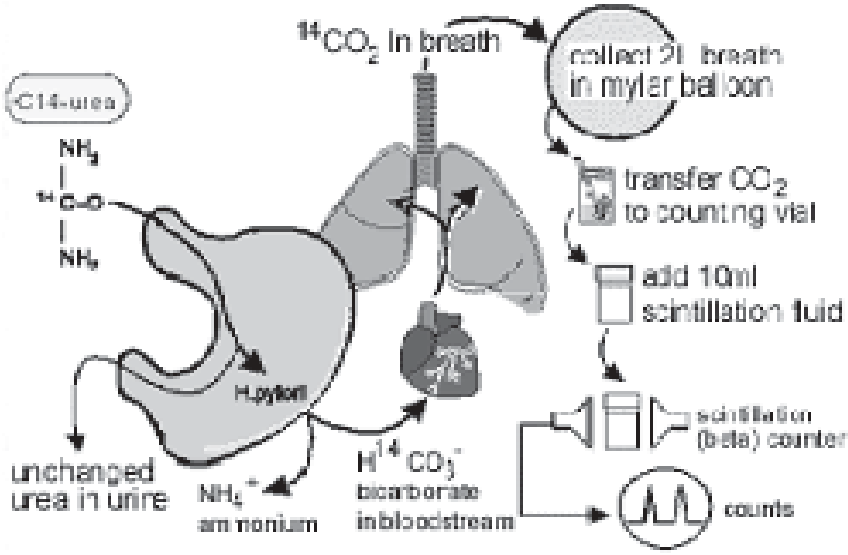


Fig. 5. Principle of the C14 Urea Breath Test (UBT)

25% of cases, aspirin. Ulcer surgery has become quite rare, and most patients with CLO are diagnosed non-invasively by their doctor and treated with just a week or two of antibiotics. No longer must ulcer sufferers be threatened with massive doses of antacid, life long medication or made to modify their lifestyles.

In the past 10 years, thousands of papers have been published on the new spiral organism, which has been given its own bacterial genus of *Helicobacter* and renamed *Helicobacter pylori*. This reflects its rather corkscrew or helical shape. Many similar bacteria have been found colonising the stomach of animals, particularly carnivores such as dogs and cats.

More than half the people in the world are infected with *H.pylori*, particularly older persons in Western countries (persons born before 1940), persons from lower socioeconomic groups, or those born in developing countries. *H.pylori* has been classed a Type 1 Carcinogen, because of its strong association with gastric cancer. Nowadays scientists have solved the treatment issues of *H.pylori* although they are concerned that antibiotic resistant strains are becoming prevalent in some countries. In the future we hope that *H.pylori* can be completely eliminated by public health measures i.e. clean water in developing countries and/or by oral vaccination methods.

References

1 Alexander, F. 1950. *Psychosomatic Medicine.* New York: Norton.
2 Pulvertaft, C.N. 1959. Peptic ulcer in town and country. *Br. J. Prev. Soc. Med.* 13:131.
3 Langman, M.J.U.S. 1979. Peptic ulcer. In *The Epidemiology of Chronic Digestive Disease,* p. 9. Chicago: Year Book Medical Publisher.
4 Doll, R., P.Friedlander, F.Pygott. 1956. Dietetic treatment of peptic ulcer. *Lancet* 1:5-9.
5 Truelove, S.C. 1960. Stilboestrol, phenobarbitone and diet in chronic duodenal ulcer. *British Medical Journal* 2:559-566.
6 Lennar-Jones, J.E., N. Barbouris. 1965. Effect of different foods on the acidity of the gastric contents in patient with duodenal ulcer. Part I: A comparison between two "therapeutic" diets and freely-chosen meals. *Gut* 6:113-117.
7 Peterson, W.L., R.A.L. Sturdevant, H.D. Frankl, C.T. Richardson, J.I. Isenberg, J.D. Elashoff, J.Q.Sones, R.A. Gross, R.W. McCallum, J.S. Fordtran. 1977. Healing of duodenal ulcer with an antacid regimen. *New England Journal of Medicine* 297:341.
8 Black J.W., W.A.M. Duncan, C.J. Durant, C.R. Ganellin, E.M. Parsons. 1972. Definition and antagonism of histamine H2-receptors. *Nature* 236:385.
9 Dreyfuss J. 1983. Smithkline's ulcer medicine "holy war". *Fortune* Sept 19, 129-136.
10 Marshall, B.J., J.R. Warren. 1984. Unidentified curved bacilli in the stomach of patients with gastritis and peptic ulceration. *Lancet* i: 1311-1315.
11 Magnus HA. 1952 Gastritis. In F.A. Jones (Ed), *Modern Trends in Gastroenterology,* pp. 323-351. London: Butterworth.
12 Freedberg, A.S., L.E.Barron 1940. The presence of spirochaetes in human gastric mucosa. *Am. J. Dig. Dis.* 7:443-45.
13 Steer, H.W., D.G. Colin-Jones. 1975 Mucosal changes in gastric ulceration and their response to carbenoxolone sodium. *Gut* 16:590-97.
14 Marshall, B.J., I. Hislop, R. Glancy, J. Armstrong. 1984. Histological improvement of active chronic gastritis in patients treated with De-Nol. Abstract from the Gastroenterological Society of Australia Scientific Meeting Marsh 1984. *Australian and New Zealand Journal of Medicine* 907.
15 Marshall, B.J., J.A. Armstrong, D.B. McGechie, R.J. Glancy.1985. Attempt to fulfill Koch's postulates for pyloric Campylobacter. *Med J Aust* 142: 436-439.
16 Marshall, B.J., J.R.Warren, G.J. Francis, S.R. Langton, C.S. Goodwin, E. Blincow. 1987. Rapid urease test in the management of Campylobacter pyloridis-associated gastritis. *Am. J. Gastroenterol.* 82(3):200-210.

Mona Ozouf

Dilemmas of the democratic idea

Dr. Mona Ozouf received the Dr. A.H. Heineken Prize for History 1998 for the challenging view of the French Revolution she developed. She has always focussed on cultural-historical and antropologic aspects of the developments and has avoided the classic approach to the usually politically charged subject of revolutions.

It may seem paradoxical that I have chosen to speak about the dilemmas facing democracy in the country which has honoured me with a prize whose prestige I acknowledge with a mixture of gratitude and confusion. After all, when the French reader reflects upon your history as he closes, for example, the book which Simon Schama devoted to the culture of your Golden Age, he is likely to believe that the Dutch have managed to devise a peaceful and harmonious way of living together, one which is sheltered from religious and nationalistic passions. In its institutions and human virtues, your civilisation – which is one of the greatest to have appeared in modern Europe – seems to have have found a way to temper the fever of democracy.

There are, however, compelling reasons for choosing this subject. The main one is that, since the fall of the Communist regimes, Europe can no longer imagine any other future than a democratic one. The restoration of the rule of law, free elections, private property and market forces to the nations of Eastern Europe shows that following the lead of the democratic West has become a common programme in European societies. The democratic idea, whose denunciation was the stock-in-trade of the totalitarians of our tragic century, now appears to be the indispensable and irreversible concept which nourishes modern society. But this apparent triumph also confronts us with the great dilemmas of democracy, and more than ever makes it necessary that we reflect upon its directions.

If I choose to examine these using the French example, this is not because I do not recognise the possibility that the democratic idea has other cradles than the French Revolution. The American Revolution, for example. But that was a restoration as much as a revolution: its objective was to recover ancient but lost freedoms. Moreover, the Americans did not have to overturn an aristocratic society, nor to guillotine a legitimate sovereign. They simply left them behind. By contrast, the French – who had to break with their history and rewrite their social contract from scratch – created a more radical experiment in democracy, and so were faced with its dilemmas to their full extent. The French example allows us to understand how the democratic faith in individual equality and liberty, and in the individual's freedom to choose his own activities and beliefs, could immediately become subject to pessimistic predictions drawing attention to the immense difficulty of knowing how to rebuild a community out of all these now-independent individuals. It is this anxious scrutiny which I would like to review with you.

We owe the analysis of the despotic tendencies of democracy to Burke, in his famous Reflections on the Revolution in France. This is a text which is all the more striking in that it dates from 1790 – which might be called the 'happy year'

of the Revolution, when its twists and turns had not yet produced the proof of his central hypothesis. But Burke immediately realised what you put at risk when you take as your basic principle individuals who are at the same time equal and unique, and then also abolish all reference to tradition – which is the main feature of the French experience. Social links are no longer to be found, either in the intermediary powers or in the actual associations – organisations and communities – which had been sanctioned by a long history but now abolished. What Burke is highlighting here is the social void and the abstraction of democracy, a theme which for almost two centuries would feed both revolutionary and counterrevolutionary thought – that of Maistre and Taine as much as Marx.

From this abstract constructivism of the French Revolution, Burke deduced its disastrous consequence: despotism. In a society stripped of its structure, one can only find the body politic in the abstract exaltation of a state invested with the sovereignty of the people – and even more dangerous. Faced with this sovereign state, isolated and desocialised individuals are defenceless, directly dependent upon a power which nothing can temper any more. At one stroke, they are able to free themselves from the traditional constraints which tied them to their communities but the degree of authority exercised over them barely diminishes. On the contrary, in fact: this increased in extent and efficiency. So much so, says Burke, that if a monarch were one day to be restored to the French throne he would exercise the most authoritarian power ever seen in this earth. This was a remarkably accurate prediction, because at the end of the revolutionary decade an administrative and military dictatorship was to appear which was infinitely more despotic than the old monarchy.

The course of the Revolution would provide Burke's reflections with a striking historical illustration. The revolutionary leaders did not overlook the need to create a body of beliefs which would unite people; indeed, this was a task which in their view was all the more urgent because they had broken with the Catholic Church and felt that they had to compete with its power over the soul. But they could only create social unity based upon something which demonstrated individual equality; that is, the figure of the citizen, which is difficult to reconcile with that of the individual, who is always susceptible to egoistical thoughts and private interests. In their view, individuals had to be reshaped in order to turn them into citizens. This is the old Rousseau problem: after acknowledging that the rights of the individual are inalienable, they are then inextricably bound up with collectivism. The French revolutionaries therefore set about forging a common patriotic and moral conscience, and then creating the reshaped citizen:

an entirely new man. 'Make of man what you want him to be,' is how Saint-Just summed up this founding programme.

The aspirations were immense. They resembled a quasi-religious hope, although unlike that they accepted the test of historical verification. And it is not too much to say that they assumed a pedagogical authoritarianism. Because, as Madame de Staël so profoundly observed, the objective of the revolutionary legislators was not only to achieve outward conformity of behaviour but also the inner consent which is essential to the very principle of democracy, so that when they obey the law men are in fact simply obeying themselves. Tyranny requires the consent of the tyrannised – and even, if possible, their enthusiasm. This is a requirement which, by erasing all barriers between the public and the private, carries with it a totalitarian potential. It assumes that legislators are able to govern men's whole lives, to oversee both private homes and public places, to monitor words as well as deeds, and as well as words even those thoughts only whispered privately to oneself. This because, even more than counterrevolutionary intent, it is indifference which should be feared. 'He who thinks nothing, thinks evil,' said Saint-Just. The task is thus so boundless that it explains the descent into the Terror: faced with extreme difficulty in creating the moral unity of which they dreamt, and in producing a reshaped humanity, the expeditious and summary solution to which these men resorted was the exclusion from the body politic – by violent means – of those elements which questioned their mission. This explains the paradox highlighted by Edgar Quinet: that a Revolution born like a dawn of freedom died in the night of the Terror.

In this pathology of the democratic idea, excessive ambition, the deification of political action and voluntarism breed failure and, at the same time, fury which is expressed through repression. But another pathology can also come about: not this time one of excess, but of flawed ambition. Or, to be more precise, of the yawning gap between the abstract promises made by democracy and the actual situation which it delivers. Without the means to do something, is not the right to do it nothing more than a false freedom? What good is declared liberty when nature and society everywhere create differences? So much so that the democratic experience carries with it its own objection. Never as democratic as it claims to be, it feeds incurable dissatisfaction. Because unlike earlier societies, in which in inequality was legitimised, democracy renders all inequality illegitimate. Men now know that they equal, but find that they unequal. Awareness of this infidelity in the very principle of democracy foreshadows an uncontrollable and unstoppable dynamic. To the despotic potential of democracy must therefore be added its utopian potential; I use the adjective 'utopian' here in the sense in which

it describes the way the democratic idea no longer has a foreseeable end or a defined objective, but has to be constantly reassessed and revived.

Once again, this possible direction was first the subject of an historical analysis which history subsequently managed to illustrate perfectly. Before democracy had even been born, Rousseau imagined what democratic man would be like. The portrait he drew was an anguished one. This modern man, with whom we still live to this day, is the incarnation of the democratic paradox: a figure perpetually angered by the differences he discovers between society itself and its principles – principles which themselves make him regard the tiniest deviation from them as illegitimate. Haunted by a guilty conscience, tortured by the madness of comparison – the source, according to Rousseau, of human misery – always more sensitive to what separates individuals than to what unites them, and tormented by jealousy, he embodies an incurable social resentment. This theme would have a good future in Western thought. One only has to think of de Tocqueville or Saint-Simon: 'The misfortune of men in democracy,' said the latter, 'is that they are unable to quell their exaltation of the idea of equality.'

History more than confirmed this democratic torment. The course of the Revolution itself symbolises this tendency. The French are very quick to abandon one revolution, which they consider failed, in favour of another which at the same time completes and negates the first. The revolutionary calendar provides the evidence, because it splits the history of the decade into two by inserting year I of Liberty right in the middle. And from this year I, the symbol that all has been started anew, the objective is no longer to found democracy upon the rule of law but to ensure – through the Terror – the victory of the revolutionaries over their enemies. This relaunch heralded a long period of instability, of which the political history of France during the 19th century provides ample illustration, but it also expressed one of the central characteristics of the democratic idea: its innate vulnerability to the utopian mirage, which is born out of the notion that if it fails or disappoints then it is not because it has gone too far but because it has not gone far enough.

It is this sympathy for the need to make a new and more robust revolution in order to give fresh substance to democracy which appears in the Babouvist movement at the end of the revolutionary period: the socialist idea as a critique of and an improvement upon the democratic idea. Both the judge and the far horizon of democracy, socialism thrives on the certainty that it is not enough to have destroyed the hereditary aristocracy. Many other aristocracies threaten equality! That of the rich, or course. But also – why not? – those of the talented, the intelligent, the beautiful and the healthy. So the hope for true equality retreats as the

extent of equality advances, as de Tocqueville noted in stating that the more the inequality of men declines, the more the feeling of inequality grows, fuelled by awareness of new differences. So dissatisfaction increases, but so too does the hope that formal democracy, which is so disappointing, will one day give rise to a real democracy which keeps its promises. This wait, which the European left has shared for the past two centuries, introduces the foment of endless upheaval into political and social life.

There is no better way to understand the idea of equality and the mirage which it produces than to leave the French example for a moment to look at that of America. This is far better inoculated against the mirage of a new society, since the Americans find it difficult to imagine any society other than their own. But there, egalitarian pride has found a new outlet in minorities' claims. It is the inequalities between groups, and no longer between individuals, which have prompted renewed activism and generated demands for collective measures in favour of those communities which have suffered under the cultural hegemony of whites or men. This transformation in the egalitarian zeal has caused a new social utopia to appear, one which shares the characteristics of every utopia: the erasure of the boundaries between the public and the private, the desire to place citizens' personal lives under the yoke of equality, artificialism and the denial of nature. In its radical version, American feminism – which is suspicious of nature and sexuality, and seeks to legislate in every field, including that of loving consent – is a perfect illustration of this new direction in the democratic idea. It has appeared in a country which is little given to theoretical constructions, but this only demonstrates even better the propensity of democracy to create utopias which simultaneously contradict and revive it.

There remains but a narrow path between despotic tendencies due to inordinate ambition and utopian tendencies resulting from unfulfilled ambition. The dissatisfaction which utopia expresses may seek a cure – and find a remedy – in a recourse to despotism. This is because the certainty that one can submit collective and individual existence to rational organisation, that the social can be mastered from beginning to end, and that the reshaping of individuals can be accomplished by their own free will is common to both the despotic and the utopian systems.

There is yet another direction to the democratic idea, one which is much less threatening to liberties but also more insidious, and which is born less from the failures of democracy than from its successes. It is what I call – for want of a better term – democracy's prosaic potential. De Tocqueville, too, identified it: 'This same quality which renders the individual independent of each of his fellow citizens also leaves him particularly isolated and defenceless when faced with the

actions of the greater number.' In this world governed by advertising – with its creation of artificial needs – and in which consensus reigns, constraints can hardly be said to have disappeared. But they are soft and silent constraints, which manage to impose uniformity of behaviour and thought not through the threat of some punishment but through ridicule. One can place this conformist society on trial in the name of aesthetic taste. What the great novelists – from Musil to Henry James – soon realised was that democratic society tends to foster a confusion of roles and conduct, a blurring of values, a mixing up of age groups, of the sexes, of class and of power. After all, nothing is more alien – or even hostile – to literature and to art than this denial of individuality, this worship of conformity.

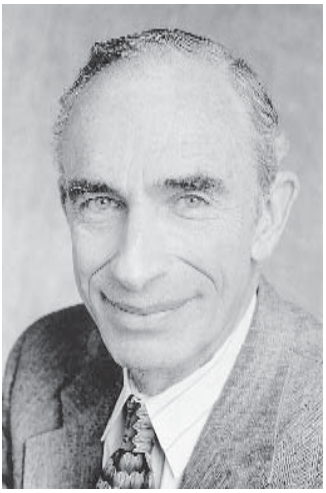
An aesthetic deficit, therefore, but also a civic one. The idea of the common good fades in democracy because, immersed as they are in the relative, everyone has his own personal image of the public interest – so much so that sacrifices in favour of the collective good become almost unintelligible. Today's societies offer us countless examples of the abandonment of the idea of autonomy – which is essential to democracy since it reaffirms that the law, far from being laid down by some transcendental power external to humanity, must actually of necessity be self-imposed – in favour of the very different notion of independence. What democratic men deem to be the value of an act is nowadays much less the bestowal of personal consent upon a standard than independence from all standards, which are regarded as unacceptable repression. Paradoxically, therefore, the more our democratic societies become homogeneous, the more the individual tries to assert his independence in respect of any standard. The pursuit of 'authenticity', which Michel Foucault called 'concern for oneself' results in one turning in on oneself and ignoring greater causes, greater passions and greater projects. Everyone thus nurtures their own egotistical well-being in a narrow private world, with no regard for the collective good.

In summarising the directions taken by the democratic experience, we are in the company of the great minds in Western thought: Rousseau, Constant, Burke, Kant, Hegel, de Tocqueville and Marx all commented upon them. Their analyses are still of great value to us. However, they do not lead us to condemn democracy itself, nor to conclude that every democracy will ultimately veer into despotism. They do not force us to abandon that ideal of equality which makes our civilisation great, which is its prize. Nor do they lead us to believe that men will give up believing in a society different from that in which they live, that they will no longer have any ambitions for the future (Europe, although still a little too young to completely fulfil this vision, could nevertheless do so eventually). But

these worried and suspicious analyses are immensely interesting in that they demonstrate how fragile the tissue of democracy is and the potential which exists for the breakdown of our society. They have the added advantage that they show the extreme difficulty of reconciling the two ultimate objectives promised by democracy: liberty and equality. These objectives have yet to be achieved in any modern society and when – as in the socialist systems – supposed attempts have been made to keep the promises made by democracy these have backfired not only against liberty but also against equality. We must therefore live with democracy as an idea which does not carry with it an end as such: one whose entire benefit is in the dynamism with which it imbues social activity, but which must be handled with care. The murderous follies of our tragic century have at least had the one beneficial result that they have encouraged in our modern European nations that spirit of moderation of which your country – through the works which it has given us to admire – has long provided the shining example.

Paul R. Ehrlich

Recent developments in environmental sciences



The Dr. A.H. Heineken Prize for Environmental Sciences 1998 was awarded to Professor Paul R. Ehrlich for the unique and erudite way in which he makes his scientific knowledge of aspects involved in the decline of the environment accessible to the general public and policy makers.

The past decade has been a critical one for the environmental sciences in three changing areas: continuing growth in the scale of the human enterprise, what is happening to the biosphere as a result of that growth, and how the community of environmental scientists is approaching the problems of achieving sustainability. As a result, it has been both an exciting and worrying time for ecologists like myself. In this brief paper, I want to deal with each of these three areas of change in turn.

The scale of the human enterprise, as measured by energy use, has increased some 20-fold since 1850.[1] The environmental impact (I) of that scale can be viewed in tenns of the I=PAT identity, where P is the size of the Population, A is Affluence (or consumption), and T is a measure of how environmentally malign are the Technologies and the economic, social, political and political arrangements involved in servicing the consumption. [2] Because the A and T factors are very difficult to sort out from available statistics, it is customary to substitute per capita energy use for A × T in the identity. In the past decade, the scale of the enterprise has increased about 5 percent, despite one quite positive development in the factors affecting that scale.

That development has been a small but significant decline in fertility rates in many nations of the world. For example, in 1988 the global population stood at 5.13 billion, the rate of natural increase for the world was 1.7 percent, and the total fertility rate (TFR)[3] was 3.6. In mid-1998 the population had grown to 5.93 billion, but the growth rate had declined to 1.4 percent, and the TFR was down to 2.9. Most important, in the rich countries, where overconsumption per individual puts enormous pressure on human life-support systems, average TFR dropped from 1.9 to 1.6, and their populations had virtually stopped growing. At the same time the TFR in the developing world (excluding China) declined from 4.9 to 3.8 – more than a full child per family. [4]

All of this is a start in the right direction, but even on the population front the world still has a long way to go. The decline in the P factor in that decade simply moved the projected date at which the population will pass 8 billion from 2019 to 2024. To put this in context, you must remember that estimates of the *long-term* carrying capacity of Earth with relatively optimistic assumptions about consumption, technologies, and equity (A × T), are in the vicinity of two billion people. [5] Today's population cannot be sustained on the 'interest' generated by natural ecosystems, but is consuming its vast supply of natural capital – especially deep, rich agricultural soils, 'fossil' groundwater, and biodiversity – accumulated over centuries to eons. In some places soils, which are generated on a time scale of centimeters per century, are disappearing at rates of centimeters per year. Some

aquifers are being depleted at dozens of times their recharge rates, and we have embarked on the greatest extinction episode in 65 million years.

Despite all this, the drop in vital rates in Europe has been a cause not for rejoicing but for hand-wringing among those who are ecologically illiterate, hand-wringing that

has been echoed in the American press. [6] The last time Europeans panicked over demographic decline was during the depression of the 1930s. But Europe's population *expansion* has been unprecedented: despite huge waves of emigration to the Western Hemisphere, the population of Europe quadrupled between 1750 and 1950. Even since the depression, Europe has added on the order of 75 million people – more than the combined present populations of the United Kingdom, Sweden and Denmark. Now growth has finally stopped and a slow decline is beginning – a cause for celebration on this vastly overpopulated continent. This European decline is especially cheering because of the extremely high consumption rates and huge 'ecological footprint'[7] of European nations.

Outside of the population statistics, on the A ×T front, most of the trends over the past decade have been negative, however. Consumption in many rich nations continues to grow, much of it reasonably classed as 'overconsumption' in comparison to the material goods available to the average human being. The most serious population growth in the world is occurring in the United States, the third most populous nation in the world. The USA still has a natural increase of 0.6 percent, a TFR of 2.0, and a growth rate (thanks largely to immigration) of over one percent. Most importantly, it has an extremely high level of consumption per person – on the order of ten to thirty times that of people in developing nations. Thus the addition of each person to the American population, whether by birth or immigration, is many times the disaster for the world as a birth in Kenya or Bangladesh. Despite this, there is no sign of any official policy for population limitation in the nation in which, from a global viewpoint, it is most needed. And the United States is even further from a program of consumption control, which is even more badly needed. [8]

Most developing nations, in contrast, have recognized their population problems and taken steps to deal with them. But the A × T element in those nations can be a source of serious problems as well. In the rich sectors of otherwise poor economies, like that of China, patterns of consumption are converging on those of the developed nations. In China, for example, increased meat consumption has been signaled by a 70 percent increase in the percentage of total available grain fed to livestock between 1985-87 and 1995-97.[9] China has already surpassed US consumption *per capita* of both pork and eggs.[10] Indeed, in special

cases, the pressures generated by countries like China can often exceed those of the West and Japan. Hong Kong, for instance, is a major consumer of the living resources of the sea. Some 6 million residents devour 300,000 tons of seafood (about 50 kg per person) annually. They are partly responsible for the destruction of the world's coral reefs from dynamite and cyanide fishing. Live reef fishes are in enormous demand – Hong Kong Chinese wishing to display their affluence will pay up to 1000 Hong Kong dollars (US $130) for a plate of lips from a large Napoleon wrasse (a reef fish).[11] One can easily imagine the impacts on natural systems of increasing affluence in proportionately small but numerically large subpopulations in China and other developing countries. The spread of American consumerism is a global threat, and the prospect of ever greater disparities in living standards not only between nations but within nations bodes ill for the environment, which in most circumstances benefits as equity increases. [12]

Thirty years ago, finding ways to slow and halt population growth were near the top of the agenda of the environmental science community. It is now slowly dawning on us that curbing runaway consumption may be even more difficult. And socioeconomic and political constraints make it very difficult to institute desirable changes in the mix of technologies used to supply the consumption. In my view, for example, it would be wise to reduce human exposure to a wide array of hormone-mimicking synthetic organic chemicals,[13] but economic forces such as plastics manufacturers and users powerfully resist such a reduction. Similarly, political power purchased by the coal industry in Australia has kept that nation on the fossil fuel treadmill, even though there has been strong public sentiment to switch to solar and other more environmentally benign technologies in order to slow global warming. Much the same can be said of the United States. Indeed, the only major success in the technological arena in the last ten years has been the implementation of the 1987 Montreal ozone protocol to limit the use of freons. Achieving that was relatively simple, since a 'smoking gun' was in hand in the form of the ozone hole, and the relatively few corporations involved could make even bigger profits manufacturing chlorofiuorocarbon substitutes. Limiting the flux of greenhouse gases from energy consumption, deforestation, and agriculture will be orders of magnitude more difficult.

Now let's turn to the second topic – what's happening to the biosphere. What can be said about the past decade's increases in our understanding of the consequences of expansion of the human enterprise? Perhaps most dramatic has been the growing evidence of anthropogenic climate disruption. The 1995 report of the scientific committee of the Intergovermnental Panel on Climate Change (IPCC), cautiously stated that the warming measured over the last century 'is

unlikely to be entirely natural in origin… the balance of evidence suggests that there is a discernable human influence on global climate.' [14] Despite a determined campaign of denial by certain elements of industry and a small group of dissident scientists, [15] it has become increasingly clear that the IPCC is correct. One key piece of scientific evidence that had been considered anomalous, satellite observations showing a cooling trend in the troposphere, turned out to be due to the failure of scientists interpreting the satellite data to take into account the steady lowering of the satellite's altitude caused by atmospheric drag. When corrections were made for this, satellite and surface data appeared in agreement. Top atmospheric scientists wrote that: 'warming trends of both the surface and troposphere are now sufficiently clear that the issue should no longer be whether global warming is occurring, but what is the rate of warming.' [16] There are, of course, many suspicious signs of rapid change in the climate itself, from an increased frequency of extreme weather events in North America [17] to a widespread meltdown in Alaska where glaciers are in rapid retreat, long-standing permafrost is melting, and widespread forest-death, caused by interacting stresses from permafrost soils being converted to swamps and newly abundant insect pests attacking already weakened trees.[18]

Arguably equally important is the growing documentation by biologists of the degree to which human activities are modifying the biosphere – and broad acceptance of the conclusion that human influences are increasingly disrupting the functioning of ecosystems.[19] For instance, humanity has now approximately doubled the annual natural rate of addition of nitrogen to the terrestrial nitrogen cycle, creating potentially serious problems for the maintenance of soil fertility, accelerating losses of biodiversity, contributing to acid deposition, and enhancing the greenhouse effect.[20] Humanity has recently been calculated to be using over half of the reasonably accessible freshwater runoff,[21] and some 43 percent of Earth's terrestrial vegetated surface has lost some of its capacity to supply humanity with benefits – overall about a 10 percent reduction in potential value – as a result of human actions. [22]

The last decade has also seen an accelerating loss of populations and species of other organisms that are involved in supplying crucial natural services to society, as natural areas are more and more displaced by human activities. Thus tropical forest [23] destruction continues throughout most of the developing world. Destruction of oceanic fisheries has come to wide public attention in the same period, as stock after stock is [24] overfished, and often the physical/biological infrastructure that supports the fisheries is destroyed. There are also growing signs that the toxification of the planet is causing serious effects on wildlife and human

health through the release of hormone-mimicking synthetic organic chemicals, although demonstrating the causal links is difficult. [25] And ecosystem services that are essential for maintaining agricultural production, such as pollination, [26] are faltering in many areas.

Third, what are environmental scientists doing that is new? Their activities constitute the best news outside of the lowering of birth rates. Building on advances in basic ecology over the past half-century, they are making important gains in understanding the significance of the negative environmental trends, finding ways to counter them, and helping to move humanity onto a path to sustainability. One outstanding example is the substantial progress that has been made in analysing the relationship between the loss of biodiversity and the delivery of essential ecosystem services. Increasingly, research by community ecologists like David Hooper, John Lawton, Shahid Naeem, David Tilman, and Peter Vitousek indicates that the long-term stability of the services will depend on maintaining a mix of species to provide redundancy in each of various roles organisms play in natural and agricultural [27] ecosystems. Another gain has been the development, under the leadership of population biologist Gretchen Daily, of the new field of 'countryside biogeography,' which seeks ways of maintaining critical elements of biodiversity in human-dominated landscapes. This is an especially important field, since every cubic centimeter of the biosphere has already been altered by humanity to some degree, and most areas have been modified dramatically from their state before humanity became a significant ecological force. Since it is clear that relatively few parts of the planet can be kept even relatively undisturbed, special efforts must be made to maintain critical elements of biodiversity – not just species but, just as importantly, populations [28] of other organisms.

Perhaps most heartening of all is the rapidly growing cooperation of economists and ecologists in efforts to find policy instruments to help preserve humanity's natural capital.[29] While the trend traces to the early efforts of Heineken Laureate Herman Daly, beginning in the 1960s, the last decade has seen an explosion of activity. At Stanford University, weekly seminars now bring together economists and ecologists (as well as engineers, historians, members of the faculties of law and business, and others) to discuss the environmental dimensions of the human predicament. I now frequently share postdoctoral students with Larry Goulder of Stanford's Department of Economics. The Beijer Institute of Ecological Economics has had an extremely active program of discussion and research in this area, and has produced a long series of important publications bringing the two disciplines together.[30] And the International Society of Ecological Economics has

grown enormously after starting its journal, *Ecological Economics*, just a decade ago.

Related to this is a growing realization among my colleagues that one cannot depend on working with governments alone to solve the growing environmental crisis. Instead the emphasis is shifting to recruiting the business community into the struggle to achieve a sustainable society. While there is a long way to go in that process, there are encouraging signs such as the Natural Step program, begun by Dr. Karl-Henrick Robèrt in Sweden, and the writings of businessmen Paul Hawken and Stephan Schmidheiny. [31] Some businesses have already demonstrated that it is possible to make more money operating in a manner that is ecologically sound than in one that ignores the impact of operations on the environment. One outstanding example is Interface, a company that (under the inspired leadership of CEO Ray Anderson) supplies commercial carpeting on a rental basis. When the carpet is worn, Interface replaces it and completely recycles the old material, rather than dumping it into a landfill. The company is enormously successful, grossing more than $1 billion annually. Through such examples, other corporations may learn that they can do well while doing good.

It is important to recognize, however, that just converting business to a powerful force for environmental quality cannot solve our predicament as long as the scale of the human enterprise continues to grow. What is needed now is to involve people in solving local and regional environmental problems and in encouraging their governments to cooperate more in seeking resolution of global problems. Business leaders have both heavy responsibilities and great opportunities in these areas – and they have a great deal of expertise in putting theory into practice. They and their children and grandchildren are fully as dependent for their lives on the services supplied by natural ecosystems as everyone else. They depend on those systems to make the air breathable, to supply freshwater and prevent floods, to dispose of their wastes, and to support the agricultural enterprise that nourishes them by generating and maintaining soils and providing free pest control and pollination services. And perhaps more than anyone else, they are experts in the critical area of consumption – and in a position to help curb the growth of the energy use and material throughput involved. Technological changes such as electronic communications instead of travel and substitution of environmentally more benign energy sources for the dominant fossil fuel technologies of today can help – but changes in lifestyle and human ambitions will be needed here also. The business community also has the political power to lead a transition toward a sustainable global society – one with a smaller population supplied with both necessities and substantial luxuries. I

urge businessmen everywhere to learn about the current environmental situation and then accept the challenge. And scientists, politicians, and ordinary citizens should do the same. Nothing less is at stake than the fate of human civilization.

Notes

1 J.P. Holdren. 1991. Population and the energy problem. *Population and Environment* 12:231-235, and personal communication (1998).

2 J. Holdren and P. Ehrlich. 1974. Human population and the global environment, *American Scientist* 62:282-292; P. Ehrlich and A. Ehrlich. 1990. *The Population Explosion*, New York. Simon and Schuster. 'Roughly the average completed family size.'

4 Demographic statistics from Population Reference Bureau, *World Population Data Sheet*, 1988 and 1998.

5 G.C. Daily, A.H. Ehrlich, and P.R. Ehrlich. 1994. Optimum human population size. *Population and Environment* 15:469-475.

6 On July 10, 1998, a long, incompetent article appeared in the *New York Times* was entitled 'Population implosion worries a graying europe.' Charles Krauthammer followed up in the *Washington Post* with another of his exquisitely ignorant environmental columns on the same general theme (July 17). Its headline said it all: 'Saved by immigrants; the US fertility rate is barely at replacement level.'

7 M. Wackemagel and W. Rees. 1996. *Our Ecological Footprint: Reducing Human Impact on the Earth.* Gabriola Island BC: New Society Publishers.

8 P.R. Ehrlich, et al. 1997. No middle way on the environment. *The Atlantic Monthly* 280 (6):98-104.

9 World Resources Institute. 1998. *World Resources 1998-99.* Oxford: Oxford University Press.

10 L. R. Brown. 1998. The future of growth. In L.R.Brown et al., *State of the World 1998,* New York: W.W. Norton.

11 C. Safina. 1997. *Song for the Blue Ocean.* New York: Henry Holt and Company.

12 G. Daily and P. Ehrlich. 1996. Socioeconomic equity, sustainability, and Earth's carrying capacity. *EcologicalApplications* 6(4):991-1001.

13 A steady flow of recent information has made ever more pertinent the 1996 warning of T. Colbom, D. Dumanoski, and J.P. Myers in *Our Stolen Future* @Dutton, New York).

14 Intergovernmental Panel on Climate Change (IPCC), 1996. *Climate Change 1995,* Summary for Policymakers, Working Group 1, pp. I 0- I 1

15 Although there has been some genuine scientific debate, much of this campaign has been outright disinformation (see P. Ehrlich and A. Ehrlich. 1996. *Betrayal of Science and Reason: How Antienvironmental Rhetoric Threatens Our Future*, Washington DC: Island Press. R. Gelbspan. 1997. *The Heat is On: The High Battle over Earth's Threatened Climate*, Reading, MA: Addison-Wesley). The most recent incident involved the circulation of a fake reprint designed to look like an article that had been published in the *Proceedings of the National Academy of Sciences USA*.

16 J. Hansen, M. Sato, R. Ruedy, A. Lacis, and J. Glascoe. 1998. Global climate data and models: a reconciliation. *Science* 281: 930-932.

17 T.R. Kari and R.W. Knight. 1998. Secular trends of precipitation amount, frequency, and intensity in the USA. *Bulletin of the American Meteorological Society* 79:231-242.

18 W. Stevens. 1998. As Alaska melts, scientists consider the reasons why. *New York Times* 18 August.

19 P. Vitousek, et al. 1997. Human domination of Earth's ecosystems. *Science* 277:494-499.

20 P. Vitousek, H. Mooney, J. Lubchenco, and J. Meiillo. 1997. Human alteration of the global nitrogen cycle: sources and consequences. *Ecological Applications* 7:737-750.

21 S. Postel, G. Daily, and P. Ehrlich. 1996. Human appropriation of renewable freshwater. *Science* 271:785-788.

22 G. Daily. 1995. Restoring value to the world's degraded lands. *Science* 269:350-354.

23 N. Myers. 1996. The world's forests: problems and potentials. *Environmental Conservation* 23:156-168.

24 D. Pauly. 1998. Fishing down marine food webs. *Science* 279:860-863.

25 E.g., J. Toppari, et al. Male reproductive health and environmental xeno-estrogens. *Environmental*

26 *Perspectives* 104 (suppl. 4):741-803. E.g., S. Buchmann and G. Nabhan. 1996. *The Forgotten Pollinators.* Washington DC: Island Press; G. Nabhan and S. Buchmann. 1997. Services provided by pollinators. In G. Daily (Ed.), *Nature's Services*, Washington, DC: Island Press, pp. 133-150.

27 For a popular summary see Bob Holmes. 1998. Life support. *New Scientist*, 15 August, pp. 30-34.

28 P. Ehrlich and G. Daily. 1993. Population extinction and saving biodiversity, *Ambio* 22:2-3; J. Hughes, G. Daily, and P. Ehrlich. 1997. Population diversity: its extent and extinction, *Science* 278:689-692.

29 P. Ehrlich. 1997. *World of Wounds: Ecologists and the Human Dilemma*, chapter 5. Oldendorf/Luhe; Germany. Ecology Institute.
30 E.g., K. Arrow. et al. 1995. Economic growth, carrying capacity, and the environment. *Science* 268:520-521.
31 P. Hawken. 1993. *The Ecology of Commerce: A Declaration of Sustainability*, New York: HarperCollins; S. Schmidheiny. 1992. *Changing Course: A Global Business Perspective on Development and the Environment*, Cambridge, MA: MIT Press.

The Dr. H.P. Heineken Prize for Biochemistry and Biophysics

The Dr. H.P. Heineken Prize for Biochemistry and Biophysics 1998 was awarded to Dr. Anthony J. Pawson for his important discovery of the 'SH2 Domain' in proteins involved in signal transduction in living cells. His work has yielded a better insight in the way in which cells communicate with neighbouring cells. It appears that there is a connection between interference in the transduction of external signals into a cell and diseases such as cancer, diabetes and cardiovascular diseases. Pawson's discovery has changed our concept of signal transduction so fundamentally that it has opened up new areas for the development of medicines for these diseases.

Tony Pawson was born in Maidstone, United Kingdom, in 1952. He received his B.A degree in Biochemistry from Cambridge University in 1973. Three years later he received the Ph.D degree in Molecular Biology from London University. Presently Dr. Pawson is Head of the Department of Molecular Biology and Cancer Research of the Samuel Lunenfeld Research Institute in Toronto, Canada. Dr. Pawson is a fellow of the Royal Society of London and the Royal Society of Canada.

The Dr. A.H. Heineken Prize for Art

The Dr. A.H. Heineken Prize for Art 1998 was awarded to the young Dutch artist Jan van de Pavert for his recognizable and personal oeuvre. Van de Pavert has a strong personality and a rich and diverse palette. He is very much interested in architecture and art history. This is manifested in all forms of sculpture referring to symbols of classic Italian and modern architecture. Scale models, maps, drawings and computer animation show imaginary villas. Van de Pavert's paintings and drawings remind of the social-realism of the beginning of this century. He is inspired by the idea of ideals, which makes his work optimistic and shows the social relevance of art also until today.

Jan van de Pavert was born in Zeist, the Netherlands, in 1960. In 1979 he began his training at the Academy of Arts St. Joost in Breda. After graduating in 1982 he

studied for two years at the Academy Ateliers '63 in Haarlem. Since 1984 Van de Pavert has participated in more than seventy exhibitions in the Netherlands and abroad. He took part in the prestigious Sonsbeek '93. His work is collected by renowned museums as, in the Netherlands, the Rijksmuseum Kröller Müller in Otterloo, the Centraal Museum in Utrecht and the Van Abbemuseum in Eindhoven, in Zürich the Museum für Gegenwartskunst and the Ferens Art Gallery in Kingston upon Hull.

The Dr. A.H. Heineken Prize for Medicine

The Dr. A.H. Heineken Prize for Medicine 1998 was awarded to Dr. Barry J. Marshall for his insight to associate gastric spiral bacteria *(Helicobacter pylori)* with gastritis and ulcer diseases, which has subsequently revolutionized the treatment of peptic ulcer disease: a cure can be reached with simple medical treatment. Contrary to the established scientific view that ulcers are due to stress, Dr. Marshall went in search of the real cause and found it in the bacterium *H.pylori*. He discovered the role of this bacterium without the use of costly extensive research methods but by simple observation instead. He also found that ulcers disappear by combatting the bacterium with an antibiotic. This new treatment means that patients no longer have to undergo endless cures and still have the chance of the ulcer returning after a time.

Barry Marshall was born in Kalgoorlie, Australia, in 1951 and studied Medicine and Surgery at the University of Western Australia. In 1981 he started together with Dr. Robin Warren at the Royal Perth Hospital his research on the bacterium *H.pylori*. He has won many awards for his work and has published numerous articles and books on *H.pylori*. Dr. Marshall's current appointments are Professor of Research in Internal Medicine at the University of Virigina, USA, Burnet Professor of Medicine at the University of Western Australia and President of the Helicobacter Foundation in Charlottesville, USA.

The Dr. A.H. Heineken Prize for History

The Dr. A.H. Heineken Prize for History 1998 was awarded to Dr. Mona Ozouf for her challenging view on the French Revolution. Ozouf has always focussed on cultural-historical and antropologic aspects of the developments and has avoided the classic approach to the usually politically charged subject of revolutions. She has researched the way cultural expressions were used as a means to the revolu-

tionary end. Her book *La fête revolutionnaire 1789-1799* (1976) has changed the established perspective of this period and has shown new ways of historical research. Mona Ozouf's research is not restricted to the French Revolution. She also published on the influence of ideological and political developments on education and educational theory in France. In recent years she has been working on more literary-historical subjects.

Dr. Mona Ozouf graduated in 1955 in Philosophy at the Ecole Normale Supérieure des Jeune Filles in Parijs. Until 1968 she was a teacher in Philosophy. Since then she holds positions as researcher in History at the Centre National de la Recherche Scientifique (CNRS). Today Dr. Ozouf is director-emeritus at CNRS. She frequently publishes essays and critical comments in well-known French newsmagazines.

The Dr. A.H. Heineken Prize for Environmental Sciences

The Dr. A.H. Heineken Prize for Environmental Sciences 1998 was awarded to Professor Paul R. Ehrlich for the unique and erudite way in which he makes his scientific knowledge of aspects involved in the decline of the environment accessible to the general public and policy makers. He became internationally known with his book *The Population Bomb* (1970), in which he describes the possible ecological and social consequences of the explosive population growth. His work has been a significant source of inspiration to the Club of Rome.
Together with his wife, Dr. Anne Ehrlich, Paul Ehrlich has been presenting his ideas in numerous articles, lectures and publications. Primarily Ehrlich is a fundamental biologist, specialized in population biology and ecology of animals and the evolution of animal-plant relationships. He is a leading and renowned scientist in this field of science.

Paul Ehrlich was born in Philadelphia, USA, in 1932. Ehrlich received his B.A. degree in Biology from the University of Pennsylvania. Five years later he received his Ph.D. degree from the University of Kansas. In 1959 he started working at the Department of Biological Sciences of Stanford University in Stanford, California, where in 1977 he was appointed Bing Professor of Population Studies. Ehrlich has won many prizes and awards for his scientific work. Professor Paul R. Ehrlich is Member of the National Academy of Sciences, Member of the European Academy of Sciences and Arts and a Foreign Member of the Russian Academy of Natural Sciences.

Dr. H.P. Heineken Prize for Biochemistry and Biophysics

1964 Erwin Chargaff
1967 Jean L.A. Brachet
1970 Britton Chance
1973 Christian de Duve
1976 Laurens L.M. van Deenen
1979 Aaron Klug
1982 Charles Weissmann
1985 Bela Julesz/ Werner E. Reichardt
1988 Thomas R. Cech
1990 Philip Leder
1992 Piet Borst
1994 Michael J. Berridge
1996 Paul M. Nurse
1998 Tony J. Pawson

Dr. A.H. Heineken Prize for Art

1988 Toon Verhoef
1990 Marrie Bot
1992 Carel Visser
1994 Matthijs Röling
1996 Karel Martens
1998 Jan van de Pavert

Dr. A.H. Heineken Prize for Medicine

1989 Paul C. Lauterbur
1990 Johannes J. van Rood
1992 Salvador Moncada
1994 Luc Montagnier
1996 David de Wied
1998 Barry J. Marshall

Dr. A.H. Heineken Prize for History

1990 Peter Gay
1992 Herman van der Wee
1994 Peter R.L. Brown
1996 Heiko A. Oberman
1998 Mona Ozouf

Dr. A.H. Heineken Prize for Environmental Sciences

1990 James E. Lovelock
1992 Marko Branica
1994 BirdLife International (Colin J. Bibby)
1996 Herman E. Daly
1998 Paul R. Ehrlich