

Collated  
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## **Leonardo Tondo: Interviews with Pioneers**

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This collated document is comprised of "Leonardo Tondo: Interviews with Pioneers," beginning with a posting on Oct. 29, 2015, to explain the project, followed by two interviews and an exchange between Malcolm Lader and Tondo about the Michael Shepherd interview.

This collated document is now open to all INHN members for final comment.

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## **Leonardo Tondo: Interviews with Pioneers**

To set a foundation for education in the history of neuropsychopharmacology, it was suggested to generate firsthand information from the pioneering generation of psychopharmacologists about their research in the form of interviews. The suggestion was adopted by INHN (Ban 2015) and this posting signals the launching of our program, in which a series of interviews conducted and audio taped by me in the late 1980s and early 1990s will be presented (posted) and discussed. The presentations will not be restricted to the transcript of the edited interview but each posting will include also a biographic sketch, information about the interview, notable comments, endnotes and acknowledgments as well as a photo of the interviewee.

The program will be implemented in three steps. It will start with the posting of edited interviews and discussions of each interview after posting. This will be followed in the second step by

rendering the posted interviews accessible first as a collated document, then as an E-Book and ultimately in print. Finally, in the third step, the information contained in the interviews will be rendered accessible for integration with the information in INHN's other projects. For this, the words/concepts that qualify for entry in Dictionary in the form of a vignette will be identified; the people who qualify for Photo History, Profiles and/or Biographies listed; and the topics which warrant an essay in Controversies or in Historical Perspective, briefly discussed.

October 29, 2015

### **Leonardo Tondo: Introduction**

With this presentation, I am initiating the publication of a series of interviews with outstanding psychiatrists collected mainly between 1987 and 1992, with the unifying theme of their interests and contribution to the topic of clinical depression. Of all potential interviewees, all but one consented to participate and authorized publication of the edited interviews.

In the intervening years, Dr. David Healy published a series of books based on his taped interviews of well-known psychopharmacologists (Healy1996, 1999a,b, 2000, 2002). This work provided additional stimulus to prepare my interview material for publication. Moreover, research collaborator, Prof. Ross J. Baldessarini of Harvard Medical School and McLean Hospital in Boston, has encouraged me to publish the project deeming the material of considerable value, particularly since most of the participants were becoming elderly at the time of the interviews, and many are now deceased. He also provided valuable assistance in editing the final manuscripts.

The first three interviews have been published and will be revised to be included in this program (Tondo 2011a,b, 2012a,b).

The series begins with Sir Martin Roth, with whom I have spent several hours having lunch together and during a lift to Pisa Airport on a sunny and chilly day in January 1992. His wife, Ms. Constance Heller, was also with us for the entire interview. The main theme of this interview was about Roth's support of a differentiation between depressive disorders and neurotic disorders in opposition to unitarian approaches by Adolf Meyer and Aubrey Lewis. From this starting point, the interview dealt with the identification of some anxiety disorders, namely agoraphobia and panic disorder, and their differential diagnosis from atypical depression. During the interview, Professor

Roth expresses his not so favourable views on the taxonomy of DSM-III and on the future of psychiatry.

### *Acknowledgement*

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November 5, 2015

## **Leonardo Tondo: Sir Martin Roth On the Differentiation of Depressive and Anxiety Disorders**

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### *Biographic sketch*

Sir Martin Roth (1917-2006), the son of a synagogue cantor, moved from Budapest to East End of London to escape anti-Semitism in Hungary. During his student years, he acquired a lasting love of literature and music, and rowing. As an adolescent, he contracted a serious illness and thought his life might be relatively short. This experience may have fueled his ambition. He married Constance Heller in 1945 and had three daughters.<sup>i</sup>

He became interested in neurology and psychiatry. Following training in neurology, starting in 1943 with Lord Russell Brain<sup>ii</sup> at Maida Vale Hospital, his interests shifted toward geriatric neuropsychiatry after training in psychiatry at the Institute of Psychiatry–Maudsley Hospital from 1945. There, he worked with Sir Aubrey Lewis<sup>iii</sup>, the first professor of Psychiatry there, and especially closely with his colleague and friend Eliot Slater,<sup>iv</sup> a pioneer in psychiatric genetics. Roth then moved to the Crichton Royal psychiatric hospital in Scotland to work with Wilhelm (“Willy”) Meyer-Gross<sup>v</sup>, who had moved from Germany in the 1930s from a professorship at the University of Heidelberg.

Roth became professor of psychological medicine at Newcastle (1956–1977) and later held the first chair in a new department of psychiatry at Cambridge University (1976). From the 1960s he studied disorders found in elderly patients who had been diagnosed with senile dementia. Instead, Roth found that many were suffering from mood disorders and, therefore, were more likely to respond to treatment. In Newcastle, he collaborated with neuropathologist Sir Bernard Tomlinson (1920–) and psychiatrist Robert Kendell,

<sup>vi</sup> later professor of psychiatry in Edinburgh. This pioneering work was a founding contribution to the new specialty of geriatric psychiatry.

In addition to improving the treatment of elderly neuropsychiatric patients, he led development of a seminal diagnostic instrument, the *Camdex (Cambridge Mental Disorders of the Elderly Examination)*, first published in 1986.<sup>vii</sup> With Mayer-Gross and Eliot Slater, he wrote the influential textbook *Clinical Psychiatry* (1954–1977),<sup>viii</sup> co-edited the five-volume *Handbook of Anxiety*<sup>ix</sup>, and served on the editorial board of the *British Journal of Psychiatry* for 40 years. Although critical of the

DSM-III (appeared in 1980), Roth was not against standardized diagnostic criteria, but he did not consider them a substitute for careful clinical interviews that included empathic exploration of a person's mental life.

In 1971, Roth was elected president of the Royal College of Psychiatrists. He was awarded the Anna Monica Prize (1977), the Gold Medal of the Society for Biological Psychiatry (1981), the Sandoz Prize of the International Association of Gerontology (1985), the Kraepelin Gold Medal of the Max Planck Institute (1986), and the Camillo Golgi Medal (1995), in addition to receiving honorary doctorates from universities in UK and US.<sup>x</sup> For his achievements in psychiatry, especially in the field of geriatric psychiatry, Roth became one of only three psychiatrists to be elected Fellow of the Royal Society in modern times. The others were Sigmund Freud (1856–1939) in 1936, and Michael Rutter (1933–) in 1987.<sup>xi</sup>

#### *About the Interview*

The interview was conducted on January 24, 1990, in Pisa, Italy I met Martin Roth during a meeting on anxiety and affective disorders in Pisa in 1990. He was a witty gentleman and seemed pleased to give the following interview, which became much longer than expected. We recorded it during lunch and afterwards when I drove him and his very caring wife, Constance Heller, to the Pisa airport.

#### *The interview*

LT (Leonardo Tondo): You have been interested in the classification of affective disorders; how important would you consider this topic?

MR (Martin Roth): Yes, I think it's fundamental.

LT: Has it been fundamental only since the early steps of psychiatric classification, at the times of the first ICD or DSM?

MR: No, it goes back before that, I think it goes back to the time when I first came into contact with

Lewis' unitary concept which was really influential in psychiatry. Lewis incorporated within the affective disorders, endogenous depression, neurotic depression and all forms of anxiety disorder and neurasthenia. So there was agitated depression and neurasthenia, then was endogenous depression and reactive depression. I cannot remember the precise titles he gave them but, in fact, it encompassed anxiety disorders for which he had no respect whatsoever and regarded those as nonexistent. The concept of all disturbances, mood and affect, as unitary and very common had a very wide influence in psychiatry. Early on, from my training at the Maudsley,<sup>xii</sup> I was aware of the scientifically unprofitable nature of this concept and I was aware of Kraepelin's<sup>xiii</sup> view that this was a fundamental misconception. In [the] Kraepelinian system there was a fundamental line of demarcation between what he regarded as illnesses, psychoses— manic-depressive and schizophrenic. Endogenous and psychotic depressions were allied and, for [Kraepelin], were an illness. When it came to neuroses and psychopathies, for him, these were not illnesses at all. They were outside the scope of illness and this went deep in German psychiatry. Needless to say, that I do not agree with that: when you get outside psychosis you are dealing with problems in ordinary living. Schneider<sup>xiv</sup> put this in a letter to an American psychiatrist in 1950, that in the neuroses and psychopathies we do not deal with illnesses but rather with variants of normal living, variants of normal life-adaptation. Neuroses do not require treatment [but rather] psychotherapy. So, in clinical practice it has been clear since the early stages of my psychiatric work that, first of all, endogenous and psychotic depressions were clearly defined categories in which one was dealing with conditions likely to be biologically determined. I was influenced at this time by Slater's work on the heredity of manic-depressive disorders.<sup>xv</sup> From my earliest days at Maudsley, depressions that were non endogenous were dealt with something differently [and] were [considered to be] very closely related to the personality of the individual. Nonetheless, some phenomena were superimposed upon the abnormal adaptation patterns and characteristic forms of the primordial personality. I did not share the view of German psychiatry that psychopathy encompassed both neurosis and personality disorder and that they were all life-long phenomena. I could see that there were breaks in continuity of the adaptation of people with personality problems. I am talking here as if the reactive component was unimportant and I think this is how I viewed precipitating factors as making the condition understandable but not necessarily important. Anyway,

the point is that I adopted the Kraepelinian position with regard to the separateness of endogenous and psychotic depression from neurotic depressions. That was one Kraepelinian proposition. The second was that when we get outside the realm of psychosis we do not deal with illness but with a vague phenomenon that merges with the problems of daily living—problems that all people have, and which neurotic individuals have a little more and indeed, within the circumstances, are something that is not accepted [as illness]. My research activities in this sphere began in Newcastle. While I took this problem with me from the Maudsley, where I finished my training, I listened to the teaching of Lewis in Birmingham: affective disorders were allowed no modification. If we look at what he described as affective disorders we find an enormous territory in psychotic depression. In the meantime, I had become interested in the anxiety conditions, anxiety and phobic states. During the course of my work I had observed anxiety disorders in which phobic symptoms and depersonalization were very prominent. I must be brief, I think; otherwise it will take a whole day. To cut a long story short, we embarked on this subject by the time I arrived in Newcastle in 1956. I was concentrated then on the anxiety states and particularly on phobic and depersonalization states.

LT: Depersonalization seems to be an area of your specific interest.<sup>xvi</sup>

MR: Yes, [but] I never found the time to publish a lot of our material [on this subject]. I was describing agoraphobia but I did not describe what Westphal had described.<sup>xvii</sup> This is why I gave it another name because Westphal described men who were afraid of open spaces and were so terrified and panic stricken that they would pick strangers from the street, even prostitutes, to accompany them home. Our phobics were women almost entirely. They were not afraid of open spaces; they were afraid of leaving home, even a few yards from home [and became] overwhelmed with terror when they were at a short distance from home. They were afraid of all sorts of situations: going into shops, shopping by themselves, entering queues. If they drove and were stuck at traffic lights, they became panic stricken as well as walking in the street with crowds around. Terror was not of open spaces; the other thing was that it was not just a cross-sectional phenomenon of people who were afraid of open spaces. We were dealing with a complex life historical phenomenon. Phobia [and] depersonalization occurred at a certain specified time of stress but these individuals were not absolutely normal before they got there.

Their introversion and anxiety progressed from there and many other neurotic traits bore some resemblance to the neurotic symptoms that followed. The neurotic symptoms were a character to certain respects of what had been there before. In certain respects the neuroses presented new features that [could be] lumped with depersonalization. They were novel features, so there was a real line of division between the agitation that preceded the disability that kept them housebound for years or decades. If you look at [our] paper<sup>xviii</sup> [on that topic] you will find that I define it as pan-neurosis because these people were neurotic in so many different directions, they were also sometimes under possession of something, histrionic, and hysterical sometimes. So I was once again [left] with the problem of depression and anxiety.

Within a few years, I did publish [on this topic as] my partial entry into anxiety states.<sup>xix</sup> I was absolutely aware then of the problem of anxiety and depression and how they related to each other and how they separated from each other. Through the phobic anxiety syndrome I was aware that this problem was fundamentally important. Darwin<sup>xx</sup> made the statement of two separate emotions: anxiety and depression, [which was accepted by] everybody who had been educated with me and not under the influence of Lewis. Lewis regarded anxiety states, even obsessional states, and endogenous depression as one condition.

I have left out my work at the Crichton General [Hospital],<sup>xxi</sup> where, as I mentioned, I was under the influence of Mayer-Gross. I became very closely familiar with the Kraepelinian view of things and with German psychiatry. My perception of the psychotic-endogenous disorders as separate from the neurotic ones was deepened when I worked in Scotland for about three years. Then I left Crichton General [Hospital] for Greylingwell [Hospital]<sup>xxii</sup> in 1950 and I brought the concept with me. There I was occupied with the problems of old age. I continued my interest in anxiety disorders which culminated in the 1959 publication, but by that year we had antidepressant drugs. In the Crichton Royal [Hospital] in Newcastle we were soon embarking upon clinical trials of imipramine. They were largely undertaken in my department there but Lesley Kiloh,<sup>xxiii</sup> later professor in New South Wales, Australia, conducted a number of trials. I gave him very strong encouragement and was an author of one or two papers with him. The first trial,<sup>xxiv</sup> one of the earliest trials was undertaken with him. [It]



showed unequivocally that imipramine [Tofranil™], discovered in 1957 by Kuhn and collaborators,<sup>xxv</sup> was an effective substance and active antidepressant. It was significantly more effective in endogenous depression than in neurotic depression but was effective also in neurotic depressions. This was surprising and made it clear one was dealing not just with some problem of living. As you know, if you give imipramine to an ordinary subject he feels awful. If you give it to severely neurotic depressives, they may achieve considerable improvement, and this was very important. Now Kiloh, Ball and Garside<sup>xxvi</sup> [1962] in their early studies used multivarious statistical methods and I was already involved in using these methods for purposes of classification.<sup>xxvii</sup> They did a factor analysis to try to differentiate between response patterns of endogenous and neurotic depression and also looked into their classification. Incidentally if I can bring here a point, Kiloh and Garside later were to make an historically very important analysis of Lewis' original observations in his M.D. thesis in the University of Adelaide.<sup>xxviii</sup>

They took what Lewis described in his cases in enormous detail and were able to do a principle component analysis on Lewis' clinical observations. They showed that on Lewis's own observations, endogenous depression [was] sharply distinct from non endogenous depression. [After] this [finding] was sent to Lewis, it was published in the Australian Journal of Psychiatry.<sup>xxix</sup> [Lewis] responded by saying that multivariate statistic was an inappropriate method for studying patients; it was irrelevant and invalid to do it. Some statistical authorities have taken this view but the great majority have said [that Lewis' point] was quite incorrect. In fact, you should use these methods to separate [clinical groups]; everybody believed [that] you must *ipso facto* justify using them for classifying patients. In these analyses, you extract factors that summarize the distribution of variation within the pattern. When you plot factors, you plot along the axes; usually your first plot gives scores to each symptom, [which] may be very high or very low. When you use it to classify patients, [you] merely to add up the scores obtained with the symptoms and you plot that.

LT: I read that study.<sup>xxx</sup>

MR: Yes, I think that was one of the most conclusive pieces of evidence [in the] paper published in the early 1960s. Later on we published a number of multivariate statistical studies. In 1965, Carney,

Garside, and I published a study of the birth of classification of depression and the prediction of treatment response in the *British Journal of Psychiatry*.<sup>xxxii</sup> Briefly, it proved with multivariate techniques that it is possible to get a bimodal solution, to get clear separation, that's all. And this was a special group of patients who had been selected for treatment with ECT, but they included both neurotic depressions and endogenous depressions so it was possible to investigate their differential response. [If] the concept of unitary psychosis were valid, there [should be] evidence that schizophrenia, manic-depressive disorders, [and] paranoid psychosis, were all one and the same. [If] we had unitary neurosis, people would say that psychosis and neurosis are useless terms, [and] unitary psychosis and neurosis [would] become one term. At the neurotic end there would be what all [of] German psychiatry says and also what Kendell says: that there is no distinction, no clear demarcation between neurotic phenomena and normal. So psychiatry is confronted with one enormous continuum [in] thinking of everything. [However,] this is a sterile concept because in these continua it is not clear what you are measuring. What are you to measure? How do you measure it? How do you devise a dimension to measure? What is it that you are measuring? What do you do with your measure? How do you advance the knowledge of treatment with these unitary concepts. We are back with Griesinger<sup>xxxiii</sup> with this concept: one disease of the brain. This is, I think, the end of clinical psychiatry. I have published, for example, about the relation to mood disorders and affective disorders. Klerman<sup>xxxiiii</sup> has often contributed something to my work; [I would not agree with] everything he says about the development [of psychiatric diagnosis] and the historical changes, but I think it is very interesting and worthwhile to look at.

I must try to be a bit more concise: I was very tired when I first met you, [and should] perhaps accelerate a little, take things more in outline. This issue of endogenous depression and neurotic depression dominated discussions of the classification of affective disorders in the 1960s and in the 1970s when depression was the leading theme in relation to mood disorders. To express an opinion, I believe that great many conditions were called depression and were called so because there were effective treatments for depression, so that individuals with any kind of disturbance of affect or mood received a diagnosis and treatment for depression. We also know that many anxiety disorders and phobic disorders were treated as depression because of so-called "atypical" depression, [about which]

there is quite a literature: Sargant and Dally wrote about it.<sup>xxxiv</sup> Then there was an American group, I think Prien was one of them, though I am not absolutely sure, [who] wrote about atypical depressions [which] were heavily loaded with such features as phobic symptoms, hypochondriacal symptoms, and unreality feelings.<sup>xxxv</sup>

LT: Do you think that the dichotomy between endogenous and neurotic depression became clearer due to the response to treatment?

MR: Well, I think it was. I believe that [our studies],<sup>xxxvi</sup> on the whole, showed that endogenous depressions had a better prognosis and I believe that the evidence showed this, but I suppose it is possible for critics to say that the difference was a quantitative, not a qualitative one. Some people believed it was a matter of severity, [in] that endogenous patients were more severe. [However,] in many cases of neurotic depressions I find [antidepressants to be] effective.<sup>xxxvii</sup> So [differences based on responses to] drug treatment could be viewed as a quantitative difference and not some difference of quality.

LT: If it is a quantitative difference, why did the first trials with imipramine show better response with people in endogenous depression?

MR: The same difference was shown in the studies of Kiloh<sup>xxxviii</sup> and the Newcastle trials. I do not think it is a quantitative difference because a neurotic depression can be very much more severe than an endogenous depression and an endogenous depression can be very quiet. One morning, [a patient] goes out and blows his brains out with a double-barreled shotgun, whereas a neurotic depression maybe very severe and an endogenous depression be quiet [and] not necessarily suicidal, but not by any measure of severity it would be less severe. So it cannot be a matter of severity that the partitions are on quite different grounds. However, that was the issue. We had begun already in the late 1960s to study the demarcation line between anxiety disorders including the phobic states, and depressive states we included the phobic states. By 1970 we published the first paper in relation to the classification of anxiety and depressive disorders in which we used multivariate techniques. We showed that we could separate anxiety disorders and depressive states.<sup>xxxix</sup> Now there were several lines of evidence that the [two types of conditions] were different. First of all the clinical

phenomenology: when examined statistically, the clinical profiles of these patients were distinct and clearly separable. There were criticisms against this sort of separation of anxiety and depressive disorders because it was claimed that it was biased by the fact that we had begun by making the diagnosis, and were not entirely objective about the assessments and subsequent calculations based on analysis of symptomatology. I think that there is something in that view but it is [not] an entirely valid criticism. I do not want to enter into details, but [would] say is that if you start with a certain view that the two disorders are quite distinct and you have gotten a list of symptoms and then you submit the total matrix of symptoms to an analysis with these rather refined statistical techniques, it is quite possible for your view to be entirely refuted because you cannot possibly know in advance what weight, what score the computer will allot each one of 35 items, so the computer may decide that one item is [more] important than another and what you thought was important, virtually is not. So when you do get a bimodal distribution I think it means something. We had to use special techniques to show that there were two syndromes. We knew that such a result was tentative.

There were several other lines of evidence that showed that anxiety symptoms and anxiety disorders were different. I think we were the first people to do a follow-up investigation. Other people have looked at anxiety and depressive symptoms because benzodiazepines have come along in the meantime. [Nevertheless,] in a second line of evidence we showed in independent follow-up study with Kerr, Gurney and Schapira<sup>x1</sup> that at every stage of the three-and-a-half to four-year follow-up investigation, depressions did better than the anxiety neuroses. A third line of evidence, now being contested by the people who talk of unitary neuroses, was that there was very little crossover. In other words, agoraphobic states did not change into depressions and depressions did not change into agoraphobic states. The last line of evidence was that the predictors which we developed [in our] the predictive indices or anxiety states and depressions were quite different from each other. In [such a] study, we included the endogenous with the neurotic depressions. It could be held that the endogenous depressions served to pull the depressions away from the anxiety states. So, we did [another] study in which the endogenous depressions were excluded; that was the investigations I did with Mountjoy.<sup>xii</sup> Very much to my surprise, [we found] that even without the endogenous cases the neurotic depressions proved to be distinct from anxiety disorders. Here I come to the reemergence of the importance of the

personality setting because since drugs have come with the emergence of the era of biological psychiatry, what was falsely called noise tended to be avoided. The view that the patient's symptoms are the disease, [led to] the disappearance of historical-developmental [and] dynamic personality factors [had led] to the impoverishment of psychiatry.

LT: Probably the personality is not really suited for science.

MR: That's right partly, but you see one very distinguished biological psychiatrist, a very intelligent person (I would not mention her name) said that a biological psychiatrist of the future will be very terse in his examination. He will not conduct detailed investigations into life situation, development, interpersonal relationships, relationships with parents, childhood, adolescence, sexual life in the developmental sense. He will ask about sleep, energy, appetite, weight, mood, physical symptoms and sexual function and that will [be] quite enough. I believe that people who believe that are going to be the coffin-bearers of psychiatry who would bear psychiatry into its graveyard [chuckles].

So perhaps I should emphasize here my own attitude to these things. Somebody in a *festschrift* [suggested] that I am repeatedly referred to as a neoKraepelinian, [though] I am not a neoKraepelinian. I accept that clinical subdivision in the psychoses, in organic disorders are great but the whole of the Kraepelinian and the German school, their attitude that neuroses are identical with personality disorders and [that] both have nothing to do with illness [but are] version of normal mental life is totally remote, totally unacceptable to me; not for 35 years has [this view] been a part of my outlook. In fact, I do not think I have ever accepted that view in psychiatry, even in the psychoses. I [also do not accept] the Scandinavian concept of psychogenic psychosis, even psychogenic endogenous depression. Not that I accept that life-event [are] the whole cause. [Instead], I think you are looking at some personality problem. It had never been acceptable to me that the neuroses and personality disorders were outside the realm of psychiatry or could I even accept that even in the psychoses. You could look just at the symptoms [as] the disease, and nothing else in relation to personality method ... I am rambling a bit ... I come back to the question of personality factors. I would like to mention the work of Caetano, [who] worked with me for about five years and published a doctoral thesis in Cambridge.

LT: Who was this person?

MR: Caetano Dorjival, a Brazilian student who did a very fine study of all kinds of depression versus anxiety.<sup>xlii</sup> The important point [is that] he used the *16 Personality Factors Questionnaire* (16PF),<sup>xliii</sup> and the *Maudsley Personality Inventory* (MPI),<sup>xliv</sup> to study a very large material of patients from a consecutive sample; the other important thing is that his patients were examined with the PSE.<sup>xlv</sup> He showed that, in a group of patients who had achieved remission from their illness, using the two personality tests alone he could allocate more than 80% of the patients [to a] most confident diagnosis. Special statistical methods [used involved removing] a middle group where there is ambiguity, and you are uncertain of the diagnosis [so as to] have two clean groups. [In this way, Dorjival] was able to allocate more than 80% with the personality tests alone to the correct anxiety or depressive groups.

LT: Sometimes personality tests actually evaluate symptoms.

MR: [Dorjival] did [his study] in the phase of remission [or] recovery, and with very simple items which we excavated from the study I did with Mountjoy.<sup>xlvi</sup> At the time, we were not interested in studying personality; we used the MPI because it had been part of the protocol used by Gurney originally.<sup>xlvii</sup> But we went back and looked at this personality issue. It has become important, and just about four years ago I said, ‘Let us dig out all the items we have about historical development and personality, childhood history and so on.’ First, we did the discriminant function analysis to see whether we could separate anxiety and depression. In other words, with the personality data we had showed that patients with anxiety and depressive disorders were distinct groups. At first doing all the patients, the separation was not very impressive. Then I suggested that we should do the men separate from the women. Now this was very interesting. First of all the [diagnostic] separation in the women was far more clear than in the men. Secondly, the indices which separated anxiety from depressive states were very different in the women from what they were in the men. I think far too little attention had been paid to this [sex effect]: when we talk of anxiety disorders or phobic disorders, men are a rather different group from women. The main point was that the view of the symptoms of the entire disease is not validated and I think that people are now looking more and more into personality dimensions. Now, along comes DSM-III.

LT: When did the interest in differentiation between endogenous and non endogenous depression start?

MR: Well, Kraepelin assumed that they were different psychogenic disorders – as he called them – that were different from the psychoses. There were great debates in the 1920s between Aubrey Lewis and the distinguished psychologist Robert Gillespie.<sup>xlviii</sup> Lewis was a unitarian, he was not a good clinical psychiatrist.

LT: Was also Meyer a unitarian psychiatrist?

MR: Yes, Adolf Meyer believed in reaction types, not in diseases. Anybody could get any disorder, so scientifically his heritage was rather impoverished, scanty, and sparse. It is a good thing you mentioned [him] because English psychiatry had been heavily influenced by Meyer. Lewis went to Johns Hopkins<sup>xlix</sup> and became inspired by Adolf Meyer with his rather nebulous conception. Desmond Curran,<sup>1</sup> a famous English psychiatrist worked with Meyer in Baltimore, [as did] David Henderson.<sup>li</sup> They all came back to England with the Meyerian view which looked rather at reaction types and showed very little interest in taxonomy. Mind you, Meyer had the virtue of introducing the human being onto the stage and encouraging a new kind of dynamics; something that departed from Freudian dynamics [but fostering] an examination of the life history of every patient and insisting that this was the clue: the life history of the individual. The trouble is that if you concentrate attention on individual patients and ignore classification, you cannot get anywhere. Looking at an individual you can do nothing but gaze at him in ineffable wonder and you cannot expect any truth from, unless there is knowledge about groups. How do you dig out any facts? How do you separate signals from noise looking at the individual? So it was a worthy objective but it could not be carried into realistic effect or in actual [clinical] practice in the absence of head-headed look at classification. On the other hand, in reaction against psychoanalysis, American psychiatry came in with what they call the new Kraepelinian view [represented by] DSM-III which I [will] not go [into] too much ... It threw neurosis out of the window and it ignored the concept of psychosis.

LT: What do you mean by that statement?

MR: Well, I mean that the distinction between neurosis and psychosis does not figure [in DSM –III]: they are two entities, two groups of disorders, each with a separate little pigeonhole to be put in—a general concept without any general conceptual structure. Another important fact about the DSM-III is

that it introduced a number of axes, so in a sense you could claim that it was multidimensional. But, if you read any research clinical publication that matters you will not see many descriptions of axis-II diagnoses figuring as criteria of admission to a given study; axis II sat there in the wings waiting to be called in what was [a] cross-sectional classification. One can understand that approach to psychiatric [diagnosis], but it ruled that anxiety disorders and affective disorders were separate, quite distinct conditions; anxiety disorders suddenly began to be explored [after] 1980. Shortly afterwards there came panic and panic-agoraphobic disorder and this is where interest was taken in my original description of phobic anxiety and depersonalization because there is nothing [is] identical with agoraphobia in its acute stage.

LT: Regarding this particular issue, do you think that the inclusion of obsessive-compulsive disorder in the anxiety group of DSM-III disorders was justified?

MR: No, I don't think so. I believe it was not strictly in accordance with facts because, if there one condition which stands out as being distinctively recognizable, having a course of its own, having commanding and very high measure of inter-observer agreement in diagnosis, you would choose obsessive-compulsive psychoneuroses. But there are elements of justification for it; certainly obsessive-compulsive patients are very anxious, so like many other conditions, [including] psychotic disorders, which are not in the anxiety group. Obsessive-compulsive neurosis [has] an enormous repertoire of symptoms, like one day fearing that lightning will strike you down, next day fearing that a meteor might drop out of the sky [or that] they would suffer from contamination [and need] to wash hundreds of times: that's classical of obsessive-compulsive neurosis. But [in] general anxiety disorder, it is very common to find one obsessional thought, one fear. Although the doctors cannot find any evidence of cancer, the person may have cancer; these are not depressions, usually they are anxiety disorders in obsessive-compulsive personality setting. The answer to your question is: no, I do not think that obsessive-compulsive neurosis belong to the anxiety disorder but I believe that agoraphobia does and that cases of social phobia do.

LT: Would you consider personality as an important background in terms of further development to a clear-cut psychiatric disorder; does a special personality develop into a particular kind of disorder, or



you think that personality and disorders are independent?

MR: Very interesting and astute question, if I may say. I am sure that personality *factors* matter, but first our measures [of these] are rather crude and I am not at sure that [such] measures give us the right answer. I believe that there are mysteries about which we do not know very much. I am certain, for example, that anorexia nervosa – which I think one has to accept as a neurosis – occurs in many different kinds of personality; and agoraphobia, which I know very well, also is not confined to one type of personality dimension or profile. I believe there is something like a mystery here that needs more light to be shed on it. What I am certain of are two things: that if psychiatry develops along the line in which it is concerned with presenting symptoms and signs alone, it will become impoverished and will die of inanition. The other thing I am certain of is [that] to study the historical and developmental aspects of psychiatric patients and to try to understand the individual is indispensable for psychiatry. The term ‘understanding’ is very unfashionable; it is regarded with skepticism, even with a certain contempt [as a] totally unscientific activity; there is a very fine passage in Kraepelin which reflects Kraepelin’s thought about understanding. He said that in ordinary social life, understanding is indispensable; we cannot live without trying to understand those we meet [or] relate to, trying to work out what they like and entering into a relationship with them. In real disease, it is very open to self-deception and, except for the cases of psychopaths, by that [Kraepelin] meant neurotic and personality disorders, which he did not regard as illnesses, [in which] understanding is best avoided. I disbelieve that and I disbelieve also that understanding is fundamentally at variance with the scientifically approach in psychiatry, because the concept of understanding others by studying their behavior, their language, their facial expression does not come from me or even from Jaspers;<sup>lii</sup> it comes from Charles Darwin. You find a very good description of this in Darwin’s *Expressions of Emotions in Man and Animals*. When I spoke of personality as being important it is not that I know that personalities are the specific antecedents of different forms of psychiatric illness. Studies by von Zerssen<sup>liii</sup> showed no distinctive personality setting in [a broad] variety of illness except [for] endogenous depression.

LT: Speaking of von Zerssen, what do you think of the concept of temperament and how it is different

from personality?

MR: These are rather bad terms. Temperament refers to the emotional characteristics of the individual; the old theory of the temperaments in terms of the old Greek concept of the humors. Personality is wider and it refers not just to mood but [also] to a wide range of other things; the term relates to terms that psychologists nowadays use in their frame-dimension. You could use such things as motivation, a novelty seeking, dependency reward—in other words, [an entire] range of dimensions other than those which relate to temperament. What about character: did you ask me that or did I ask myself that? Character refers more to those aspects of personality which relate to the system of aspiration, values, self-disciplinary strategies and techniques, and the manner in which these are expressed in relationship with others. I think they are related concepts; temperament relates to mood, [but] personality is wider.

LT: In patients with panic disorder and agoraphobia we have seen traits characterized by hyperthymic temperament, over-controlling of emotions, especially among high-achievers.

MR: ‘Hyperthymic’ refers to individuals with elated states, [as] you find in Akiskal.<sup>iv</sup> However, that is interesting. I think this is a difficult area which needs much research. I believe that two things stand out for me from that background; the first is that these are individuals who may show a drive toward high achievement, may show apparently actual achievement as well as high drive toward it, but fundamentally these are compensatory activities; and emotional dependence on others is a central characteristic. It is seen in the characteristic form in the individual who is housebound, who cannot get out of the home without feeling panic and being overwhelmed, unless she is accompanied by somebody rather close to her, [perhaps] a husband. You see that this a complete negation of any physiological theory alone; here is a phenomenon where you have an individual in a state of panic with heart pounding at 160 but give her a friend and she can go away, to the end of the earth. I think this does not come on, does not commence with agoraphobia; it has been there as a personality trait long before. I have said all these things far better in many other places, I am a great supporter of biological psychiatry ... [There are] genetical discoveries in relation to schizophrenia and manic-depressive disorder, [and] recently about panic disorder. They claim to have mapped the gene for panic disorder as major locus, [possibly] on chromosome-7.<sup>lv</sup> I am a great believer in this [approach]; biological psychiatry perhaps is

at a growing point. [Its] reductionism is very powerful but it is not to be regarded as the answer to all the problems of psychiatry. I don't believe that it is likely to be able to arrive at the biological language which eliminates the language of clinical and psychodynamic observations, and certainly I don't have answer to the problem of making a scientific discipline out of the definition of personality profiles and their relation to illness.

LT: In many patients with panic disorder I have seen also over-controlling parents, mainly mothers with a lot of anxiety and very concerned that something may happen to their children.

MR: You also see under-controlling ones; that is the trouble.

LT: Dealing with power in the relationship between mothers and children; also you mentioned that mother-child separation is the first moment of agoraphobia, supporting the idea that you depend on somebody. On the same line there is the issue of early and recent losses in patients with panic disorder and depression. What do you think?

MR: Klein<sup>lvi</sup> claimed that separation anxiety occurs in high proportion of people and he has related this to [a] Bowlbian concept. I think this is a very controversial field for two reasons: first of all in the recent investigations including those by Klein himself he has not succeeded in demonstrating that a significant excess of patients with agoraphobia had had separation experiences.<sup>lvii</sup> In fact, he introduced some ad hoc explanation why [such patients have had] very controlling parents who have never let them experience separation; I don't think a great deal of that, saving your hypothesis from extinction. [Also], child psychiatrists who have published follow-ups on people who had school phobia have not confirmed [that] those who have suffered with school phobia, with the exception of a small minority who begin phobias after the age of eleven, are especially liable to neurotic disorder in later life. [That is,] follow-up of school-phobic patients does not provide very good confirmation for this theory. [Concerning] loss of a parent, George Brown's <sup>lviii</sup> work [finding that early] loss is a consistent or major causal agent in depression during adult life has been replicated by some but rebutted by more people. I have not looked at the recent research but I was familiar [with it] until three [or] four years ago. I don't think the evidence for [an association between early loss and later depression] is very good nor peculiarly productive. Of course, if you lose a mother, you suffer a disadvantage without any

question, but how much this contributes and to what disorder is another matter. I don't think that Brown's notion is very well substantiated. I suppose that Bowlby's<sup>lix</sup> idea that agoraphobia [arises from] separation anxiety is an attractive idea. One can see that [agoraphobia] is indeed the fear of being separated from home [and from] people who belong there, but it is hard to expect that some separation which occurred in childhood may lead to an [adult] illness. I do not think it has been proven.

Can I just mention [a] very important issue here which has brought back the old question of separation of anxiety and depression? [Regarding] the phenomenon of comorbidity, certainly there is quite often a depressive coloring to agoraphobic disorder, but people failed to differentiate between depression as a symptom and depression as a syndrome. Anxiety and depression are constantly working in association, but the presence of one depressive symptom does not mean a comorbidity of depressive illness with panic disorder. If an anxiety symptom in depression which does not lead to the diagnosis of a depressive illness, an anxiety symptom in a depressive illness does not lead to a diagnosis of depression [either]. In addition, depressive symptoms, one or two, which tend in any case to be transient in anxiety or phobic disorder, do not lead you to vary the diagnosis issue. What I would say is this: when you study agoraphobics for years you will find from time to time they become depressed and sometimes very depressed so that they may have to go to a hospital with the depression superimposed on their agoraphobia. [Nevertheless,] there is a refractory-resistant core that survives year after year, the agoraphobia. This is the explanation of the fact that you will get some patients with agoraphobia [even] 10, 15, and 20 years [after presenting] for the first time. The same is true of social phobia. Evidence has been advanced recently that suggests that phobia, panic disorder, agoraphobia, and depression have some common foundation in etiology. I do not think [it] is very well founded [or is of] sufficient depth [regarding] the phenomenology, course, and outcome.

LT: People who agree with the idea of comorbidity claim that the effectiveness of antidepressants for both depression and anxiety could be one of the elements supporting the association.

MR: Having a treatment that is successful in several diseases does not mean the diseases are the same; if that were the case, if you use the effect of corticoids as a principle of classification in medicine you

would have a very peculiar picture. In relation to depression and anxiety disorder what is certain is that there is a treatment that sharply discriminates between them: we are talking of the rediscovery of ECT. ECT in severe depressive disorder with suicide symptoms and with typical endogenous symptoms can be a life-saving procedure. I do not know of any evidence that ECT is an effective treatment for anxiety disorder. In fact, if you give ECT to [anxious] patients, you are likely to make them worse; frequently they may switch on to an attack of depersonalization that lasts for months or years. Have you seen this?

LT: Not in my patients because I have no access to ECT in Sardinia.

MR: No ECT in Sardinia: not allowed?

LT: Because there no facilities where to administer it.<sup>lx</sup>

MR: It is incredible.

LT: I know patients who have been treated with ECT in whom the indication probably was not 100% correct, who experienced depersonalization.

MR: I would be interested if you send me a few case histories. I think the difference [in the effect of antidepressants] is decisive. Obviously, if you find that antidepressants work in panic disorder – and I am not so sure they work in the long term in agoraphobia – I think we have a few follow-up studies of the effects of drugs in agoraphobia; if they work in panic disorder and also in depression, [there] must be some common factors, but it does not mean that they are the same disease. They may have one connecting thread: for neurotic disorder as a whole that there are threads in common between neuroses, but it would be very distractive to go from that to the inference that agoraphobia, social phobia, hysterical or conversion disorders, obsessive-compulsive states, hypochondriacal disorder, anorexia nervosa, post-traumatic stress disorder are all one condition. I do not think that [by] continuing to draw a line across distinct disorders to show by means of some matching symptom scores, you can demonstrate no visible break in the curve that connects the symptom scores of all these conditions. [This,] to me, is an empty exercise; that there is no difference it is not acceptable. Many excellent investigators argue, in principle, in favor of unity of neuroses. What they are saying is that same genes

[are associated with] different syndromes. You asked about differentiation. I think that in relation to psychopharmacology there is something rather specific about the effects of clomipramine in obsessive-compulsive states; I believe that there is a lot of evidence that it is effective in a substantial proportion [of such cases], and there is a recent review paper by Murphy.<sup>lxi</sup> There [also] is evidence social phobic states tend to benefit from monoamineoxidase inhibitors. I don't think we have yet any treatment for anorexia nervosa unless you can tell me one. Do you think we can take a five-minute break? [that was a euphemism to mean that the time was over].<sup>lxii</sup>

### *Notable comments*

Several of comments made by Dr. Roth during my 1990 interview with him were particularly noteworthy:

*The trouble is that if you concentrate attention on individual patients and ignore classification, you can't get anywhere. Looking at an individual you can do nothing but gaze at him in ineffable wonder and you can't expect any truth from unless there is knowledge about groups.*

*I am certain, for example, that anorexia nervosa, which I think one has to accept as a neurosis, occurs in many different kinds of personality.*

*If psychiatry develops along the line in which it is concerned with presenting symptoms, it will become impoverished and will die of inanition. ... To study the historical and developmental aspects of psychiatric patients and to try to understand the individual is indispensable for psychiatry.*

*Many [who] show a drive toward high achievement may show apparently actual achievement, ... but fundamentally the central characteristic is that these are compensatory activities and emotional dependence on others.*

*I don't have an answer to the problem of making a scientific discipline out of the definition of personality profiles and their relation to illness.*

*The phenomenon of co-morbidity ... Certainly there is quite often a depressive coloring to agoraphobic disorder but people fail to differentiate between depression as a symptom and depression as a syndrome; of course anxiety and depression are constantly working in association, but the presence of one depressive symptom does not mean a comorbidity of depressive illness.*

*In reaction against psychoanalysis, American psychiatry came in with what they call the new Kraepelinian view of DSM-III ... It threw neurosis out of the window and it ignored the concept of psychosis.*

*[The] biological psychiatrist of the future will be very terse in his examination. He will not conduct detailed investigations into life situation and development, and relationships with parents; childhood, adulthood, sexual life. He will ask about sleep, energy, appetite, weight, mood, physical symptoms and sexual function and that will give him quite enough. Well I believe people who*

*believe that are going to be the coffin-bearers of psychiatry ... into its graveyard [That future is now].*

## Endnotes

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i

. Photo from: Sir Martin Roth, an appreciation (Kerr TA, Kay D. Sir Martin Roth, FRS. An appreciation. *Br J Psychiatry* 2007; 190: 375–378.) The article includes more biographical notes. An even more detailed autobiography is included in a publication by the CINP (Ban et al 2000) and other notes are included in some newspaper articles: (Anonymous. Obituary: Sir Martin Roth. *Bull RCP* 2006; 10: 95; Anonymous. Obituary: Professor Sir Martin Roth. *The Daily Telegraph*, 13 October 2006; Kay D. Obituary: Sir Martin Roth. *The Guardian*, 27 October 2006; and Wischik CM. Professor Sir Martin Roth. *The Independent*, 19 October 2006.

ii

. Walter Russell Brain, 1st Baron Brain (1895–1966), British neurologist, author of *Brain's Diseases of the Nervous System* and editor of the homonymous neurological medical journal aptly titled *Brain*.

iii

. Sir Aubrey Julian Lewis, (1900–1975) was born in Australia. In 1946, he became the first Professor of Psychiatry at the Institute of Psychiatry in London. He was a great supporter of the unitarian view of depression following Adolf Meyer's ideas. Lewis was pragmatic in his approach to diagnosis: "if clinical differences did not make a difference in practice, then there was no difference". Roth, instead, was a divider who emphasized psychopathology: "if clinical syndromes could be shown to be different in phenomenology, then they are different" (Ghaemi NS. The heterogeneity of depression: an old debate renewed: *Acta Psychiatr Scand* 2011; 124: 497.)

iv

. Eliot Trevor Oakeshott Slater (1904–1983), British psychiatrist, co-editor of *Clinical Psychiatry*, the leading textbook for psychiatric trainees. He had polyhedric interests, including chess, music, poetry, painting, statistical study of literature, and euthanasia.

v

. Wilhelm Mayer–Gross (1889–1961), German psychiatrist, worked in Heidelberg and was important in the field of phenomenologic psychiatry. He moved to England in 1933, first in London and then in Birmingham, where he became very influential in British psychiatry.

vi

. Robert Evan Kendell (1935–2002), a Welsh psychiatrist trained under Sir Aubrey Lewis, chair of psychiatry in Edinburgh. Roth and Kendell argued a lot about differences between anxiety disorders and depression. Kendell claimed that, together, they formed an undifferentiated spectrum of emotional disorder, too often found together to be able to distinguish them (see: Kendell RE. *Clinical Validity*. *Psychol Med* 1989; 19: 45–55). Roth favored two distinct biological entities, with different clinical features, different genetics and different natural history. From the diagnostic point of view, and also based on modern molecular genetics, Roth's concept won and is included in DSM and ICD. Nevertheless, from a therapeutic perspective, there remains a large overlap between the two groups of disorders (see: Wischik CM. Professor Sir Martin Roth. *The Independent*, 19 October 2006.)

vii

. Roth M, Tym E, Mountjoy CQ, Huppert FA, Hendrie H, Verma S, Goddard R. CAMDEX: a standardized instrument for the diagnosis of mental disorder in the elderly with special reference to the early detection of dementia. *Br J Psychiatry* 1986; 149: 698–709.

viii

. The third edition was published in 1966 and the partial edition of 1977 was prepared by Roth and Slater since Mayer-Gross died in 1961 in Birmingham on the night before he was due to return to Germany. A fourth edition was in preparation for years but never published (Ban 2000).

ix

. Roth M. Categorical subtypes and dimensions of illness in the anxiety and related disorders. In: Noyes R, Roth M, Burrows GD, editors. *Handbook of Anxiety*, vol. 2. New York: Elsevier; 1988a. pp. 53–79.

x

. Ban T, Healy D, Shorter E. *The history of psychopharmacology and the CINP as told in autobiography*. Budapest, Animula. 2000, pp. 238–249.

xi

. Previously, other psychiatrists became Fellows of the Royal Society: William Battle (1704–1776) in 1742, Sir John Charles Bucknill (1817–1897) in 1866, and William Halse Rivers (1864–1922) in 1908.

xii

. The Maudsley Hospital in South London and is the largest mental health training institution in the UK; it is partnered with the Institute of Psychiatry of King's College. It was founded in 1907 when the Victorian psychiatrist Henry Maudsley offered London County Council the sum of £30,000 to help found a new mental hospital that would be exclusively for early and acute cases rather than chronic cases, have an outpatient clinic, and provide for teaching and research (Wikipedia, 2015).

xiii

. Emil Kraepelin (1856–1926) was a German psychiatrist considered the founder of the modern scientific psychiatry. His major work, *Compendium der Psychiatrie: Zum Gebrauche für Studierende und Aertze (Compendium of Psychiatry: For the Use of Students and Physicians)*, was first published in 1883 and was expanded in subsequent editions (total of 9) as *Ein Lehrbuch der Psychiatrie (A Textbook of Psychiatry)* until 1927. His major contribution to psychiatry was the description of a dichotomy between *dementia praecox* (later termed schizophrenia) and manic-depressive psychosis (later, bipolar disorder and recurrent major depression).

xiv

. Kurt Schneider (1887–1967) was a German psychiatrist whose main interest was the study of schizophrenia, personality disorders, and psychopathic personalities.

xv

a. Slater E, Tsuang Ming–Tso. J. Abnormality on paternal and maternal sides: Observations in schizophrenia and manic-depression. *J Med Genet* 1968; 5: 197–199.

b. Slater E, Maxwell J, Price JS. Distribution of ancestral secondary cases in bipolar affective disorders. *Br J Psychiatry* 1971; 188: 215–218.

xvi

a. Roth M. The phobic anxiety-depersonalisation syndrome. *Proc R Soc Med* 1959; 52: 587–596.

b. Roth M. Phobic anxiety-depersonalization syndrome and some general aetiological problems in psychiatry. *J Neuropsychiatry* 1960a; 1: 293–306.

c. Roth M. Depressive states and their borderlands: classification, diagnosis and treatment. *Compr Psychiatry* 1960b; 1: 135–155.

d. Harper M, Roth M. Temporal lobe epilepsy and the phobic anxiety-depersonalization syndrome: a comparative study. *Compr Psychiatry* 1962; 3: 129–151.

e. Roth M, Harper M. Temporal lobe epilepsy and the phobic anxiety- depersonalizationsyndrome: practical and theoretical considerations. *Compr Psychiatry* 1962; 3:215–226.

f. Cassano GB, Petracca A, Perugi G, Toni C, Tundo A, Roth M. Derealization and panic attacks: clinical evaluation on 150 patients with panic disorder-agoraphobia. *Compr Psychiatry* 1989; 30: 5–12.

g. Toni C, Cassano GB, Perugi G, Murri L, Mancino M, Petracca A, Akiskal H, Roth SM. Psychosensorial and related phenomena in panic disorder and in temporal lobe epilepsy. *Compr Psychiatry* 1996; 37: 125–133.

xvii

. Karl Friedrich Otto Westphal (1833–1890), German psychiatrist from Berlin coined the term 'agoraphobia', after the observation of three men with anxiety and feelings of dread associated with being in public areas. In: Westphal C. *Die Agoraphobie: eine neuropatische Erscheinung*. *Archs Psychiatr Nervenkr* 1871; 3: 138–161.

xviii

. Roth M, Argyle N. Anxiety, panic and phobic disorders: an overview. *J Psychiatr Res* 1988; 22(Suppl 1): 33–

54.

xix

a. See note 11a.

b. Roth M. Anxiety neuroses and phobic states. I. Clinical features. *BMJ* 1969; 1: 489–492.

xx



. Charles Darwin (1809–1882). His most famous book was *On the Origin of Species* (1859) in which he claimed that all living beings descend from common ancestors introducing the concept of natural selection and the survival of the fittest. In 1871 he published *The Descent of Man, and Selection in Relation to Sex*, followed by *The Expression of the Emotions in Man and Animals* (1872) which represents an important contribution to psychology.

xxi

. The Crichton Royal Hospital is the largest Scotland's psychiatric hospital. It was founded in Dumfries in 1838 by Elizabeth Crichton (1779–1862), a wealthy local widow. She persuaded the phrenologist William A. F. Browne (1805–1885) to become medical superintendent and to implement his innovative ideas of occupational therapy (Wikipedia).

xxii

. Graylingwell Hospital (formerly The West Sussex County Lunatic Asylum) was a psychiatric hospital in Chichester, West Sussex. It was completed in 1897. It closed in 2001, due to the decline of the number of patients having moved away from long stays in psychiatric wards to community-based care (Wikipedia).

xxiii

. Leslie Kiloh (1917–1997), Australian psychiatrist who studied medicine at the London University and King's College Hospital. In 1961, he coined the term *pseudodementia* to indicate a syndrome of the elderly with symptoms consistent with dementia which, instead, is a depressive syndrome.

xxiv

. Ball JR, Kiloh LG. A controlled trial of imipramine in treatment of depressive states. *Br Med J* 1959; 2: 1052–1055.

xxv

. a.. Kuhn R. Über die Behandlung Depressiver Zustände mit einem Iminodibenzyl-derivat (G22355). *Schweiz Med Wochenschr* 1957; 87: 1135.

b. Tondo L. Closer Looks. Roland Kuhn. *Clinical Neuropsychiatry* 2012; 9: 138–154.

xxvi

. Kiloh LG, Ball JR, Garside RF. Prognostic factors in treatment of depressive states with imipramine. *BMJ* 1962; 1: 1225–1227.

xxvii

. Garside RF, Roth M. Multivariate statistical methods and problems of classification in psychiatry. *Br J Psychiatry* 1978; 133: 53–67.

xxviii

. Kiloh LG, Garside RF. Depression: a multivariate study of Sir Aubrey Lewis's data on melancholia. *Aust N Z J Psychiatry* 1977; 11: 149–156.

xxix

. See note 24.

xxx

. Roth M. Depressive and manic psychoses and allied disorders. *Curr Med Drugs* 1964; 4: 3–18.

The topic was further discussed in a subsequent paper: Roth M. Problems in the classification of affective disorders. *Acta Psychiatr Scand (Suppl)* 1981; 290: 42–51.

xxxi

. Carney MW, Roth M, Garside RF. The diagnosis of depressive syndromes and prediction of ECT response. *Br J Psychiatry* 1965; 111: 659–674.

xxxii

. Wilhelm Griesinger (1817–1868), German neurologist and psychiatrist who studied at the University of Zürich and in Paris. He worked in Württemberg, Stuttgart, Tübingen, and Kiel. He was also the director of the Medical School in Cairo where he became the personal doctor of the King Abbas I. In 1845, he published *Die pathologie und therapie der psychischen Krankheiten (The Pathology and Treatment of Psychic Diseases)*. His major claims were that in order to understand a psychic symptom it is important to localize it in the brain and that all psychic illnesses were caused by a pathological alteration of the brain.

xxxiii

. Gerald L. Klerman (1928–1992), American psychiatrist and researcher who developed interpersonal psychotherapy, who directed the NIMH in 1977–1980. He was an expert of psychopharmacological treatments of

depression and anxiety disorders.

xxxiv

- . a. Sargent W. The treatment of anxiety states and depressions by the monoamine oxidase inhibitor drugs. *J Neuropsychiatry* 1962; 3: 96–103.
- b. West ED, Dally PJ. Effects of iproniazid in depressive syndromes. *Br Med J* 1959; 1: 1491–4.

xxxv

. No reference was found on atypical depression by Robert F. Prien. The first account of atypical depression in PubMed is by Anchersen (Anchersen P. Atypical endogenous depressions. *Acta Psychiatr Scand* 1961; 37(Suppl): 233–239), and the concept was reviewed by Pae et al. (Pae CU, Tharwani H, Marks DM, Masand PS, Patkar AA. Atypical depression: comprehensive review. *CNS Drugs* 2009; 23: 1023–1027.) Atypical depression refers to the depressive group meeting DSM-IV criteria for major depression or dysthymia, with significant mood reactivity, and two of the four associated symptoms: hyperphagia, hypersomnia, leaden paralysis, and rejection sensitivity.

xxxvi

- . a. see note 11c.
- b. Gurney C, Roth M, Garside RF. Use of statistical techniques in classification of affective disorders. *Proc R Soc Med* 1970; 63: 232–235.
- c. see note 23.
- d. Roth M. Classification of affective disorders. *Pharmakopsychiatr Neuropsychopharmakol* 1978; 11: 27–42.
- e. Roth M, Garside RF, Gurney C, Kerr TA. Psychotic and neurotic depression: a reply on method. *Br J Psychiatry* 1979; 135: 94–96.

xxxvii

- . a. Marshall EF, Mountjoy CQ, Campbell IC, Garside RF, Leitch IM, Roth M. Influence of acetylator phenotype on the outcome of treatment with phenelzine, in a clinical trial. *Br J Clin Pharmacol* 1978; 6247–254.
- b. Mountjoy CQ, Marshall EF, Campbell IC, Garside RF, Roth M. Prediction of response to treatment with phenelzine in neurotic patients. *Prog Neuropsychopharmacol* 1980; 4: 303–308.

xxxviii

- . See notes 20 and 22.

xxxix

. See notes 23 and 33b. Also: Roth M, Gurney C, Garside F, Kerr TA. Studies in the classification of affective disorders: relationship between anxiety states and depression illness. *Br J Psychiat* 1972; 121: 147–162.

xl

- . a. Kerr TA, Gurney C, Schapira K, Roth M. Measurement and prediction of outcome in affective disorders. *Proc R Soc Med* 1970; 63: 235–238.
- b. Kerr TA, Schapira K, Roth M, Garside RF. The relationship between the Maudsley Personality Inventory and the course of affective disorders. *Br J Psychiatry* 1970; 116: 11–19.
- c. Schapira K, Kerr TA, Roth M. Phobias and affective illness. *Br J Psychiatry* 1970; 117: 25–32.

xli

. Roth M, Mountjoy CQ, Caetano D. Further investigations into the relationship between depressive disorders and anxiety state. *Pharmacopsychiatria* 1982; 15: 135–141.

xlii

- . See note 38.

xliii

- . Cattell RB, Eber HW, Tatsuoka MM. *Champaign (II): IPAT*; 1970.

xliv

- . Eysenck HJ. *The Manual of the Maudsley Personality Inventory*. London: University of London Press; 1959.

xlv

. *Present State Examination* developed by John Wing and collaborators at the Maudsley in 1967 (Wing JK, Birley JLT, Cooper JE, Graham P, Isaacs AD. Reliability of a procedure for measuring and classifying "Present Psychiatric State". *Br J Psychiatry* 1967; 113: 499–515.) Since version-10, it has been called the *Schedules for Clinical Assessment in Neuropsychiatry* (SCAN). It encompasses a set of diagnostic items able to measure mental disorders in adult persons.

xlvi

- . See note 38

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xlvi

. See note 33b and 37a.

xlvi

. Robert D. Gillespie (1884–1965), psychologist, coauthored with David Henders on the textbook, *Henderson and Gillespie's Textbook of Psychiatry for Students and Practitioners*; Oxford University Press, 1927, and later worked at Cambridge.

xlix

. Johns Hopkins Hospital, Baltimore (MD).

l

. Desmond Curran (1903–1985), British psychiatrist, emeritus professor at the University of London. In the postwar years, he ran the weekly psychiatric case demonstrations at Hyde Park Corner (along with Sir Paul Mallinson and 'Bird' Partridge) which became nationally and internationally famous providing teaching to postgraduate students. His clinical skills were legendary and came to be regarded as an infallible prognostician (Anonymous 1986).

li

. Sir David Kennedy Henderson (1884–1965), a distinguished Scottish psychiatrist, knighted in 1947, president of the Edinburgh's Royal College of Physicians in 1949, and co-author with Robert Gillespie on a 1927 textbook of psychiatry.

lii

. Karl Theodor Jaspers (1883–1969), a German psychiatrist and philosopher, a major exponent of existentialism. His major contribution to psychiatry was the book *General Psychopathology* (1913).

liii

. Detlev von Zerssen (1926–), German psychiatrist, who studied depressive disorders, typological characters, circadian rhythms, and temperaments. See: von Zerssen D, Koeller DM, Rey ER. [The premorbid personality of patients with endogenous depression. A cross-validation of the results of an earlier investigation (German)]. *Confin Psychiatr* 1970; 13: 156–179.

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. Hagop Souren Akiskal (1944–), Armenian-American psychiatrist best known for his research on temperament and bipolar disorder.

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. Initial research showed inconclusive evidence of linkage of panic disorder to the alpha-haptoglobin locus on chromosome 16q22 (Crowe RR. Panic disorder: genetic considerations. *J Psychiatr Res* 1990; 24 [Suppl 2]: 129–134.)

lvi

. Donald Franklin Klein (1928–), New York psychiatrist who discovered the effect of imipramine in panic attacks, (Klein DF. Anxiety reconceptualized: gleanings from pharmacological dissection—early experience with imipramine and anxiety. *Mod Probl Pharmacopsychiatry* 1987; 22: 1–35,) and in childhood anxiety disorders (Rabiner CJ, Klein DF. Imipramine treatment of school phobia. *Compr Psychiatry* 1969; 10: 387–390.) Most of his research was carried out with his wife, Rachel Gittelman-Klein, a child-psychiatrist.

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a. Gittelman R, Klein DF. Relationship between separation anxiety and panic and agoraphobic disorders. *Psychopathology* 1984; 17(Suppl 1): 56–65.

b. Gittelman-Klein R, Klein DF. School phobia: diagnostic considerations in the light of imipramine effects. *J Nerv Ment Dis* 1973; 156:199–215.

lviii

lviii. George Brown (1930–), a British sociologist and psychologist, who investigated several social factors and life events associated with the origin of depression. See: Brown GW, Harris T. *The Social Origins of Depression: A Study of Psychiatric Disorder in Women*. London: Tavistock Publications; 1978.

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. Edward John Mostyn Bowlby (1907–1990), a British psychologist, psychiatrist, and psychoanalyst, famous for his interest in child development and for his work in attachment theory (see: Tondo L. Closer Looks. *John Bowlby. Clinical Neuropsychiatry* 2011; 8: 159–171.)

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. Since the year 1995, there has been a facility for ECT at the San Martino Hospital in Oristano (Sardinia) thanks

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to the efforts of Dr. Gian Paolo Minnai.

lxi

- a. Murphy DL, Pigott TA. A comparative examination of a role for serotonin in obsessive compulsive disorder, panic disorder, and anxiety. *J Clin Psychiatry* 1990; 51 (Suppl53–8): 59–60.
- b. Murphy DL, Zohar J, Benkelfat C, Pato MT, Pigott TA, Insel TR. Obsessive-compulsive disorder as a 5-HT subsystem-related behavioural disorder. *Br J Psychiatry Suppl* 1989; Dec: 15–24.

*Acknowledgments.*

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. The author is deeply grateful to Prof. Ross J. Baldessarini of McLean Hospital-Harvard Medical School, for his extensive comments and suggestions during the preparation of this report.

## **Leonardo Tondo: Michael Shepherd On Epidemiology in Psychiatry**

### **CONTENTS: Biographic sketch About the interview The Interview Endnotes**

#### *Biographical sketch*

Michael Shepherd (1923–1995) was born in Cardiff to a Jewish family originating in Odessa and Poland. He married Margaret Rock in 1947, who died in 1992, after a long illness. They had four children. He obtained his bachelor medical degree at the Oxford University, where he was influenced by John Ryle, a professor of social medicine, to pursue the social implications of mental disorders. In 1952, he started his career at the Maudsley Hospital and Institute of Psychiatry and obtained a doctorate in medicine from Oxford University, in 1954.

In 1955–56, he trained at the Johns Hopkins School of Public Health in Baltimore and visited several psychiatric centers in the United States to obtain material for a critical survey of American psychiatry. He documented a major difference in psychiatry in the US and UK as an emphasis on public services in the UK and dominant private office practice in the US. He noted that “nearly 3,000 of the 7,500 recognised [American] psychiatrists in 1951–1952 listed private practice as their major activity...one-quarter of them were engaged in the practice of psychotherapy and were not considered to meet the traditional criteria of the practice of medicine.” Moreover, he found that American

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psychiatrists seemed to have a “distaste for the tracts of detailed knowledge dismissed as ‘descriptive psychiatry’; an antagonism to many of the facts and concepts associated with the study of heredity; a neglect of much biological investigation; and...in many centers, a biased ignorance of the evolution and the historical roots of modern psychiatry.” He also pointed out the “frosty reception... for the ‘tranquilizing’ drugs” by US psychiatrists, along with the dominance of psychoanalysis, noting that many US centers, “ingested the whole system, python-like, into the body of academic opinion,” This dominance led to “an interest in mental health only in the individual and much less for the society in which he lives,” as he further noted in a report on the use of psychotherapies in Britain.

In 1961, he became Reader in psychiatry at the Institute of Psychiatry, where in 1967, he was conferred a chair in epidemiological psychiatry. He remained there for the remainder of his professional career. He became Fellow of the *Royal College of Physicians* in 1970, and in the following year, he was among the founders of the *Royal College of Psychiatrists*. Later, he was also named Fellow of both the *American Public Health Association* and the *American Psychological Association*. He was the founding editor of the journal *Psychological Medicine*, in which he invested an enormous amount of energy until 1993, when he resigned from his position of editor-in-chief.

Michael Shepherd’s interest in social issues associated with mental problems was stimulated by the teaching at the Maudsley Institute of Aubrey Lewis,, who insisted that the collection of social data was more important than personal details about individual patients. Shepherd had a special respect for Lewis as his mentor, to whose qualities he aspired for himself. He described Lewis as, “the style of a man,” referring to the richness of Lewis’ writing. It has been suggested that Shepherd’s style of writing was even better, lighter, more vivid, and amusing.

Shepherd was one of the most influential and internationally respected psychiatrists of his time. He was Professor of Epidemiological Psychiatry at the Maudsley Institute of Psychiatry. He was the author of 30 books, among which, *Psychiatric Illness in General Practice* (1966), and of more than 200 scholarly articles. He masterminded the development and production of the monumental, five-volume *Handbook of Psychiatry* (1982). His main interests certainly were in the epidemiological approach in psychiatry and on the effects of social issues in the lives of individuals.

Shepherd also was convinced that better mental health care could be achieved by better training and support for general practitioners in the British National Health System. This position was not entirely appreciated by his psychiatric colleagues and it stirred a debate that lasted many years before eventual acceptance of his opinions.

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Among his works, his collection of biographical essays, including on John Ryle, Aubrey Lewis and Jean Starobinski have received special praise. He was described as the *Hammer of Psychoanalysis* owing to his critical view of the Freudian approach as a scientific method. He brilliantly expressed his perspective in the essay *Sherlock Holmes and the case of Dr Freud*, in which he coined the neologism *method* to describe a combination of method and myth with minimal scientific value. This essay demolished psychoanalysis as a scientific discipline, and incidentally relegated Conan Doyle to the category of very minor writers.

He was not an enthusiastic supporter of Kraepelin's classification of mental disorders. According to the German psychiatrist, major functional mental disorders fell into two main groups: dementia praecox and manic-depressive insanity. Shepherd considered this scheme to be "a primitive exercise ... with so many methodological flaws as to render it unacceptable to any editor of a peer-review journal." Shepherd's view of Kraepelin's work had a strongly political cast: "At the same time attention is drawn to the limitations of his general outlook and to his political views, which in their historical context carry disturbing overtones of proto-fascism. It does not detract from the value of his work as a clinical scientist to conclude that his philosophical amblyopia, allied to an ineradicable chauvinism that was shared by many Germans of his class and status, resulted in a failure to demarcate the boundaries of his professional expertise and distorted his judgment on the wider implications of his own achievements." The accusation of "*proto-fascism*" reflects the fact that Kraepelin died, in 1926, before the tragedy of Nazism emerged, whereas Shepherd wrote in 1995 from a very different historical perspective that included having lived through World War II and the Holocaust.

According to many colleagues who knew him well, Shepherd was highly cultivated, as witnessed by a pleasant and startling paper on psychohistory. He was fluent in several European languages and familiar with German and French, as well as Anglo-American psychiatry. His legacy certainly is tied to understanding the social origins and the political context of psychiatry. "No other individual in British psychiatry could move with such felicity and wisdom from an analysis of the racism inherent in the thinking of Emil Kraepelin to an exposition on the Sherlock Holmes-type fantasy at the heart of the great Freudian mythology."

#### *About the Interview*

I met Professor Michael Shepherd on May 30, 1987, during the 16th Congress of the Italian Association of Psychiatry, held in Cagliari, Sardinia, where he had been invited to give a lecture titled *Psychogeriatrics and the Neo-Epidemiologists*. The venue was the Forte Village, a posh sea resort in

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the south of Sardinia. We dined together the night before the congress, along with his wife, a gentle and affable lady. Professor Shepherd struck me for the tranquility he communicated; he had a peaceful expression, with the subtle smile of people who practice irony diligently and eyes that hardly left the prey. The next day, on a sunny and warm morning, during which he never thought of taking off his winter jacket, we spoke for nearly an hour.

*The interview*

LT: What do you think about the current importance of epidemiology for affective disorders? I have read that epidemiology is considered the most important aspect of health organization in your country.

MS: As you know, there are several different dimensions of investigation which are covered by the one word ‘epidemiology.’ It is a word with several meanings, although probably for most people the principal significance of epidemiology in the field of mental disorder has been as a method of making an accurate assessment of the amount of mental illness which exists in a defined population and providing the necessary information on the extent of the disease, the strategy for screening, and the resources for effective intervention. It is what we call ‘head-counting,’ and what it has done for the psychiatric profession is to demonstrate that psychiatrists see very little mental illness because they know nothing about the existence of mental disorder in the general population. If you take a public-health point of view—and epidemiology is the science of public health—then you ask not how many patients are in the hospital, but how many patients and illnesses you find in the whole population. And in descriptive terms, the most important category has been affective disorders. We have discovered through epidemiological enquiry that affective illnesses constitute easily the largest group of disorders in the general population, and this [conclusion] has come almost entirely from epidemiological research. However, a major obstacle in the way of epidemiological inquiry has been the dominance of subjective phenomena, always difficult to measure accurately.

LT: Have affective disorders changed in prevalence from the beginning of this century when a kind of objectification of psychiatry started with the work of Kraepelin? I am interested particularly in the possible change of prevalence of affective disorders considering that this century has seen two world wars. Do you think that these major events changed the prevalence of affective disorders in any way?

MS: I think that unfortunately you cannot answer this question on the basis of published

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information because what you call ‘objective’ enquiry in psychiatry was almost exclusively confined to hospital conditions. Kraepelin knew nothing about the general distribution of illness. He, like most of the older clinicians, appears to have been virtually innumerate. What has emerged by the epidemiological studies is that the less severe forms of depression far exceed in number the major variants which come to hospital and that they are identified and managed chiefly by non-psychiatrists, particularly by general practitioners. This would mean that the role of general practitioners needs to be reinforced, as well as the collaboration with the psychiatrists as recommended by the World Health Organization (WHO) and the Committee for the Prevention & Treatment of Depression. However, the contributors nowhere acknowledge the epidemiological foundations of which their discussions are based. The function of the psychiatrist was to deal with severe mental disorder and I think it has been only since the end of the Second World War that people have begun to make systematic observations on affective disorders and insufficient time has elapsed to give you a time trend.

LT: What is your own opinion on the possibly increased need for psychiatric consultation on affective disorders? Is this because affective disorders have increased dramatically in the last forty years or because there are simply many more psychiatrists now?

MS: I do not believe in personal opinions except for general discussion. But for what it is worth, I would say that there have been two factors: the first is the increase in epidemiological studies everywhere which makes people understand that many members of the general population suffer from what we call ‘minor’ affective disorders, and do not go to psychiatrists. They see their general practitioners or they ask their mothers what they should do. And now we understand that there are many such subjects. During a meeting in 1974, one speaker remarked that possibly in 40%–50% of all patients consulting a general practitioners for any reason, no organic causes for their symptoms can be found. That raises the question as to whether all these patients should be regarded as psychiatric cases. The answer is ‘no’. The second reason has been the arrival of drugs which are used widely for this purpose. And if you describe a drug as an antidepressant, for example, and the patient or an individual takes the drug, then he becomes ‘depressed’ —because he is taking an antidepressant.

LT: The Oedipus Effect?

MS: I think it is more than the Oedipus Effect. It is an Oedipus effect with commercial implications. And it is true in every country. I have a colleague who likes to say that the diagnosis is benzodiazepine and the treatment is anxiety and one knows what he means. You make the diagnosis through the drug and because there are now so many drugs which are supposed to be used for affective



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illness, we have apparently an increase.

LT: Might it be possible that in thirty years we will not talk about anxiety but rather about benzodiazepine plus or minus something?

MS: Yes. Certainly I think that we will learn a great deal about neural transmission and about the pharmacological activities of centrally-acting drugs. But whether we learn about depression, well let's wait thirty years and see! Even the concept of depression is quite scattered, appearing as it does, in the categories of psychosis, neurosis, personality disorder, alcoholism. The patterns or syndromes in terms of the phenomena of the illnesses, their outcome and their response to treatment is a sore need for the elucidation of depressive states.

LT: Can psychiatric epidemiology give an answer to the contributions of environment in causing affective disorders?

MS: It is not possible to provide an answer to that at the moment, but it may help to make observations, which will enable one to make more accurate statements than are made at the present time, by selecting populations which differ in their environmental conditions. For example, if you have two populations, which differ in their environmental conditions, two populations where one is subject to a lot of stress and the other is not, where one is urban and one is rural, you can use a comparison of the prevalence rates of affective disorder to outline the environmental component. By exclusion, because you cannot do this directly with the epidemiological method, you can introduce the element of constitutional factor. I mean a recent example of an American genetic study of depression is a very good example of using a special population with a biological technique, which could not have been possible if the environment had not been as stable as it was. So, that in theory, yes. But at the moment, it is only in limited areas has this been done.

LT: Do you think that in the United Kingdom epidemiological psychiatry is more important than in other European countries or the United States?

MS: I do not know whether it is important but I think it has a different emphasis. And I think there are several reasons for this. The first is the existence of a national health service, which makes it possible to carry out enquiries more easily than in other countries and the second is that there is a tradition in the United Kingdom which makes epidemiology part of clinical activity, so that many of the people who work in this field, for example myself, are also clinicians. It is possible to be an epidemiologist in psychiatry without being medically qualified. Statisticians, sociologists,

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psychologists, stenographers, geneticists, all use the epidemiological method. But what has happened in Britain is that it has become part of the clinical teaching and the importance of this is that many of the hypotheses of epidemiology arise from clinical observation. If you don't see patients, you have no opportunity to know what type of hypothesis to examine. I think that gives the subject some distinguishing features in the United Kingdom.

LT: I seem to understand that you make use of somatic treatments, but it would appear that you are in some way skeptical about long-acting drugs. You mentioned that these medicines can cover spontaneous remissions for a disease due to the fact that 25% of the population can go into spontaneous remission. Do you agree with this?

MS: You are now speaking of schizophrenia, not affective disorders.

LT: I am speaking of long-acting drugs.

MS: But of course the example concerns schizophrenia and the study which I described was based on the claim that intramuscular injections of fluphenazine were most effective because they avoided the problem of non-compliance. And we were struck by the number of patients who seemed to be receiving these injections unnecessarily because once you begin to receive it, it is very difficult to stop. It was suggested that fluphenazine for schizophrenia is like insulin to diabetes. You MUST continue. We thought that there was no pharmacological evidence to support this and so we did a comparative study. From the results, I think we were right to do this because other people have since made similar observations. But it is not so much the study itself I was trying to emphasize, as the approach to answering a question about treatment. And I think that one could generalize from this small study, although it took five years to do, to every branch of psychiatry.

LT: Do you think the same speaking of affective disorders, for example, using treatment with lithium salts?

MS: Oh yes. Of course we have published material on this matter, as well as with lithium and other forms of antidepressant medication. The method is exactly the same. And it seems to me that until this type of study has been carried out, it is unjustifiable to suggest that patients should receive drugs indefinitely. And as you know, there are now very grave doubts about lithium being expressed in several centers. You probably know that some years ago, I unintentionally caused problems about this; we wrote a paper questioning the evidence before lithium was widely introduced, and Dr. Schou was very agitated. And I see more and more reports in the clinical literature raising doubts about the long

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term efficacy of lithium. I think it would have been better to do this type of study before it became generally the practice to give patients with manic depressive disease lithium for a long period of time.

LT: Do you suggest withdrawal of the treatment from time to time?

MS: In some cases, I think that is certainly justified. The difficulty, of course, is that from a purely clinical point of view, it is not always easy to do this because the patient has become dependent partly on the lithium and partly on the ritual of lithium administration. And it is not always easy to persuade the patient that he does not need the drug. Because he may need the injection and the attention and everything that goes with it. It is a little like the treatment of long-term hypertension. But, in principle, my answer would be that all cases should be carefully looked at.

LT: What is your concept of normality in psychiatry and in affective disorders? Do you have something more than a personal opinion of normality?

MS: I can only answer this in general terms. There are two radically different notions of normality. One is a statistical matter, which would require quantitative information of a large population; the other is the type of question that arises if you ask what is a normal blood pressure, You cannot answer this without taking the blood pressures of 10,000 people and giving the normal range. You have a range, which is regarded as normal in purely quantitative terms. And the other is to ask simply whether or not the person in the end develops morbid affective phenomena. And that is using the same notion of normal/abnormal but in a different way. I think that the first is what a chemical epidemiologist would imply and the second is the way you function as an ordinary clinician.

LT: Thank you very much.

MS: Thank you.

*Notable comments:*

*Kraepelin knew nothing about the general distribution of illness.*

*I would say that there have been two factors: the first is the increase in epidemiological studies everywhere which makes people understand that many members of the general population suffer from what we call 'minor' affective disorders, and do not go to psychiatrists. They see their general practitioners or they ask their mothers what they should do.*

*And if you describe a drug as an antidepressant, for example, and the patient or an individual takes the drug, then he becomes 'depressed'—because he is taking an antidepressant.*

*It is an Oedipus effect [about the use of more psychotropic medications] with commercial implications. And it is true in every country. I have a colleague who likes to say that the diagnosis is benzodiazepine and the treatment is anxiety and one knows what he means.*

*And, as you know, there are now very grave doubts about lithium being expressed in several centers. You probably know that some years ago, I unintentionally caused problems about this; we wrote a paper questioning the evidence before lithium was widely introduced and Dr. Schou was very agitated.*

*You have a range which is regarded as normal in purely quantitative terms. And the other is to ask simply whether or not the person in the end develops morbid affective phenomena. And that is using the same notion of normal/abnormal but in a different way. I think that the first is what a chemical epidemiologist would imply and the second is the way you function as an ordinary clinician.*

#### Endnotes

<sup>1</sup> Biographical information from Russell G.: Michael Shepherd, Obituary in: *Psychiatric Bulletin* 1996; 20: 632–637; Clare Anthony: Michael Shepherd, Obituary. *The Independent* August 30, 1995 (access: September 21, 2015).

<sup>2</sup> John Alfred Ryle (1889–1950), British physician and epidemiologist, Fellow of the Royal College of Physicians since 1924, became the chair of the Institute of Social Medicine at the University of Oxford in 1943. He was also physician of the King George V.

<sup>3</sup> The Maudsley Hospital in South London and is the largest mental health training institution in the UK; it is partnered with the Institute of Psychiatry of King's College. It was founded in 1907 when the Victorian psychiatrist Henry Maudsley offered London County Council the sum of £30,000 to help found a new mental hospital that would be exclusively for early and acute cases rather than chronic cases, have an outpatient clinic, and provide for teaching and research (Wikipedia 2015).

<sup>4</sup> a. Shepherd M. An English view of American psychiatry. *Am J Psychiatr* 1957; 114: 417–420.

b. Shepherd M. A critical appraisal of contemporary psychiatry. *Compr Psychiatry* 1971; 12: 302–320.

<sup>5</sup> Shepherd M. Psychoanalysis, psychotherapy, and health services. *Br Med J* 1979; 15: 1557–1559. The paper introduces the issue with an amusing quotation from *Time* magazine (Psychiatry on the couch, April 2, 1979, p.74) in which psychoanalytical psychiatry is presented in the role of a patient with the following clinical aspects:

*History: European born. After sickly youth in the US, traveled to Vienna and returned as Dr. Freud's Wunderkind. Amazing social success for one so young. Strong influence on such older associates as Education, Government, Child Rearing and the Arts, and a few raffish friends like Advertising and Criminology.*

*Complaint: Speaks of overwork, loss of confidence and inability to get provable results. Hears conflicting inner voices and insists that former friends are laughing behind his back.*

*Diagnosis: Standard conflictual anxiety and maturational variations, complicated by acute depression. Identity crisis accompanied by compensatory delusions of grandeur and a declining ability to cope. Patient averse to the therapeutic alliance and shows incipient over-reliance on drugs.*

*Recommended treatment: requires further study.*

*Prognosis: problematic*

<sup>6</sup> The journal was established in 1969 by Michael Shepherd who remained its editor in chief until 1993. Shepherd insisted on the the term ‘psychological’ instead of ‘psychiatric’ apparently in continuity of the *Journal of Psychological Medicine* founded by Forbes Benignus Winslow (1810–1874) in 1848.

<sup>7</sup> Sir Aubrey Julian Lewis, (1900–1975) was born in Australia. In 1946, he became the first Professor of Psychiatry at the Institute of Psychiatry in London. He was a great supporter of the unitarian view of depression following Adolf Meyer’s ideas. Lewis was pragmatic in his approach to diagnosis: “if clinical differences did not make a difference in practice, then there was no difference” and very little interested in classification of mental disorders. (see also interview with Sir Martin Roth).

<sup>8</sup> Rawnsley K. *The Contribution of Michael Shepherd. In The Scope of Epidemiological Psychiatry: Essays in Honour of Michael Shepherd.* London: Routledge; 1989, pp. 509-21.

<sup>9</sup> See Russell in note 1.

<sup>10</sup> Several publications are devoted to this main research theme for which a small but prestigious selection is provided:

- a. Shepherd M, Cooper B. Epidemiology and mental disorders: A review. *J Neurol Neurosurg Psychiatry* 1964; 27: 277–290.
  - b. Shepherd M. Epidemiology and clinical psychiatry. *Br J Psychiatry* 1978; 133: 289–298.
  - c. Shepherd M. The application of the epidemiological method in psychiatry. *Acta Psychiatr Scand Suppl* 1982; 296: 9–16.
  - d. Shepherd M. Psychiatric epidemiology and the classification of mental disorder. *Int J Epidemiol* 1982; 11(4): 312–313.
  - e. Shepherd M. Psychiatric epidemiology and epidemiological psychiatry. *Am J Public Health* 1985; 75(3): 275–276.
  - f. Shepherd M. Urban factors in mental disorders – an epidemiological approach. *Br Med Bull* 1984; 40: 401–404.
    - g. Shepherd M. Historical epidemiology and the functional psychoses. *Psychol Med* 1993; 23: 301–304.a.
11. a. Shepherd M. The prevalence and distribution of psychiatric illness in general practice. *J R Coll Gen Pract* 1973; 23(Suppl 2): 16–22
  - b. Shepherd M. General practice, mental illness, and the British National Health. *Am J Public Health* 1974; 64: 230–232.
    - c. Shepherd M. Who should treat mental disorders? *Lancet* 1982; 1(8282): 1173–1175.
    - d. Shepherd M. Mental illness and primary care. *Am J Public Health* 1987; 77: 12–13.
12. a. Shepherd M. A representative psychiatrist: the career and contribution of Sir Aubrey Lewis. *Am J Psychiatry* 1977; 134: 7–13.
  - b. Shephard M. Aubrey Lewis: the making of a psychiatrist. *Br J Psychiatry* 1977; 131: 238–242.
  - c. Shepherd M. From social medicine to social psychiatry: the achievement of Sir Aubrey Lewis. *Psychol Med* 1980; 10: 211–218.
  - d. Shepherd M. A representative psychiatrist: the career, contributions and legacies of Sir Aubrey Lewis. *Psychol Med*

Monogr Suppl. 1986; 10: 1–31.

<sup>13</sup> Jean Starobinski (1920–), Swiss literary critic.

<sup>14</sup> See note 5.

<sup>15</sup> See Russell in note 1.

<sup>16</sup> a. Shepherd M. Kraepelin and modern psychiatry. *Eur Arch Psychiatry Clin Neurosci* 1995; 245:189–195.

b. Shepherd M. The two faces of Emil Kraepelin. *Br J Psychiatry* 1995; 167:174–183.

<sup>17</sup> Shepherd M. Clio and Psyche: the lessons of psychohistory. *J R Soc Med* 1978; 71: 406–412.

<sup>18</sup> See Clare in note 1.

<sup>19</sup> See notes 16 a and b.

<sup>20</sup> Thirty years are almost passed and we still know very little about biological mechanism of depression.

<sup>21</sup> Cadoret RJ, O’Gorman TW, Heywood E, Troughton E. Genetic and environmental factors in major depression. *J Affect Disord* 1985; 9: 155–164.

<sup>22</sup> Several studies by Shepherd indicate that treatments with long-term injections are not superior to oral treatments. In particular, in one there was no difference between the two treatments (Falloon I, Watt DC, Shepherd M. A comparative controlled trial of pimozide and fluphenazine decanoate in the continuation therapy of schizophrenia. *Psychol Med* 1978; 8: 59–70); one more showed that patients on pimozide were significantly more favourably rated on aspects of sociability, use of leisure, warmth of personal relationships, household tasks and child-rearing. (Falloon I, Watt DC, Shepherd M. The social outcome of patients in a trial of long-term continuation therapy in schizophrenia: pimozide vs. fluphenazine. *Psychol Med* 1978; 8: 265–274), and a last one showed that the use of pimozide was associated with improvement in various measures of social outcome (Shepherd M. Medico-social evaluation of the long-term pharmacotherapy of schizophrenia. Comparative study of fluphenazine and pimozide. *Prog Neuropsychopharmacol* 1979; 3: 383–389).

<sup>23</sup> a. Blackwell B, Shepherd M. Prophylactic lithium: another therapeutic myth? An examination of the evidence to date. *Lancet* 1968; 1(7549): 968–971.

b. Shepherd M. A prophylactic myth. *Int J Psychiatry*. 1970-1971; 9: 423–425.

c. Glen IA, Johnson AL, Shepherd M. Continuation therapy with lithium and amitriptyline in unipolar depressive illness: a randomized, double-blind, controlled trial. *Psychol Med* 1984; 14: 37–50.

The controversy is going on still at these days and can be followed in *Lithium Controversy* in Controversies in INHN’s website.

<sup>24</sup> The rather harsh, dismissive, and highly critical paper by Blackwell and Shepherd on the prophylactic effect of lithium actually encouraged another controlled study by Mogens Schou on the prophylactic effect of lithium in mood disorders in which the efficacy of this treatment well demonstrated. Since then, several other studies have confirmed the efficacy of lithium.

December 24, 2015

## **Malcolm Lader's comment on Leonardo Tondo's interview with Michael Shepherd**

I am honoured to have been asked to comment upon this interview of Michael Shepherd with Leonardo Tondo in 1987.

I first met Michael Shepherd in January 1960 when I was interviewed by him for a junior research post. He was co-holder of an NIMH grant with Heinz Schild and Hannah Steinberg. I last met Michael in December 1994 when we were members of an advisory panel invited to Taiwan to discuss mental health facilities with the Taiwanese president. In the 35 intervening years, I was treated by him with exceptional kindness, consideration and help with my career.

The interview is mainly related to Michael Shepherd's epidemiological interests and expertise. But his psychopharmacology interests were also a major part of his activities. Perhaps the best example is his lead authorship of one of the first textbooks of clinical psychopharmacology. I was still a junior doctor when he asked me to collaborate with him on this, together with a biochemist, Richard Rodnight. Michael provided the overall strategy and the philosophy, Richard the technical aspects of biochemical pharmacology, and I worked assiduously writing the clinical aspects. The book was quite successful.

Later, Michael became involved in 2 aspects of psychopharmacology and therapeutics, both concerning long-term therapy. He fuelled the lithium controversy and cast doubt on the superior efficacy of depot neuroleptics. The latter were very extensively used in the UK because of the structural organisation of the National Health Service. I recall numerous discussions with Michael about both topics. We agreed that the model for a prophylactic therapy differed greatly from that of the treatment of an acute illness. The main complication was spontaneous natural remission which would promote the discontinuation in due course of an acute treatment but could lead to indefinite prolongation of a prophylactic treatment with long-term dangers. Michael therefore thought that the burden of proof for long-term treatments had to be greater than for short-term interventions.

After my three years' research training with Schild, Shepherd and Steinberg, I decided to

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undergo the formal three years' of psychiatric training at the Maudsley Hospital. My first year was with Michael. He was a brilliant diagnostician but less proficient in treatment. He was concerned to establish the diagnosis in unequivocal terms and to that end he would carry out lengthy searching interviews that often bewildered the patients. His senior assistant, James Birley, was a sympathetic and humane clinician, who later became president of the Royal College of Psychiatrists. After each ward round we would go round and reassure the disconcerted patients that we would arrange the most appropriate and hopefully up-to-date treatments.

Michael's greatest and most enduring lesson for me was the broadening of the concept of normality. I would suspect some subtle psychopathology but he would show me that this was within the bounds of normality and was really British eccentricity. He was an expert on all sorts of obscure and esoteric cults.

Michael was at great pains to emphasize that hospital psychiatry was only a small and unrepresentative part of wider psychiatry as practised by General Practitioners in the UK National Health Service. He had many contacts and friendships with academic and practising GPs. This led to resentment on the part of his fellow hospital consultants who conspired to oppose him as the successor to Aubrey Lewis in 1966. Instead, the following year he was given a personal Professorship in Epidemiological Psychiatry as a consolation prize. He never forgave his colleagues.

Michael was a shy man who often became quite anxious in company. His main attribute was not to suffer fools gladly but he made this quite obvious instead of trying to hide his exasperation. He spoke and read several languages fluently. He was a true polymath and his knowledge of philosophies and literature was unparalleled. Although critical of American psychiatry (Shepherd 1957), he often spoke fondly of his time in the United States where he made friends who remained close throughout his life.

His anathema was Emil Kraepelin (Shepherd, 1995), whom he regarded as not just a proto-fascist but a proto-Nazi in that his racial prejudices and rigidity provided a pseudoscientific rationale for the World War II atrocities in which mentally ill people were exterminated, as were the Jews and the Roma.

I quickly realised and accepted that I was neither intelligent enough nor eclectic enough to fully appreciate the towering intellect of Michael Shepherd. The only time that I felt any superiority was in Taiwan when it was apparent that he was unable to use chopsticks while I was quite adept.



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Shepherd, M, Lader, M, Rodnight R. *Clinical Psychopharmacology*. London: English Universities Press; 1967.

May 19, 2016

### **Leonardo Tondo's reply to Malcolm Lader's comment**

I deeply appreciate the comments of Malcolm H. Lader, currently Emeritus Professor at the King's College in London. His reflections on Shepherd, with whom he worked for a long time, reveal information on Shepherd's personality. From Lader we learn that Shepherd was strongly attached to his opinions and obsessed with the diagnostic process to the point of forgetting that diagnosing is not just an aimless philosophical exercise that provides little help for patients but is needed for delivering treatment.

From his comments I understand that his mentor dealt with psychopathology somewhat in the realm of British eccentricity and we, continental Europeans, may agree with him although sometimes with a bit of admiration for the overseas lifestyles. Lader confirmed also my impression that Shepherd favored the involvement of general practitioners in the treatment of psychiatric patients, envisioning an attitude more and more common today that is probably also efficient and cost-saving. In fact, minor psychiatric problems may not need a specialist's consultation. I am sorry to know that his view was opposed by the psychiatric establishment that was defending its privileges.

Shepherd criticized American psychiatry because it adopted psychoanalytical theories he considered unsubstantiated and applicable only to some privileged people. On the other hand, Shepherd's criticism of Emil Kraepelin (1856–1926) is uncalled for. The German psychiatrist died years before Hitler became Chancellor in 1933 and Kraepelin's theories on mental illnesses, which may be seen as proto-fascist today or even thirty years ago, represented the prevalent view of a positivistic perspective on psychiatric disorders.

From Lader's comment the portrait of an erudite, multilingual, curious (to the point of leaning

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to esoteric), humane, democratic man emerges, as well as that of a gentleman very fond of his Britishness, and therefore somewhat anti-American.

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*Collated by Olaf Fjetland (September 14, 2017)*