Lionel Penrose: some aspects of his life and work

Sir Cyril CLARKE, KBE, MD, FRCP, FRS,
President of the Royal College of Physicians of London

Lionel Sharples Penrose was born in London on 11th June 1898. His father was a portrait painter, James Doyle Penrose, and his mother Elizabeth Peckover. She was directly descended from Edmund Peckover, who served in Cromwell's army. Some landmarks in Lionel Penrose's life are given in Table 1.

TABLE 1. Some landmarks in the life of Lionel Sharples Penrose, 1898–1972

1908–1911	The Downs School, Colwall.
1912–1916	Leighton Park School, Reading.
1916–1918	Friends' Ambulance Train, NW France.
1919–1921	St John's College, Cambridge. Moral Sciences Tripos (this included Psychology). 1st in Logic, Part II.
1921–1925	Post-graduate studies in psychology, chiefly in Vienna.
1925	Cambridge again, to start medicine. 1st and 2nd MB.
1928	Qualified St Thomas's Hospital.
1928	Married Margaret, daughter of John Beresford Leathes, FRS, Professor of Physiology, The University of Sheffield.
1928–1931	Research Studentship, City Mental Hospital, Cardiff. MD on schizophrenia (single patient).
1931–1939	Research Medical Officer, Royal Eastern Counties Institution, Colchester, sponsored by the Pinsent-Darwin Trust and the Medical Research Council. MRC Colchester Survey.
1939–1945	Director of Psychiatric Research, Ontario. During these years published papers on the evaluation of shock treatment in mental disorder, and relationship of mental health services to the incidence of serious crime.
1945–1965	Galton Professor of Eugenics. 'The Galton' became a world-famous centre and Penrose received many honours and awards. (FRS, 1953).
1949	First edition of *The Biology of Mental Defect*.
1965–1972	Director, Kennedy-Galton Centre, Harperbury. Research continued to the end. Of particular interest was the discovery that the average total ridge count on the fingers progressively decreases with increasing numbers of sex chromosomes, the effect of an additional X chromosome being about three times as marked as that of an additional Y.

The families of both his parents had been Quakers for more than 200 years, and Lionel and his three brothers were brought up strictly according to Quaker principles—no games or reading of fiction on Sundays (the study of natural history and astronomy was allowed). Lionel always remained a member of the Society of Friends, not particularly zealous over attending

Meetings, and no doubt his upbringing profoundly influenced his character. He always hated show and pretentiousness of any kind, and he had an extremely pacifist outlook, but not where scientific matters were concerned.

The courtship of Lionel's father and mother was amusing. The young artist had sat for a long time regularly behind the Misses Peckover at Meeting and wondered how to get to know them. Finally he plucked up courage and wrote a letter to the most beautiful of them, Elizabeth Josephine, asking if he might call on her. The young lady dutifully showed the letter to the aunt in charge of her, who replied 'Let thy conscience be thy guide'. So what I think most scientists would regard as an unmeasurable character was responsible for Lionel seeing the light of day.

A word about Lionel and his brothers. Alec, the eldest, was an East Anglian landowner known as 'Squire Penrose'; Lionel was number two; Sir Roland Penrose, very well known as a collector of paintings and friend of artists, was the third, 'Painter Penrose'. The fourth, Bernard, who went before the mast, was 'Sailor Penrose'. Lionel was always referred to by Alec as 'respectable Penrose', but I think that this was more an index of Alec's way of life than of Lionel's orthodoxy. Others referred to Lionel as 'Loony Penrose' but much more suitable would have been 'Genius Penrose'.

Lionel went to Leighton Park School as a scholar, and while there he was put in charge of the newly-built observatory where he calibrated the telescope. Among his contemporaries in the school were T. F. Fox and R. W. B. Ellis, an indication of the intellectual strength of the Friends.

After leaving school, Lionel served in the Friends' Ambulance Train of the British Red Cross in France and was only demobilised after the end of the war in 1918. Life on an ambulance train is described by quoting from verses about it from a book compiled by the workers on the train.

AMBULANCE TRAINS

. . .
You're the trains. What remains
Of the best of British brains
Is collected on the good old A.T.S.*
Though the churches may deplore you,
And the *Daily Mail* ignore you,
You're the Army's one unqualified success.

Though you're spared the front line trenches where the whizz-bangs never stop,

* A.T.S.—Ambulance Train Service.

And you never have to 'stand to' or go across the top,
What with Frenchmen on the engines, and the Gothas on the hop,
You have your share of dangers all the same.

(From *Ambulance Train No. 5 in the Great War.*)

While in the Unit he showed his artistic ability and manual skill by making woodcuts showing scenes of the countryside (Fig. 1).

After the war, Cambridge, studies abroad, qualification, marriage, and research at Cardiff, came his first important post, that of Research Medical Officer at Colchester. There he carried out a most important and detailed study of a large series of all types of mentally defective patients. At that time little was known about mental deficiency and its causes, as the following story of Penrose's will show.

A member of the Royal family was scheduled to open a new wing at Colchester, but it was stipulated by the civil servants who made the arrangements that the Royal Duke who was to perform this office was not to see any of the patients. The reason given for this precaution was that the Duchess was pregnant and imprinting was feared. However, a way round was found, and the Duke was greeted by a proud guard of honour composed of patients who all belonged to the hospital troops of Boy Scouts and Girl Guides. It had been possible to persuade the authorities that any pre-natal impressions of imbecility that the Duchess might receive would be innocuous from such paramilitary sources.

In his survey, Penrose set about doing something that was then quite new, collecting accurate information about the patients and their families—parental age, birth order, stillbirths, incidence of other abnormalities, defects among relatives and IQ—and analysing them statistically. When he graded the patients in terms of their mental ability, he found that the four groups into which he divided them did not altogether match the legal gradings in which the patients had been certified. Some had been classified as feeble-minded simply because of anti-social or difficult behaviour. He also found that there were many more defective mothers than fathers but discounted this as a genetic finding because mental defect in a mother (rather than in a father) was frequently decisive in persuading a local council to take action to certify.

In these days, when time off is so important, it is salutary to realise the enormous amount of work involved in the survey. Penrose and a very small team investigated no fewer than 1,280 patients, and these had 6,629 sibs, quite apart from other relatives, and the ascertainment was remarkably complete. In 920 of the 1,280 propositi they were able to get complete data.

Fig. 1. 'Aubremetz'—a woodcut by Lionel Penrose, 1918. (From *No. 5 Ambulance Train in the Great War.*)

The major general conclusions that came out of this Colchester Survey are now accepted and seem obvious, but they were important new contributions then. The most relevant were the absence of any sharp dividing line between

mental deficiency and the so-called normal state, the evident heterogeneity of mental defect, and the multiplicity of causes, both genetic and environmental, that could be involved in its causation. Furthermore, there was a sevenfold increase in the incidence of mental defect among the parents and sibs of patients compared with the general population.

It was while Penrose was at Colchester that Fölling discovered that certain patients with a severe degree of mental defect continuously excreted large amounts of phenylpyruvic acid in their urine. Penrose immediately appreciated the importance of this, and his family studies suggested that the condition was inherited as an autosomal recessive. He set to work trying to find a diet without phenylalanine that was nourishing enough to keep the patient alive. He consulted Gowland Hopkins, who estimated that it would cost £1,000 to feed one patient for a week, so the matter was put on one side.

Penrose's work on epiloia at this time was a pioneer effort to clear up the mystery of this very variable disease which yet appeared to be determined by a single abnormal or mutant gene. He postulated a common, non-allelic modifying gene which might or might not be inherited with the major gene. This study of epiloia also led to one of the earliest methods of calculating the mutation rate in man.

Following Colchester, he held an important post in Canada and in 1945 was appointed Galton Professor of Eugenics at University College, London. During the whole of his time there he had a paramount interest in mongolism, and his advances merit more detailed discussion.

Penrose first showed the importance of maternal age and maternal age only. Until the 1930s it had been thought that paternal age and birth rank might also be aetiological factors, but Penrose showed that these were simply concomitants of being an older mother, and not causal.

This answer, which we all know now and which sounds obvious, involved a great deal of complex mathematical calculation. Another current belief then was that there was a long gap, i.e. a period of diminished fecundity, between the mongol and the preceding birth, but Penrose showed that the interval was not significantly different from that between the birth of the mongol and the next child.

Penrose also showed that, although mongolism was usually sporadic, occasionally it was familial, and this was long before the chromosomal discoveries in mongolism. In 1951 he published a paper in the *Journal of Mental Science* called 'Maternal age and Familial Mongolism', and the most important finding was that the maternal ages in cases of familial mongolism were on average significantly lower than in cases of mongolism taken as a whole and that the effect was particularly striking where the inheritance of the condition

was through the mother. Lionel is particularly well known for his studies on mongolism and palm prints. It had been known for a long time that there were abnormalities in the ridges, but what Penrose did was to quantify a particular aspect which he called the *atd* angle (Fig. 2). Using an *atd* angle of

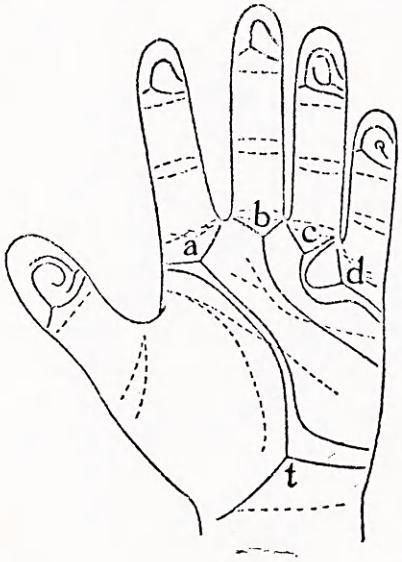

Fig. 2. Left hand of normal adult male showing the *atd* points (Penrose, 1972). (Courtesy Sidgwick & Jackson, London.)

57° as a point of discrimination, he found that about 80 per cent of mongols had values greater than this, compared to about 8·5 per cent of the controls. Among the relatives of mongols, just over 13 per cent had angles greater than 57°, which was significantly different from the controls.

After the chromosomal discoveries were made on the subject of mongolism, all Penrose's findings were explained. The maternal-age-dependent mongols were trisomic for chromosome 21, the familial ones were due to a translocation of 21 on to another chromosome, and the increase in the *atd* angle in relatives was due to mosaicism, some of the somatic cells containing the normal 46 chromosomes and some 47.

This is a sketch of the basic work but there is a lot more to it now, particularly the fact that cases of mongolism in which elevated maternal age appeared not to have been of aetiological significance form a heterogeneous group.

At the time of the first chromosome discoveries, Penrose and his colleagues found a case of mongolism and Klinefelter's syndrome in the same patient, who had a chromosome complement of XXY, trisomy 21.

Penrose's writings were usually very restrained but he occasionally let himself go and in his book, *Mental Defect*, he thought 'foetalism' was a better

name than 'mongolism' for these retarded individuals. 'The peculiar temperament of the affected persons, their secret source of joy, may be akin to the sort of happiness which the foetus might be supposed to experience in its blissful intrauterine surroundings.'

Mental Defect was the forerunner of *The Biology of Mental Defect*, published in 1949 and reaching a fourth edition in 1972. It is an extraordinarily interesting volume, which I can strongly recommend. I have not space to say anything about it in detail except to quote two extracts from prefaces to it by J. B. S. Haldane. They are typically J.B.S.

> 'I have only one warning to readers of the book. Penrose has the habit of presenting views, which he does not share, with scrupulous fairness. It is thus often necessary to read his book with care in order to discover what he thinks himself. In my opinion this is worth doing.'

And again

> 'In Sir Thomas More's *Utopia* no one who did not love fools and treat them well was allowed the privilege of keeping one in his house. Professor Penrose genuinely loves fools. When I presented him with certain calculations he accepted them with every mark of interest and pleasure. Soon afterwards I saw him examining the drawings of a defective, and expressing the same emotions. He was right. It is perhaps more remarkable that a boy who can hardly speak should be capable of excellent drawing than that one professor should be capable of helping another to analyse his data.'

In his Galton period Penrose was particularly interested in the supposed decline in intelligence in the population, because it was known that the more intelligent people are, the less fertile they tend to be. It seems self-evident therefore that if people of above normal intelligence have fewer children than those of under-average intelligence, the average intelligence of the population must decline, and eugenic measures should be applied to counteract it. Lionel, however, was sceptical of this view and showed, by means of an admittedly over-simplified model, that it is quite possible for the general intelligence of the population to remain unaltered in this situation. He suggested a pair of alleles, those individuals homozygous for which (AA), had slightly lowered fertility but normal intelligence. The heterozygotes Aa are of lower intelligence, but high fertility, whereas aa people are idiots, and are always infertile. There is completely assortative mating. In this model the IQ remains unaltered, because Aa mated to Aa will produce one highly

intelligent child, two like themselves and one idiot, and the last does not contribute at all to the next generation. The situation is, of course, much more complicated than this in practice, and Penrose elaborates the hypothesis using many genes, but the principle remains the same.

Where many genes are involved, it is known that the IQ of children of parents both of whom are above normal intelligence tends to be nearer the population mean and, conversely, that of children of lower than average parents tends to rise towards the mean. However, geniuses evidently form an exception, for Lionel and Margaret, though both unusually intelligent, not only had four children, but Oliver is Professor of Mathematics at the Open University, Roger is Rouse Ball Professor of Mathematics at Oxford and also an FRS, Jonathan is an international chess master, and Shirley a paediatrician. Another interesting pedigree, also of a genius (and again against all the rules) is that of Charles Darwin. He married his first cousin, had numerous offspring who lived happily ever after and, from both the Darwin and Penrose pedigrees, Fellowship of the Royal Society looks like a Y-linked trait.

Mention of Y-linkage brings me to a story that typifies Lionel's suspicion of showiness. The Porcupine Man (Fig. 3), Edward Lambert, was the example of Y-linkage in *Homo sapiens*, and the pedigree was copied from book to book without question. The dénouement came in 1956 when Curt Stern was spending a short sabbatical at the Galton Laboratory and was preparing a new edition of his textbook. Penrose had always doubted the validity of Edward and he expressed his doubts to Stern, so they decided to investigate the matter, Stern searching the early literature while Lionel went into the original parish records in Suffolk, where the critical members of the family had lived more than 150 years earlier. The results were that some of those children of Edward were found to be girls, and that John and Richard had not only had seven unaffected sisters, but four unaffected brothers. Furthermore, it was shown that the last two generations of the pedigree were fabrications. Mrs Penrose remembered this very well because she helped in the search of the registers, and at the end of it Penrose made a characteristically dry remark. 'Until now it was thought that outstanding problems of human heredity could be adequately investigated without moving from an armchair. This method is now believed to be inefficient.'

I saw quite a lot of Lionel in the later part of his Galton period, but I shall never forget the first time I actually met him, in 1952 or 1953. I had given an elementary butterfly genetics talk at the Royal Entomological Society, and afterwards Hans Kalmus, who was present, asked me to give a seminar at the Galton. I expected to talk about the work in a light-hearted way to some

New SPECIES of MAN.

Among the Wonders of Nature, which have from time to time tempted the Curiosity of the Public, perhaps no object more worthy of attention has been offered to their notice, than a Singular Variety of the Human Species, now exhibiting at the ***Great Room, 182, Fleet Street,*** near St. Dunstan's Church. This Young Man is 30 years of age, *covered with Scales*, with the exception of the face, soles of the feet, and palms of the hand, which are like those of any other man. These Scales, nearly half an inch long, are so hard and firm, that with a touch of the finger they make a sound like stones striking together; those on the stomach are short, round, and distant; those on the arms, on the contrary, approach each other like the bristles of an hedge-hog. The great grandfather of the singular family to which this young man belongs, was found savage in the woods of North America. The peculiarity descends only in the male line. (*For a description of this Species see the Works of Buffon.*)

Physicians and Natural Philosophers will find an extensive field opened to their enquiries, and every arrangement is made with regard to Dress to aid their researches, without violating Decency.

ADMISSION, One Shilling each person. Doors open from 9 o'Clock in the Morning till 8 o'clock in the Evening.

Fig. 3. Handbill advertising the showing of the 'Porcupine Man' at 182 Fleet Street, London, in 1820 (courtesy Royal College of Surgeons of England).

students, but was paralysed to find sitting in the front row Fisher, Haldane, and Penrose.

No account of Penrose's scientific work would be complete without some mention of the extraordinary series of wooden self-replicating machines that he made. The purpose behind these models was to try to find some very simple self-reproducing mechanism by which the most primitive forms of life that evolved on earth could have arisen. The first models consisted of wooden pieces of two types which, if initially separated, would remain so when shaken at random on a track. However, if a correctly joined pair of pieces was inserted among them in the track, the random shaking would cause other pairs also to be assembled in the same way as the first. The first pair could also be assembled in an alternative arrangement, and then the shaking would cause other pairs to link together in the new way. Later, by designing more complicated pieces, Penrose was able to extend the number of alternative configurations that would self-replicate. He even built pieces that could form chains of arbitrary length in one dimension and with a width of two or four pieces in another. Pieces could be added to the sides of these chains until the width was doubled. Then the whole chain would split down the middle and two chains, each identical with the original one, would result.

It would not be hard to argue that the analogies between chemical bonds and wooden ratchets are totally superficial, but the demonstration that certain assemblages of shapes can be made to reproduce themselves is of serious interest and could, if followed up, provide a totally new approach to the problem of self-replication.

David Garnett, in Lionel's obituary in *The Times*, said he thought that the prime motive of his mind was intellectual amusement and that the reason he was such an original scientist was because he had an instinct for playing with ideas, as a kitten plays with cotton reels. An example of his versatility was his book, *The Objective Study of Crowd Behaviour*. In these days of endless meetings this well repays study, for it shows how it only needs a few resolute people to carry a motion (though this assumes random voting in the rest). Put formally, it is that if there are, say, 25 people on a committee and the square root of this (i.e. 5) forms the resolute bloc, in 100 divisions for voting the resolute bloc will win 84·1 times.

He used this argument when he was writing about power politics for the Medical Society for the Prevention of War, which he, with others, had founded. He first regarded war as a wasteful and damaging form of human activity and believed that it presented an analogy with disease, and could be dealt with scientifically. Later, however, he came to realise that whereas the removal of disease requires no substitution, the abolition of war does, in order

to fulfil some profound impulse in the human race. Sport is an obvious sublimation, and chess, at which he excelled, is a good intellectual substitute.

In 1951 Penrose had written on the function of science as a bridge between East and West. It is sad to think that in 1973 the bridge still appears to be somewhat shaky. But, as Penrose says: 'Scientists are tenacious people: their bridge, though narrow and obscured by fog, is still there and it will hold'.

One of Penrose's other non-genetic interests was membership of the Shakespearean Authorship Society. He was anti-Shakespeare and probably favoured the Earl of Oxford, one of the reasons for this being that by testing the lengths of the words used in the plays against those of other writers he thought the Earl of Oxford fitted best. Penrose probably agreed with Freud that only someone who had been through the psychological trials of Hamlet could have written the play, and the Earl of Oxford had been through them. The chief anti-Shakespeare argument, however, lies in the wide culture and knowledge of the world that is shown in the plays and which an impecunious player from Stratford could not have possessed. The fact that the authorship had to be concealed was at that period a quite natural phenomenon; noblemen did not publish, and to voice opinions could be dangerous.

An interesting sidelight is Penrose's paper on Shakespeare's knowledge of medicine. Most authorities attribute this to his relative-in-law, Dr John Hall, but Hall seems to have been an ignorant fellow; it is doubtful if he was even an apothecary and he was certainly not a Fellow of the Royal College of Physicians. As evidence of his incompetence, he diagnosed his wife's illness as 'scurvy accompanied with pain of the loins, corruption of the gums, stinking breath, melancholy, wind, cardiac Passion, binding of the Belly'. If the author of the plays had little to learn from Hall and was not influenced by him, from whom did he derive his knowledge and his medical attitude? The answer may be 'from the nobility'. For example, the Earl of Derby was famous for 'chirurgie, bone setting and hospitalitie', the Marquis of Dorchester, whose library the College possesses, became a Fellow of the Royal College of Physicians, and Lord Lumley (who founded the Lumleian lecture) possessed a large library of medical works. The Earl of Oxford was a relative of Lord Lumley, and could have used this library. Also, Lumley is thought to have written that 'Among noble gentlemen who have written excellently well, but whose doings have not been made public, the Earl of Oxford is the first'.

EPILOGUE

In 1968 the Penroses gave their usual hospitality to many refugees from Czechoslovakia. One was a child called Anita Lax, who later, when she was 15 years old, was asked to write a school essay on 'An interesting character'.

She wrote:

'He was an old Professor of genetics (human genetics) but he may just as well have been a professor of almost anything under the sun, beginning with music, mathematics, chess, art and ending with woodwork. He used to invent ingenious puzzles for his innumerable grandchildren and then he would make them from wood in his little workshop, always considering carefully the ages of "all these little boys", which, as he said laughingly, changed every year and you had to be careful to keep track of them!

'He lived in a tremendously large, old and extremely cold house, the number of rooms of which he never could remember. His equally absent-minded and exceptionally kind wife would continuously have several foreign students and other visitors staying (simply because "they had nowhere else to go") but neither she nor the professor were ever quite sure who they were or whether they hadn't already left.

'One of the rooms, however, was the professor's study, where, among the pictures, self-reproducing machines, puzzles and books, many of which he had written himself, there was a small, 18th century spinnett on which he loved to play. While you were listening, he would give you one of his ingenious puzzles "to keep you amused". If you managed to solve it (and what he never realised in his charming modesty was, that not everyone was endowed by a mind as great as his), his blue, deep-set eyes would twinkle behind his spectacles, and he would run off to bring you a new, slightly more difficult one, laughing in his very characteristic way. He found everything amusing, even the most difficult (or possibly particularly the most difficult) mathematical or scientific problem.

'During their free weekends—and there were not many of these, because they were always organising doctors' meetings for the prevention of war, if not chess matches or amateur orchestras—he and his wife would go to Thorrington where they had a beautiful old sixteenth century home. On the way they would probably spend two hours on the road repairing the almost also sixteenth century car which very rarely reached any place without breaking down. (There was never any time to buy a new one—too many more useful things to do.)

'Once at Thorrington, the professor would settle down among the trees of the mysterious and beautiful old garden (he was always amused by the one with the roots growing upwards), equipped with crayons and sketching pad and would draw the most detailed and meticulous sketch of a plant or landscape. He always saw more in everything than everybody else did—by simply observing. His power of observation was one of his

most prominent characteristics—whether it applied to his patients, colleagues or the kite he happened to be flying with the children.

'Then he would sit on a bench, in the same old brown-grey worn little jacket which he always seemed to be wearing, wherever he was, in his black down-at-the-heel shoes, pull out a little notebook with a coloured cover, and start calculating and proving a recent mathematical law or working out a chess problem, or even inventing new games and "machines" for his mongol patients of whom he was so fond.'

How right Anita was, and what a perfect summing up. This is how many of us, as well as Anita, remember Lionel and it seems appropriate to leave him here.

Fig. 4. Lionel Penrose (courtesy Professor A. G. Bearn).

Acknowledgements

I am deeply grateful to Professor Harry Harris, FRS, for allowing me to draw freely from his biographical memoir of Penrose for the Royal Society. This was published in November 1973 and was reprinted in the March 1974 issue of the *Journal of Medical Genetics*. The review is most valuable and contains much detailed information about Penrose's work as well as giving the references to all his scientific papers arranged in years from 1925 to 1973.

I am also much indebted to Mrs Penrose for giving me many most interesting anecdotes and for the loan of relevant books, photograph, and films.

I am also very grateful to Dr D. A. Pyke for the Leighton Park School information and to Professor A. G. Bearn for Fig. 4.

This article is based on the Penrose Memorial Lecture delivered at the joint meeting of the Royal College of Physicians and the Clinical Genetics Society in Liverpool in November 1973.

References

No. 5 Ambulance Train in the Great War. Selections from *La Vie Sanitaire*. August 1916—February 1919. Blackburn: Geo. Toulmin & Sons Ltd.

Harris, H. (1973) *Biographical Memoirs of Fellows of the Royal Society*, Vol. **19**, p. 521.

Harris H. (1974) *Journal of Medical Genetics*, **11**, 1.

Penrose, L. S. (1933) *Mental Defect*. London: Sidgwick and Jackson.

Penrose, L. S. (1938) *A Clinical and Genetic Study of 1280 Cases of Mental Defect*. MRC Special Report Series, No. 229. London: HMSO.

Penrose, L. S. (1949) *The Biology of Mental Defect*. London: Sidgwick & Jackson.

Penrose, L. S. (1951) *Journal of Mental Science*, **95**, 685.

Penrose, L. S. (1952) *The Objective Study of Crowd Behaviour*. London: H. K. Lewis.

Stern, C. (1960) *Principles of Human Genetics*, 2nd edn. San Francisco: Freeman.