BIOGRAPHICAL MEMOIRS

Sir Martin Roth. 6 November 1917 — 26 September 2006

Sir Michael Rutter and Sir Aaron Klug

Biogr. Mems Fell. R. Soc. published online May 26, 2010

Supplementary data
"Data Supplement"
http://rsbm.royalsocietypublishing.org/content/suppl/2010/05/25/rsbm.2009.0018.DC1

P<P

Published online 26 May 2010 in advance of the print journal.

Email alerting service
Receive free email alerts when new articles cite this article - sign up in the box at the top right-hand corner of the article or click here

Advance online articles have been peer reviewed and accepted for publication but have not yet appeared in the paper journal (edited, typeset versions may be posted when available prior to final publication). Advance online articles are citable and establish publication priority; they are indexed by PubMed from initial publication. Citations to Advance online articles must include the digital object identifier (DOIs) and date of initial publication.
SIR MARTIN ROTH

6 November 1917 — 26 September 2006
SIR MARTIN ROTH

6 November 1917 — 26 September 2006

Elected FRS 1996

BY SIR MICHAEL RUTTER1 FRS AND SIR AARON KLUG FRS2

1MRC Social, Genetic and Developmental Psychiatry Centre, Institute of Psychiatry, King's College London, De Crespigny Park, London SE5 8AF, UK
2MRC Laboratory of Molecular Biology, Hills Road, Cambridge CB2 2QH, UK

Martin Roth was distinguished for his major contributions to the understanding and classification of mental disorders in the elderly. These led to a new discipline, psychogeriatrics, as the problems of late life became recognized as constituting a major medical and social problem. His pioneering investigations led to the crucial demonstration of the differences between the dementias and the affective and other mental disorders of old age. The quantitative neuropathological and psychological studies undertaken by Roth and his colleagues established the pathology of Alzheimer disease as indicative of a disease separate from normal ageing and from other psychiatric disorders. These early studies led to collaborative molecular studies that pointed to a possibly causal pathological process.

EARLY YEARS

Martin Roth was born into a long-lived, highly musical Orthodox Jewish family in Budapest on 6 November 1917. In 1925 the family moved to London, where his father, the Reverend Samuel Roth, a cantor with a highly renowned singing voice, accepted a position in a synagogue in the East End. Samuel had been born in what is now Czechoslovakia, spent some time as a young man in Palestine, and then settled in Budapest, Hungary, where Martin and his brother Ferenc were born. Martin’s mother, Regina, was born in Hungary; she was a warm and hospitable person, a devoted mother, and an excellent cook. After the move to the UK, her Hungarian friends and relatives were frequent visitors to the family home. Ferenc first trained as a lens maker, but after serving in the British Army during World War II he bought and ran a hotel with his wife. He was also a talented jazz pianist. Martin’s younger sister, Charlotte, was
born in the UK and became a secretary in a company. She also played the piano well. Musical talents have continued in several of Martin’s grandchildren.

Martin attended the Davenport Foundation school, famous for educating talented boys (mainly Jewish) who went on to become outstanding professionals—especially in medicine. Martin excelled both scholastically and musically. Even as a boy, he was a highly talented pianist and, for a while, he contemplated a career in music. In the event, he opted for medicine instead but he remained an excellent musician who treasured musicality and musical vision much more than mere technical accuracy. The same quality of valuing true understanding was evident in the whole of his approach to science. Empirical evidence was crucial, but the accumulation of ‘facts’ meant nothing if it did not lead to an appreciation of mediating mechanisms. He lacked respect for academic fads and fashions that were based on claims of ‘authority’ rather than empirical evidence and experimental testing. A creative and original thinker, he was always willing to try out and test new ideas, even if (perhaps especially if) they seemed unconventional at first. But most of all he was a synthesizer who used considerable intellectual powers to integrate diverse findings and open up new avenues of understanding. Moreover, he never lost sight of the importance of applying scientific insights to improving the health and wellbeing of patients.

**MEDICAL TRAINING AND PSYCHIATRIC EXPERIENCE**

Martin undertook his medical training at St Mary’s Hospital Medical School, graduating MB BS in 1942. He then worked at Park Prewitt (an outpost of St Mary’s), then a military hospital, proceeding rapidly to gain his MRCP in 1944 and his MD in 1945. He trained in neurology at Maida Vale Hospital, where Sir Russell (later Lord) Brain (FRS 1964) was a crucially important mentor. At that time, Martin planned a career in neurology, gaining neuropathological experience while at Maida Vale. Brain, the outstanding neurologist of the day, had not only a brilliant intellect, an encyclopaedic knowledge and an amazingly retentive memory but also a breadth of interest that included psychoanalysis and psychiatry. Curiously, although Martin’s first studies were into neurological disorders, it was Brain’s broader interests that led Roth to switch his focus to psychiatry—albeit with a major interest in neuropsychiatric interconnections.

His psychiatric training was undertaken at the Maudsley Hospital, where he was most influenced by Dr Eliot Slater, who taught him statistical methods and fostered his skills in logical reasoning. Martin also visited Grey Walter in Bristol and acquired some skills in the use and analysis of the electroencephalogram (brainwave measurements). His clinical duties at the Maudsley were heavy, and Martin felt that there was little time for dedicated research, despite the research emphasis in the training. He clashed with Sir Aubrey Lewis, the then Director, whom he considered too critical and not sufficiently supportive. Accordingly, he left the Maudsley prematurely in 1947 to go to Crichton Royal Hospital, where he was hugely influenced by Professor W. Mayer-Gross, who was Director of Research there. Mayer-Gross, who had been the leader of German psychiatry before emigrating to the UK to escape Nazi persecution, was a creative, dynamic individual who combined intellectual rigour with a warm, helpful, supportive style. He had been much influenced by E. Kraepelin and K. Jaspers, and he brought Martin into contact with an extensive range of very influential European psychiatrists. In addition, he fostered and encouraged Martin in the scientific value of clinical epidemi-
logical studies and emphasized the importance of biochemistry. Throughout his career, Martin combined key elements of the German and British traditions of neuropsychiatry.

**THE INNOVATIVE TEXTBOOK OF CLINICAL PSYCHIATRY**

Martin’s two and a half years at the Crichton Royal proved to be a major turning point in his career—for two rather different reasons. First, it led in 1949 to an invitation to join Slater and Mayer-Gross in writing a new comprehensive textbook, *Clinical Psychiatry*, that was unlike all previous psychiatric textbooks in seeking to integrate science and clinical work (3)*, to present a way of thinking about the conceptual issues involved in that integration, and to challenge the key theoretical notions that lacked empirical support. Its impact internationally was immense when it was published in 1954; it was translated into five different languages and went through three editions, the last (in 1977) largely written by Martin himself.

Second, the period at Crichton Royal, and especially the collaboration with Mayer-Gross, convinced Martin that accurate classification of mental disorders provided the first step towards understanding causation and that this was especially needed in the diagnosis of mental disorders in the elderly, which at that time was in a muddled state with a lack of an empirical base for diagnosis. His commitment to bringing clarity to diagnosis and classification was also applied to the field of anxiety and depressive disorders, which constituted a major focus in the decades ahead and led to the Anna Moniker award.

**PIONEERING STUDIES OF PSYCHIATRIC DISORDERS IN OLD AGE**

In 1950, while still in his early thirties, he was appointed as Director of Clinical Research at Graylingwell Hospital in Sussex, where he remained for five years. There were heavy clinical duties (thus, he had to write a report on every patient for the Board of Control every three months), but these facilitated his interest in the natural history of mental disorders in old age. He and his colleagues first examined the case records of patients admitted some years earlier and studied what happened to them over the next two years. His working hypothesis at that time was that affective (depressive) psychosis differed from senile psychosis (Alzheimer disease), from paraphrenia (a disorder similar to schizophrenia), from acute confusional states and from arteriosclerotic or multi-infarct psychosis (namely, a dementia involving the death of brain tissue as a result of a loss of blood supply). Systematic follow-up showed that most patients with affective psychosis were discharged from hospital. The death rate was below 20%, as it was also for paraphrenia—the rate being much the same as that for mentally intact persons of a comparable age (4). The cloudy confusional states had an intermediate outcome, but the multi-infarct psychoses had a high mortality. Epidemiological studies with Martin’s colleague, David Kay, told a similar story (5–7). The findings ran counter to the prevailing view at that time that all the psychoses in the elderly ultimately resulted in dementia. Martin decided that the necessary test of the hypothesized group differences was likely to lie in the neuropathology. Although some preliminary research was undertaken at Graylingwell, the real

* Numbers in this form refer to the bibliography at the end of the text.
opportunity was provided by Martin’s appointment to the Chair in Psychological Medicine at Newcastle (initially Durham) in 1955, where he remained for 21 years, building up a powerful interdisciplinary Medical Research Council (MRC) research group.

The group included Barbara Hopkins, the psychologist with whom he collaborated at Graylingwell in studying patterns of cognitive test performance in the same five groups (1, 2). It was found that the psychotic patients with affective disorder, and those with paraphrenia, showed IQ distributions very similar to those of normal controls, whereas those with either Alzheimer disease or arteriosclerotic dementia had much lower scores that scarcely overlapped with those of controls. Once again, confusional states occupied an intermediate position. This early psychological research laid the foundations for the much later development of a standardized instrument for assessing mental disorders in the aged (14).

A major step forward was taken through the quantitative neuropathological studies undertaken with Tomlinson and Blessed (9–11). Alzheimer was the first to describe the abundant occurrence of plaques and tangles in the brains of individuals who had suffered from senile dementia. Corsellis (1962) was the first to show that clinical groups of psychoses in old age corresponded fairly well to neuropathological findings—with marked differences between the dementias and functional disorders. The research of Martin and his colleagues took matters to a new higher level, however, because of the rigorous quantification, the use of strictly blind conditions, and the demonstration that measurement was reliable. Moreover, the neuropathological research was planned on a hypothesis-testing strategy based on the systematic longitudinal and psychological studies undertaken by Martin and his colleagues.

The neuropathological findings of Roth et al. showed the expected difference in the occurrence of plaques between the brains of demented and non-demented patients, but there were four really novel, and important, findings. First, there was a significant, and substantial, correlation (0.77) between the severity of the dementia and the mean plaque count score. This finding strengthened the inference that the plaques (or neural changes associated with them) might be causing the dementia. Second, the very high association did not apply to all cases of dementia; instead, it applied mainly to those with Alzheimer disease. Third, the associations were not just a function of increasing age. This meant that Alzheimer’s distinction between pre-senile and senile dementia was probably invalid. Fourth, plaques were found in non-demented subjects, and the differences were quantitative rather than qualitative. This raised the possibility that there might be an aetiological continuity between milder degrees of cognitive impairment in old age and severely handicapping senile dementia. The late 1960s and early 1970s saw the beginning of the abundant flow of international honours that came to Martin Roth and continued throughout the remainder of his career.

The Alzheimer story was not taken forward in a major way by the Roth group until, in 1977, he moved to take the Chair of Psychiatry in Cambridge (see below). Martin himself was not a basic laboratory scientist, but it is a mark of his strength that he recognized the need to go beyond the correlational neuropathological studies to molecular investigations that could identify causal processes more directly. With that in mind, he approached Aaron (now Sir Aaron) Klug FRS, then Director of the Laboratory of Molecular Biology in Cambridge, to ask for help in determining the possible role of the paired helical filament (PHF) formed in tangles in the causation of the dementia associated with Alzheimer disease. The initial problem was that the PHF is biologically inert and, hence, there was a need to break down the insoluble tangles to determine what might be different about the varieties of PHF that could bring about dementia. Claude Wischik (Martin’s former student) was primarily responsible for the science
required to solve the problem. The initial paper (13) showed that the PHF had the structure of a twisted ribbon and that it was most unlikely that it was formed by a simple collapse of normal cytoskeletal elements such as neurofilaments. Five years later (15), antibodies were used to examine neurofibrillary degeneration in Alzheimer disease to distinguish between intracellular and extracellular protease digestion in vitro. Thus, tangle degradation seemed to involve a change in tau immunoreactivity and partial proteolysis of tangle-bound tau in extracellular tangles. Further studies concerned the selective inhibition of Alzheimer-disease-like tau aggregation by phenothiazines (17) and alterations in tau protein phosphorylation in Alzheimer disease (16). The findings were important in two main respects. First, they showed that the biologically inert PHF could have variants showing fragmentation and, second, they showed that a multi-phase transformation (that is, a process involving several phases) leading to Alzheimer disease might be taking place. Since these early studies prompted by Roth, the Cambridge group of Wischik, Goedert, Klug and others (see Goedert et al. 2006) showed that tau protein was the major component of the PHF and that the latter was made of six tau isoforms, each full length and hyperphosphorylated. This finding pointed to what was abnormal in the PHF varieties associated with Alzheimer disease but fell short of proving a causal process leading to dementia. Genetic evidence dealing with an autosomally dominant form of frontotemporal dementia with Parkinsonism constituted the missing link that needed to be filled. Further research (Spillantini et al. 1997, 2006) provided evidence that mutations in the tau gene were associated with a diverse group of neurodegenerative diseases regarded now by many people as ‘tauopathies’.

The story of Alzheimer disease that began with Martin’s longitudinal investigations, associated with psychological studies and followed by the quantitative neuropathological research, had led on to molecular investigations that pointed to a possibly causal pathological process. After Martin had left the research team, genetic research took the story further to a point at which a genetically driven causal process could be inferred. Nevertheless, uncertainty remains on what is distinctive about Alzheimer disease.

Particularly given Martin’s admiration for his mentor, Eliot Slater, a pioneer in quantitative genetics, it is curious that Martin’s papers over a 50-year period involved little or no discussion of the potential value of genetic research in tackling causal questions. Of course, Martin was well aware of genetic findings and fully accepted the importance of genetic influences on mental disorders. What seems to be missing is an appreciation of how genetic findings may inform causal investigations.

As we have noted, an interest in diagnosis and classification, as well as in treatment, was a main driver of Martin’s research. We have placed our emphasis on his contributions in the field of the psychiatry of old age because that is where his conceptual and synthesizing skills made a decisive contribution that remains as important today as it was when it was undertaken in the 1950s, 1960s, 1970s and 1980s. It is not that any single discovery is attributable to him, but rather that his vision changed the field and that his appreciation of the diverse kinds of research that was needed led to collaborations with distinguished colleagues who provided the detailed expertise that he lacked but for which he had the wisdom to see the need, together with the drive and entrepreneurial skills that made change happen. Deservedly, this work led to numerous prestigious awards—including the Paul Hoch Award of the American Psychopathological Association in 1979, the Gold Medal of the Society of Biological Psychiatry in the following year, the Sandoz Prize in 1985, the Kraepelin Gold Medal in 1986, the Gold Medal of the Alzheimer’s Disease International Society in 1992 and the Camillo Golgi Medal in Neuroscience in 1993.
RESEARCH INTO AFFECTIVE DISORDERS

Over the same period, Roth undertook an extensive body of research into anxiety and depressive disorders. It is clear from his writings that he saw this as making an equally important contribution. We beg to differ, and need to explain why. In brief, Martin was prompted to investigate diagnostic distinctions by observations that patients differed in their response to antidepressant medication and to electroconvulsive therapy (ECT). He hypothesized that this inter-individual variation might be a function of heterogeneity in the types of affective disorder. The investigative tool used was provided by principal components analysis (a form of factor analysis) leading to a discriminant function analysis to differentiate the postulated ‘neurotic’ and ‘endogenous’ varieties of depression. The data used stemmed from ratings based on a combination of clinical interview, case notes, and observations by nursing staff. One study (8) showed that depression of the so-called ‘neurotic’ and ‘endogenous’ types could be differentiated by their response to ECT as assessed at three-month and six-month follow-ups. A later paper (12) applied the same techniques (but this time using a structured clinical interview (the Maudsley Personality Interview)) to differentiate between anxiety and depressive states. It was concluded that anxiety and depressive states were largely separate.

The research was carefully conducted and presented, but there were several crucial differences from Martin’s studies of psychoses of old age. First, the studies of affective disorders relied on one particular statistical strategy that provided no basis for causal inferences. By contrast, the studies of old age involved a range of complementary strategies that allowed the testing of alternative hypotheses. Second, the hypothesis was expressed in terms of an old-fashioned and misleading contrast between disorders that are genetic in origin and those that are environmentally determined. Again, although genetic research was in its infancy in the 1970s and 1980s, it is a curious omission not to have made use of genetic research strategies. Third, many of the key findings have not stood up to the test of further research (although some have—for example, response to ECT). Most crucially, Martin’s basic concepts no longer influence the field in any major way.

We need to turn next to Martin’s many other contributions that make use of science but did not themselves constitute science. Mention has been made already of his textbook with Slater and Mayer-Gross. It played a substantial role in changing thinking in psychiatry, and for a quarter of a century it dominated the field.

COMMITTEE WORK

From the 1960s onwards, Roth was much in demand to serve on national and international committees (see, for example, figures 1 and 2). Thus, he was a member of the Council of the Royal College of Physicians (for which he was an examiner) and a member of the Royal Medico-Psychological Association (RMPA) and the MRC during the mid 1960s; and from 1958 onwards he served as a consultant to the World Health Organization in various capacities. He served on multiple editorial boards and did much reviewing of grant proposals and articles submitted for publication in scientific journals. He had prodigious drive and energy and was much respected for the breadth and depth of his knowledge. He had strong opinions and worked best in leadership roles. His colleagues sometimes teased him about his reviews of proposals and articles being longer than the proposals or articles themselves. It mattered...
Figure 1. Martin Roth at the 30th anniversary meeting of Soroptimist International held on 12–14 March 1980 at Palazzo Congressi Firenze. (Photographer unknown.)

Figure 2. Martin Roth addressing the 35th Congresso Nazionale di Psichiatria held at Forte Village, Cagliari, on 27 October to 1 November 1982. (Photographer unknown.)
Biographical Memoirs

greatly to Roth both that his views prevailed and that he was given the respect and acknowledge that his stature required. Although his views were not always accepted, he always had telling, pertinent points to make, and more often than not he won the day by the force of his logic.

Presidency of the Royal College of Psychiatrists

The next major contribution came from his presidency of the Royal College of Psychiatrists between 1971 and 1975. After much tricky negotiation with the Privy Council, the RMPA was upgraded to become the Royal College of Psychiatrists—the first of the new Royal Colleges to be set up. The RMPA lacked the expertise to make the transition easily and a major crisis was brewing because a large number of able, articulate, younger psychiatrists were opposed to the establishment of a new membership examination (as required by the Privy Council). Several leading academic psychiatrists banded together to persuade Martin to stand for election as president, which he did, and he was elected on the first ballot. It was crucial that leadership be provided by someone of high scientific standing who was used to walking the corridors of power and who had both the wisdom and the charisma to bring about success—qualities that Martin had in abundance.

However, interestingly, the challenge brought out other qualities possessed by Martin. He recognized that it was vital to obtain the support of the whole body of psychiatrists, including the young rebels. Martin was a wonderful raconteur, with talents of mimicry. It turned out that his judgement on what was needed was on target. He told a long story about the fearsome competitive examinations for entry to the Civil Service in ancient China. For three days some 12,000 people were held in a confined space with no one allowed out of the entrance gates. The strain led some candidates to become unhinged so that they submitted their last will and testament rather than completed exam papers. Any corpses had to be hoisted over the wall rather than carried through the gates. Martin never acquired the art of talking or writing briefly, but on this occasion a long, involved, very funny story delivered with all of his charismatic style was just what was needed. The laughter engendered by Martin’s talk cleared the air and defused the anger.

Of course, it was necessary afterwards to engage in detailed negotiations and to make some compromises. The difference from the failed discussions that had previously taken place was the change in atmosphere. Martin’s logic and powers of persuasion were then able to operate. The new College paved the way for the other colleges in setting standards of training and in establishing problem-solving ways of raising standards. The College, under Martin’s leadership, also did much to develop community care to replace the old asylums and to deal with the growing problems associated with drug abuse and dependency. An even bigger challenge was presented by the need to acquire a building for the College, and the funds to purchase it. Martin’s entrepreneurial skills and good connections brought success.

Cambridge University, the Royal Society and the Academy of Medical Sciences

In 1977, Martin moved from Newcastle to become the first holder of the Chair of Psychiatry in Cambridge University. Cambridge, of course, was a highly distinguished university, but at
that time it did not house a first-rate medical school. Martin, building on his experience in Newcastle, sought to make Cambridge psychiatry the best in the country—again, appreciating the need for interdisciplinary collaboration in most forms of research.

There is no doubt that Martin’s election to the Fellowship of the Royal Society in 1996 meant a lot to him. It reflected the importance of his research into the disorders of old age that made modern geriatric psychiatry possible. The failure to be asked to be a founder Fellow of the Academy of Medical Sciences (AMS), when it was established in 1998, rankled, and it was a surprising omission. Those setting up the AMS were keen to bring in the academic leaders of the future rather than retired senior statesmen (Martin having retired in 1985). Nevertheless, Martin greatly appreciated his (albeit belated) election to the AMS in 2001. It represented public recognition of the enormous range of his many scientific contributions that served to put the psychiatry of old age onto the map.

Although not widely known, Martin suffered throughout much of his adult life with Crohn’s disease—a particularly troublesome disorder. He dealt with this with his customary fortitude but, in the end, he died from complications of this disease. He is survived by his wife, Constance, an outstandingly able woman in her own right, who has served as a magistrate and on Mental Health Tribunals, as well as the Warnock Committee on the Education of the Handicapped, and whose support over the years meant a great deal to Martin. He is also survived by three daughters, Priscilla (known informally as Scilla), a consultant psychiatrist; Ilona, an academic psychologist; and Naomi, a publisher.

APPOINTMENTS AND HONOURS

1950 Fellow of the Royal Society of Medicine
1964–68 Scientific member of Medical Research Council
1968–69 President of the Section of Psychiatry of the Royal Society of Medicine
1972 Knight Bachelor
1977 Fellow of Trinity College, Cambridge
1977–90 Vice-president, Medical Defence Union
1985 Emeritus Professor and Fellow of Trinity College, Cambridge
1996 Elected Fellow of the Royal Society
2001 Elected Fellow of the Academy of Medical Sciences

ACKNOWLEDGEMENTS

We are most grateful to Dr N. D. Minton for the DVD of his hour-long interview with Martin in 1991; to Thomas Bewley for his history of the Royal College of Psychiatrists; to Eugene Paykel for his account of Martin’s period at the University of Cambridge; to Katherine Bick for her interview with Martin, published in 1980; to Claude Wischik for his address at the Memorial Service; and to Ilona Roth for the eulogy delivered at the funeral service. We are also indebted to Martin’s own address at a meeting to celebrate his eightieth birthday, and to the obituaries written by Claude Wischik (in The Independent), by Eugene Paykel and Henry Rollin in the British Journal of Psychiatry and the anonymous obituary in the Daily Telegraph.

The frontispiece photograph was taken in 1996 by Prudence Cuming Associates and is reproduced with permission.
Biographical Memoirs

REFERENCES TO OTHER AUTHORS


BIBLIOGRAPHY

The following publications are those referred to directly in the text. A full bibliography is available as electronic supplementary material at http://dx.doi.org/10.1098/rsbm.2009.0018 or via http://rsbm.royalsocietypublishing.org.
