L. S. Penrose FRS (1898–1972)

Psychiatrist and professor of human genetics

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Some individuals, though pre-eminent in their subject, fail to receive recognition of their merit and continuing value. W. H. Rivers and Adolf Meyer come to mind as psychiatrists and with them we can include Lionel Penrose. The accolade he has received as a powerful mover in the meteoric progress of human genetics since the beginning of this century has perhaps cast his psychiatric accomplishments into shadow. The centenary of his birth this year is an appropriate time to look over and consider his work in this field. In psychiatry his principal contributions are large surveys of: (a) 1280 mentally defective patients and their families, the results of which include clinical and genetic data; and (b) almost 5500 pairs of related individuals who had been admitted to an Ontario hospital with psychosis and were studied together with their families. He used a measurable aid to diagnosis and estimated the effectiveness of treatment and the constancy of diagnosis among affected relatives of people with psychosis. Using age of onset of illness as a measurable aid to diagnosis he estimated the effectiveness of shock treatment, as indicated by patient discharge from hospital, among the same population. He also conducted a sustained and successful rebuttal of the eugenists' claim and widespread popular belief that the proportion of mental defectives and problem families could be effectively reduced by constraining their fecundity and that of their parents.

PENROSE'S EARLY INTEREST IN PSYCHIATRY

Penrose was an undergraduate at St John's College, Cambridge during 1919–1921 where he first read mathematics, but later changed to the Moral Sciences Tripos, which allowed him to study mathematical logic (under Bertrand Russell) and psychology. Later in his course he concentrated on logic where he obtained a first class degree and then did a year of psychological work with F. C. Bartlett. He worked for a time in Fulbourn Mental Hospital and became acquainted with John Rickman, a former pupil of his Quaker public school who later became a well-known psychoanalyst. He also attended the lectures of W. H. Rivers whose contributions to the theory of psychotherapy derived from his treatment of psychiatric casualties in Craiglockhart Hospital during the First World War, of which a historically-based novel gives an account (Barker, 1994).

Penrose became interested in discovering whether psychoanalysis could be investigated scientifically, a question he addressed several times in writing (Penrose, 1953). In 1922, following the example of John Rickman, he went to Vienna where he met Freud, Wagner Jauregg, Paul Schilder and other leading psychiatrists. He worked in E. Bühler's laboratory on memory and perception (Harris, 1973) and was himself psychoanalysed by Siegfried Bernfeld (further details available from the author upon request).

Penrose decided that in order to pursue the field of mental disorder and abnormal psychology he must qualify in medicine. He therefore undertook preclinical studies at Cambridge and later went to St Thomas's Hospital in London where he remained until his qualification in 1928 and then took up a research scholarship at Whitechurch Hospital, Cardiff which at that time was pre-eminent for psychiatric training in Britain. He produced a thesis for his MD about a group of people with schizophrenia, one of whom had a duration of illness of 50 years. He later published a paper about this person including a clinical description followed by an extended formulation comprising a discussion of symptoms with the Kraepelinian diagnosis 'paraphrenia expansiva'. Nevertheless his discussion of aetiology derives largely from speculations in psychoanalytic theory (Penrose, 1931*a*).

On his return from Vienna he approached Ernest Jones of the Institute of Psychoanalysis on whose recommendation he became a member of the London Psychoanalytical Society (J. Duncan, personal communication, 1993) and undertook a brief period of supervised psychotherapy as a clinical student of the Institute (Penrose, 1926). Roazen (1975) points out that: "Like Freud, Jones thought that one could not be an analyst unless one practised full-time"; so he felt that Lionel Penrose had too many other interests and Penrose agreed not to pursue an analytical career.

However, he eventually concluded that psychoanalytic theory and treatment was not amenable to a scientific approach (Kevles, 1985); his conclusion anticipated the medical consensus of about half a century later. He advised one of his post-graduate students not to waste her time undertaking psychoanalysis which he said all depended on transference and could be learned in a few weeks (further details available from the author upon request). He was not, however, an overt critic of psychoanalysis; he founded a Clinical Essay Prize and remained a paying member of the London Institute of Psychoanalysis until his death (J. Duncan, personal communication, 1993).

THE COLCHESTER SURVEY

In 1931 Penrose was appointed by the Medical Research Council to undertake research to increase existing knowledge of the causation of mental deficiency. This took place at the Royal Eastern Counties Institution and took the form of a detailed clinical and genetic study of the 1280 patients of this large hospital for mental deficiency. The initiation of the plan and its execution gained by the support of the humane and progressive medical superintendent Frank Turner (Kevles, 1985). Besides examination of the patients, their 6629 siblings, as well as parents, children and spouses were systematically interviewed during the seven-year duration of the project. Harris, a later colleague, noted that: "Mental deficiency was at that time the Cinderella of the public health services . . . little systematic scientific research had in fact been carried out . . . the subject seemed too far removed from the mainstream of psychiatry. Certainly there appeared to be few conventional career prospects on embarking on research in this

field, but to Penrose the apparent disadvantages and difficulties were probably among its main attractions" (Harris, 1973). The overall results of this study were published in a report to the Medical Research Council (Penrose, 1938).

J. M. Berg, a colleague of Penrose's involved in studying mental deficiency for over a decade, said of this report: "Only careful direct scrutiny of the 159 page report provides an adequate picture of its wealth of data, analyses and insights. Very briefly it can be said that the report clearly demonstrated that mental defect is not a homogeneous, neatly circumscribed entity; that it is a graded continuum from the most profound degree (called idiocy at the time) to levels not precisely separable from normality; that there is a wide range of physical and behavioural accompaniments and that multiple interrelated aetiological factors of varied genetic and environmental kinds are involved. This may now all seem fairly obvious to many, but that this is the case is in no small measure due to Penrose's meticulous investigations and analyses" (Berg, 1998).

Among specific items of work during the Colchester period the following are outstanding.

Down's syndrome

Frequent replacement of the distal and medial creases of the fifth finger by a single one (Penrose, 1931*b*).

The role in aetiology of advancing maternal age (in contrast to paternal age, birth order and time interval between births).

Observations of maternal age-independent occurrences of the syndrome, often associated with familial incidence (explanation of which is related to the detection of regular trisomy 21, translocations and mosaicism).

Penrose suggested in the 1930s that a chromosomal aberration of some kind might be a biological basis of Down's syndrome (Penrose & Smith, 1966; Smith & Berg, 1974) at least 20 years before Lejeune *et al* (1959) first reported such an aberration.

Dermatoglyphics had long preoccupied Penrose (Loesch, 1973) and his first publication on the subject reported that the handprints in families with a Down's syndrome member deviated towards a characteristic feature of palm prints in Down's syndrome, particularly with trisomy 21 mosaicism (Penrose, 1949). He also found a graded reduction in the total finger ridge-count as the number of X chromosomes increased.

Inborn errors of metabolism

Soon after Fölling (1934) reported an inborn error of metabolism associated with mental retardation, Penrose tested the urine of 500 inmates of the Royal Eastern Counties Institution and discovered a 19-year-old male who, with his brother, was affected with phenylketonuria (Penrose, 1935*a*). He helped to show that this was an autosomal recessive disorder (Penrose, 1935*b*).

Persistence of an autosomal dominant condition producing infertility is shown in tuberose sclerosis, a condition with very varied manifestations which often includes idiocy and psychosis, and which was calculated by Gunther & Penrose (1935) to be often due to repeated new mutations the rate of which they estimated.

Intelligence

Penrose, throughout his career, gave much attention to this central feature of mental defect including its definition, determinants, measurement and distribution in populations. Two examples of this arise from his work in Colchester. In 1933 he published an analysis of inheritance of intelligence in 100 families containing members with subcultural mental defects. Estimates of the mental abilities of the members of these families gave evidence of the higher intelligence of parents of individuals with severe recessively-determined mental defect compared with parents of those with mild mental defect resulting from polygenic inheritance. He further estimated that of individuals in families with a mentally defective member 45% are of normal intelligence. Of the remaining 55% the majority had one parent who was dull or defective; in 6% both parents were dull or defective; 2% of the siblings of a mild or dull defective were of superior intelligence, 44% were of normal intelligence and 16% were dull or defective (Penrose, 1933*b*). He deduced from his findings that the inheritance of this type of mental defect (including those who cannot be distinguished from dull normals) is not the result of a single gene but of a number of 'alternative additive factors'. He also found that the mental level of mentally retarded offspring was more often related to that of the mother than of the father and suggested that this might result from the differential assortative mating of parents with respect to mentality whereby a woman of normal intelligence and a mentally retarded man do not appear to mate whereas the opposite combination is found, thus increasing the proportion of defective mothers. These findings constituted an important ingredient of the arguments which Penrose brought to bear against the widespread eugenic idea that measures to limit the supposed greater fecundity of defectives than of subjects of superior intelligence should be instituted to prevent an overall decline in national intelligence (Watt, 1998).

CANADA

Penrose was appointed as Director of Psychiatric Research in the Ontario Department of Health, took up the position in 1939 and held it for six years. Here his chief interest passed from mental deficiency and he turned his attention to the patients in Ontario mental hospitals among whom patients with schizophrenia and affective disorder (depression and mania) constituted the majority.

Features of his method are as notable as his results: for instance he used age of onset to differentiate schizophrenia and affective disorder, thus using a measurable item to meet the difficulty of diagnosis that was wholly dependent on mental symptoms and therefore unreliable.

Of those admitted to any Ontario psychiatric hospital during a fixed period he identified patients who had one or more relative who also had been admitted or had committed suicide and made a comparison between about 5500 pairs of affected relatives in respect of age at first admission (as an approximation of age at onset) and of the constancy of diagnosis in affected members of a family. He also compared outcome in respect of discharge at two and three years after treatment of 1600 of these patients who had undergone induced convulsion therapy with the outcome of the remaining patients who had not undergone this treatment. Once again, he used a measurable variable to support the less ascertainable and less reliable clinical judgement.

The results of these large surveys were reported to the Ontario Department of Health (Penrose, 1944*a*,*b*) and, although not fully published by Penrose, were obtainable from the Department. Fortunately, T. J. Crow obtained a copy which he published (1991) with an introductory

comment indicating the value of Penrose's findings to his own research. Some years after returning to Britain, however, Penrose drew on his Canadian findings in several papers including, 'Critical survey of schizophrenic genetics' (1968), which represents mature reflection on his work there. It shows the superiority of induced convulsion treatment to any contemporary treatment and to natural remission, its limitations in the longer outcome of affective disorder and the lack of effect of either coma or convulsion treatment on the outcome of schizophrenia (Penrose, 1944*a*,*b*). He also demonstrated that married couples showed a greater frequency of both parents being admitted to a mental hospital with the same psychosis diagnosed and with ages of onset closer to one another than would occur by chance; possibly due to assortative mating (1944*c*).

GALTON CHAIR (1945–1965)

His appointment to the chair, originated by Galton, marked a resurgence of his work with mental deficiency and his contributions to the burgeoning field of medical genetics. I have recorded elsewhere his steady constructive criticisms of eugenics (Watt, 1998). He developed a close working relationship with Shapiro the superintendent of Harperbury Hospital for mental defectives in Hertfordshire, giving him welcome access to patients. He also became editor of the publication which under him became the *Annals of Human Genetics*.

BIOLOGY OF MENTAL DEFECT

A huge contribution was made to the formation of a comprehensive rational view of mental deficiency and of its biological significance which attained a full development in his book *The Biology of Mental Defect* (Penrose, 1949). To its subsequent three editions (1953, 1963, 1972) fresh material from mental deficiency research, largely from his own work and that of his students and colleagues, provided, as Harris (1973) notes, "a remarkable picture of the developments that took place during these 40 years".

THE KENNEDY–GALTON CENTRE (1965–1972)

When Penrose retired from his University Chair at the age of 67 years he was able to transfer his full-time research to the facilities which he developed during his relationship with Harperbury Hospital. He used money he had been awarded from the Joseph P. Kennedy Foundation to set up in 1965 'The Kennedy–Galton Centre for Mental Deficiency Research and Diagnosis' with himself as director (Harris, 1973). The name, he declared, "implies that the scientific researches on the causes of mental deficiency, to which it is dedicated, should be of high objective standard and as imaginative in conception as would be demanded by the association of the name of Francis Galton" (Penrose, 1973). About 20 full-time staff and collaborators were associated with staff at the centre with cooperation of physicians from neighbouring mental deficiency hospitals (Cell Barnes, Leavesden and others more distant; Stoke Park, Caterham and South Ockenden) while material was also obtained from referrals to the Centre which has now been transferred to the Medical Research Council hospital at Northwick Park.

Dermatoglyphics (involving finger, palm and foot printing) formed a large part of the work of the Centre, and Penrose devised a new method of classifying prints resulting in a number of deductions with clinical applications and aetiological implications (Loesch, 1973). Penrose (1973) explained: "It is clear, when there is any marked chromosomal error, the normal dermatoglyphic picture is distorted, often in a stereotyped way. In fact any disturbance of limb growth, caused by genes or toxins, in very early foetal life is likely to influence these patterns. Abnormal genes, whose effects come into action later, do not have any such effect and the prints of patients with biochemical effects are normal."

Penrose's work is a pre-eminent example of the valuable research based on and carried out in mental defective and mental hospitals which could not be readily done outside them. Penrose alludes to this in expressing his regret that: "At present there is a widespread opinion that mental deficiency hospitals should be 'run down' and eventually closed: it is consequently unsuitable in future, to plan scientific researches in these institutions. In the meantime, we continue to work hopefully on the assumption that such fascinating and, as we think, useful investigations will not be discouraged, although they may not easily fit in to standard administrative practices" (Penrose, 1973).

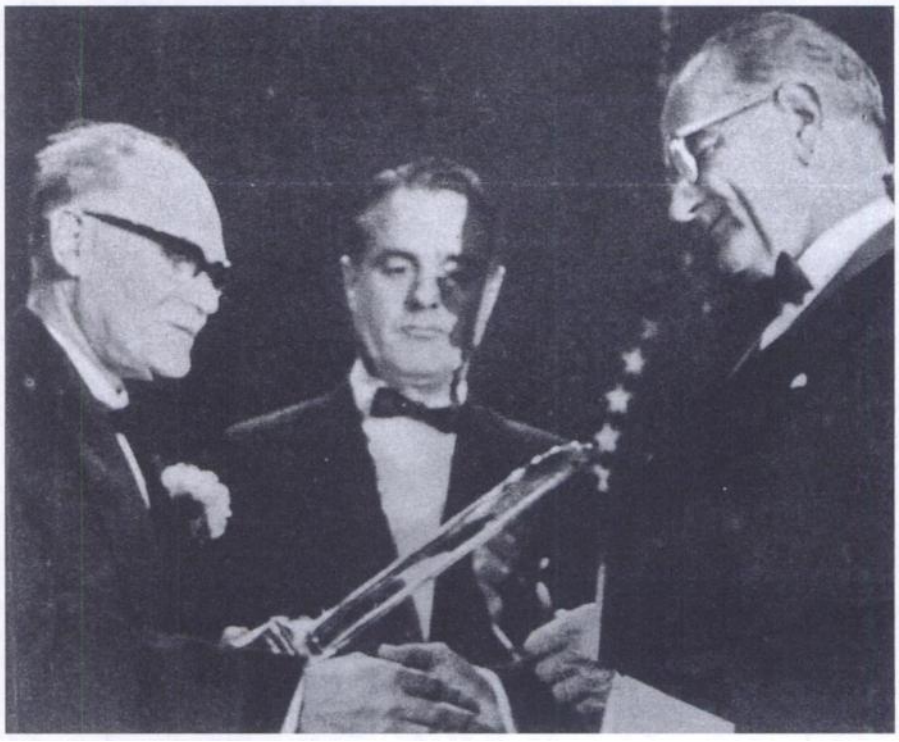

Fig. 1 Penrose (left) receiving the award of the Joseph P. Kennedy, Jr Foundation in 1964 from Lyndon Johnstone, President of the United States. (Printed by kind permission of Dr Shirley Hodgson.)

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