

Ramanujan's illness

D. A. B. Young

A January night in 1913 found the two renowned Cambridge mathematicians G.H. Hardy and J.E. Littlewood, in the latter's rooms in Trinity College, poring over an unsolicited manuscript of mathematical formulae, which had arrived that morning in Hardy's mail. The letter was from a 25-year-old Hindu clerk, Srinivasa Ramanujan (1887-1920), who lived in Madras and was as regards mathematics entirely self-educated. Many mathematicians receive letters from cranks and hoaxers, but it was at once obvious that this author was no crank, since not one of his theorems, as E.H. Neville later pointed out, could have been set in even the most advanced mathematics examination in the world. The suspicion of a hoax by a competent mathematician, where familiar theorems are skillfully disguised, was dispelled by Hardy's recognition that a few of the results defeated him completely; he had never seen anything the least like them before. 'A single look at them is enough to show that they could only be written down by a mathematician of the highest class. When they parted that night both Hardy and Littlewood was comparing him with Jacobi, the great German master of formulae.

This famous episode bore immediate fruit for Ramanujan. Hardy at once joined forces with others in Madras in obtaining a research studentship for him so that he could pursue mathematical research full-time, and in arranging his coming to Trinity College, Cambridge in April 1914 to work with Hardy and to have first-hand contact with European mathematicians.

The war and Ramanujan's life in Cambridge.

These intentions were frustrated by the outbreak of war within four months of his arrival in England. Contact with much of continental mathematics abruptly ceased, and soon many Cambridge mathematicians, most significantly Littlewood, left on war service.

Another consequence, slower in impact but more serious for Ramanujan's well-being, was food shortages, especially of Indian comestibles. He was a Brahmin Hindu and strict vegetarian, and although in coming to England he had compromised certain Brahminical strictures including crossing the seas, he remained punctilious about dietary observance. In the absence of another Brahmin to cook for him, he had to buy and cook all his food. If he had established a routine in his life, he could have coped. But he was obsessional about his research, working for 30 hours at a stretch and then sleeping for 20. 'Cooking only once a day or two', as Alice Neville remembers his habit, must have resulted in malnutrition.

For three years his own mathematical research and that with Hardy resulted in a rapid succession of papers of the highest quality; and then, as Hardy states, things went wrong:

It was in the spring of 1917 that Ramanujan first appeared to the unwell. He went into a Nursing Home at Cambridge in the early summer, and was never out of bed

for any length of time again. He was in sanatoria at Wells, at Matlock, and in London, and it was not until the autumn of 1918 that he showed any decided symptom of improvement. Early in 1919 he had recovered, it seemed, sufficiently for the voyage home to India, and the best medical opinion held out hopes of a permanent restoration.

However, the improvement was short-lived. By the time he landed in Bombay at the end of March 1919 he had a relapse and his health deteriorated remorselessly until his death in April 1920. The best medical opinion had been quickly contradicted; clearly, the correct diagnosis had not been made. What then was the correct one?

The mis-diagnosis of tuberculosis

Many may wonder that any mystery attends Ramanujan's illness, for until 1984 it was generally believed that tuberculosis was the cause of death, and that his illness had been explicitly treated as such in the various English sanatoria and nursing homes. However that diagnosis originated, not in England, but in India with Dr P. Chandrasekhar of the Madras Medical College, who attended Ramanujan from September 1919 until his death on 26 April 1920. The ever-worsening emaciation and pulmonary symptoms that followed his relapse on arriving in India have been powerfully persuasive. The verdict of the English doctors was quite the opposite, but its publication had to wait until Rankin brought the hitherto unpublished material together in his 1984 papers. It quite clearly contradicts, for example, the statement in Ranganathan's book that 'by the end of 1918, it was definitely known that tuberculosis had set in'. It was disappointing that it was set in. It was disappointing, therefore, that Kanigel in his biography, although acknowledging the doubts, nevertheless chose to perpetuate the undue emphasis on tuberculosis.

Ramanujan's medical treatment in England

In May 1917 Ramanujan was admitted to the Nursing Hostel in Thompson's Lane, Cambridge. He left there on 20 September, but remained in Cambridge. Early in October he went briefly (2-3 weeks) to the Mendip Hills Sanatorium, near Wells in Somerset. In November, after a short break spent in Cambridge and London, he entered the Matlock House Sanatorium, at Matlock House Sanatorium, at Matlock in Derbyshire. Like Mendip Hills, this was a sanatorium for patients with tuberculosis, although it was a much more professional establishment. Ramanujan was a patient of Dr. L. Ram, but was in the immediate care of the medical superintendent, Dr F. Kincaid.

At some time after the end of June 1918 Ramanujan left Matlock and entered Fitzroy House, a hospital in Fitzroy Square in central London, a situation permitting greater access to medical expertise. According to a letter dated 26 November 1918 from Hardy to Francis Dewsbury of Madras University, Ramanujan had been in London for the previous few months and had seen several specialists. Towards the end of the year he moved into Colinette House, a private nursing home in Putney, south-west London. Hardy's well-known story of the taxi-cab Number 1729 relates to his visit to Ramanujan in this nursing home. About a month later, on 24 February, he was well enough to attend to the business

of obtaining his passport and had his photograph taken. On 13 March 1919 he boarded the P&O ship Nagaya for Bombay.

Unfortunately, no official medical records of Ramanujan's illness during his time in England have survived, so any attempt to a retrospective diagnosis must depend on information in letters and reminiscences.

The only account we have that approaches a description of the illness is in a letter from Hardy written in February 1918 to Sir Joseph Thomson:

Batty Shaw found out, what other doctors didn't know, that he had undergone an operation about 4 years ago [actually 8 years]. His worst theory was that this had really been for the removal of a malignant growth, wrongly diagnosed. In view of the fact that Ramanujan is no worse than 6 months ago, he has now abandoned this theory – the other doctors never gave it any support.

Tubercle has been the provisionally accepted theory, apart from this, since the original idea of gastric ulcer was given up. There is a perfectly regular rise a temperature every night, and persistent weakness. But there is certainly no crude lung trouble: no coughing or spitting. And Dr. Kincaid, who runs Matlock, told me he is quite doubtful still, thought it might be some obscure Oriental germ trouble imperfectly studied at present.

This brief account can be supplemented from other sources. With regard to the night-time fever, Ramanujan began a letter in June 1918 to a recent visitor: 'the whole of last night I had a fever and my temperature this morning was about 102°[F]. Such a prominent reference suggests this symptom was no longer a regular feature; and it had disappeared by November 1918, when Hardy wrote to Dewsbury:

There is at last, I am profoundly glad to say, a quite definite change for the better. I think we may now hope that he has turned the corner, and is on the road to a real recovery. His temperature has ceased to be irregular, and he has gained nearly a stone in weight. The consensus of medical opinion is that he has been suffering from some obscure source of blood poisoning, which has now dried up; and that it is reasonable to expect him to recover his health completely and if all goes well fairly rapidly.

His relapse on the return to India must have brought a return of the fevers, since the confident diagnosis was that of tuberculosis.

Pain is a symptom only implied by Hardy in his account, i.e. the mention of gastric ulcer. Obviously there must have been severe and characteristic pain to have given rise to that diagnosis. In contrast, in India Pain was a prominent symptom, and his wife remembered that he often complained of severe pain in the stomach.

A significant symptom was loss of weight leading to emaciation. Before his illness Ramanujan was stout. But by June 1918 he had lost so much weight that a visitor who had not seen him since 1914 reported to Hardy that he was shocked to find him so weak and emaciated. As we have seen, he had gained weight by November and his condition continued to improve until he left for India. Yet the passport photograph taken in February 1919 shows him much thinner than before his illness, his clothes being far too large for his shrunken frame. On his arrival in India his old friends were disturbed by how thin and ill he looked and his wife seeing him so emaciated and coughing up phlegm, a new symptom, realized how sick he was. She described him as being towards the end 'only skin and bone'.

The illness: analysis

Although we have but little information about Ramanujan's illness, there is much that can be inferred from it. The illness began with an acute episode that was diagnosed as gastric ulcer. Later, the condition eased and the symptomatology must have changed significantly, for this diagnosis was rejected and that of tuberculosis favoured. The sign prompting this was probably the onset of intermittent pyrexia, which eventually became the regular nighttime fevers described by Hardy. Intermittent pyrexia is found in a group of otherwise diverse diseases, by far the most important of which at that time was tuberculosis. Expert opinion was accordingly sought from Dr H. Batty Shaw (1867-1936), a London specialist in consumption and chest diseases. His verdict, given probably in August 1917, was that it was not tuberculosis but metastatic liver cancer, derived, he believed, from a malignancy of the scrotum excised some years before. Time proved him wrong, but it must be very significant that he did not favour tuberculosis. By the summer the bouts of intermittent fever had become less frequent, and they ceased altogether during Ramanujan's stay at Fitzroy Square. Here, doubtless, advantage was taken of the wealth of medical expertise and facilities available in London. The consensus of medical opinion mentioned by Hardy in his November letter, namely that Ramanujan had been suffering from some obscure source of blood poisoning, entails that, at a minimum, blood counts were carried out. These are procedures that were, even then, a matter of routine. Then following discussion is a diagnosis by exclusion, and is limited to clinical detail and diagnostic procedures available in 1918, as presented in the 1917 edition of Munro's textbook.

Blood poisoning here would refer to septicaemia or toxaemia due to either an abscess or a source of inflammation. Both would give rise to intermittent pyrexia, but more specifically to neutrophil leucocytosis, an absolute increase in the polymorphonuclear fraction of the white blood cells. This fact would rule out several other diseases associated with intermittent pyrexia: tuberculosis, brucellosis, kala-azar (an example of Dr Kincaid's 'obscure Oriental germ') and pernicious anaemia. The last, whether due to absence of intrinsic factor or to a dietary deficiency of vitamin B₁₂, causes symptoms similar to Ramanujan's and has been suggested as a diagnosis. Malaria must also have been considered and blood smears examined accordingly, together with the sensitivity of the fever to quinine.

In four other diseases, however, intermittent pyrexia is accompanied by neutrophil leucocytosis. The first is subacute bacterial endocarditis; but although signs of cardiac involvement may not be seen at the outset, eventually evidence of valvular disease together with petechiae and bacteriaemia (proved by blood culture) would permit a correct diagnosis. The second is Hodgkin's disease (lymphadenoma); but enlargement of the lymphatic glands is characteristic and biopsy of them was prescribed for a definite diagnosis. The third is metastatic cancer of the liver, which was Dr Shaw's diagnosis in 1917. This argues strongly for blood counts having been carried out at the Nursing Hostel in Cambridge, and would account for Dr Shaw's scepticism about tuberculosis. That Dr Shaw made the diagnosis of secondary liver cancer in August 1917 means that Ramanujan's symptoms then included pain, continuous and not related to food, and enlargement and tenderness of the liver. The character of the pain must have changed from the found in May/June 1917 when gastric ulcer was diagnosed and accounts, along with the onset of intermittent pyrexia, for the rejection of that diagnosis. Jaundice is eventually an invariable consequence of liver cancer and its failure to appear, together with Ramanujan's survival beyond 6-12 months, would suffice to eliminate liver cancer.

The fourth disease is hepatic amoebiasis and the fact that it has been arrived at here by a process of elimination should not disguise the high probability that it could have been the cause of intermittent fever in someone of Ramanujan's background. For as a 'Always suspect hepatic amoebiasis in a patient with obscure pyrexia coming to me would be pain with tenderness in epigastrium, enlargement of the liver, and weakness. Progressive emaciation leading to cachexia is characteristic of the disease. If hepatic amoebiasis was suspected, the effect of emetine for 8-10 days on the patient's symptoms was the easiest way to confirm the diagnosis; and it remains so today, although metronidazole would now be preferred to emetine. It should be noted that although hepatic amoebiasis was not diagnosed in Ramanujan's case, it is contained in the comprehensive diagnosis of blood poisoning, for the 'obscure source' of toxæmia would be the amoebic abscess in the liver. Lastly, remembering Dr Shaw's diagnosis, it is of interest that in the differential diagnosis of hepatic amoebiasis, carcinoma of the liver may cause great difficulties.

Ramanujan and amoebiasis

Amoebiasis is a protozoal infection of the large intestine that gives rise to dysentery. The disease is widespread in India, particularly in and around the large coastal cities of Calcutta, Bombay and Madras. The prevalence of the disease, though very high, is imprecisely known since most of those infected are symptomless carriers, who are responsible for the spread of the disease through excretion of the cystic form of the amoeba.

Although Ramanujan was born and grew to manhood in the Madras region, he went to live in Madras for the first time only when he left home in 1906. He was attending senior school again when, in the second half of the year, he contracted a bad bout of dysentery that forced him to return home for three months. This was probably amoebic dysentery, the most common form in India at the time, where the onset is usually gradual and the symptoms progressive but generally limited to abdominal discomfort and some diarrhoea,

often preceding frank dysentery by days or weeks. The dysentery may then continue for several weeks before subsiding, in many cases only to reappear in one or more mild dysenteric episodes. Constitutional disturbance is often surprisingly slight, the patient usually remains ambulant and might well be able to make a journey of 200 miles. Bacillary dysentery, in contrast, is sudden in onset and is accompanied by fairly high fever, vomiting, intense abdominal symptoms, dehydration and headache. The patient inevitably takes to bed, and it seems unlikely that he would either be able or want to attempt a long journey. The disease usually clears up spontaneously in 7-14 days and recovery is rapid.

Amoebiasis, unless adequately treated, is a permanent infection, although many patients may go for long periods with no overt signs of the disease. Relapses occur when the host-parasite relationship is disturbed. Ramanujan experienced such a relapse, I believe, in 1909 when according to his friend R.R. Ayyar:

Ramanujan, who was living in [Madras], became seriously ill... As a patient he was obstinate and a patient ... he was obstinate and would not drink hot water and insisted on eating grapes which were sour and bad for him. [The doctor] after examining him, asked me to send him to his parents as his condition required constant nursing.

How ill Ramanujan felt at this time is indicated by his giving his host for safe keeping the two large notebooks he kept with him all the time and in which he had been recording his mathematical results; the same notebooks that are now famous as a major legacy of his genius.

Later that same year (1909), while still at home with his family, he developed a hydrocele, which was operated on in January 1910. The condition seems to have had some urgency, which is unusual for a newly-developed hydrocele, and it could in fact have been a lesion arising from the relapse, for amoebae can spread into adjacent tissues in the anogenital area. This can occur either internally to cause abscesses (examples have been reported for both epididymis and testis IS, 23.26), or more frequently externally through a skin abrasion to cause ulceration, which may give rise to an amoeboma. The last is a granulomatous tumour closely resembling a neoplasm, satisfactory treatment of which, despite the efficacy of modern amoebicides, may still require excision. Dr Shaw's suspicion that the operation was the excision of a malignant growth, depending as it must have done on Ramanujan's exact description of the lesion, certainly favours the explanation of a scrotal amoeboma rather than a hydrocele.

When in the spring of 1917 Ramanujan became acutely ill, gastric ulcer was diagnosed. This could have been a recurrence of intestinal amoebiasis, this time in the transverse colon, where it can give rise to symptoms closely resembling those of gastric ulcer, but without dysentery. This could have then led to hepatic amoebiasis, with the changed symptomatology already discussed.

However, since the clinical picture of hepatic amoebiasis rarely develops during an intestinal attack and is well known for arising many years after the last relapse, it is more

likely that the acute illness was the onset of the hepatic disease. Furthermore, malnutrition is said to predispose for this complication and was a worrying feature of Ramanujan's life in the months before his illness. The hepatic disease begins when amoebae carried via the portal circulation from asymptomatic intestinal lesions form foci of infection in the liver. These foci enlarge and coalesce to form a small abscess. The contents, which are the products of tissue necrosis, are largely free of amoebae. The latter are found in the tissue immediately surrounding the abscess, actively enlarging it by cytolysis. At some stage there will be an onset of symptoms; in the abrupt form, these include low-grade fever, liver enlargement with pain and tenderness (often felt in the epigastrium), anorexia, nausea and vomiting, and moderate neutrophil leucocytosis. This corresponds to Ramanujan's condition in the Cambridge nursing home. As the abscess enlarges, the fever becomes more marked and takes on an intermittent character, until a regular diurnal intermittent fever (38.7-40°C) peaking at 10 pm is established, with night sweats, insomnia, anorexia, malaise, weakness due to secondary anaemia, a marked loss of weight and a greater degree of leucocytosis. This corresponds to his condition at Matlock during the winter of 1918.

Contrary to expectations in untreated hepatic amoebiasis Ramanujan's condition improved in late 1918. Fever gradually disappeared, there was gain in weight and strength, and leucocytosis must have been much reduced since the verdict was that the source of blood poisoning had dried up. A spontaneous resolution of a liver abscess without amoebicide therapy is said to be infrequent, although in this case, of course, it was only temporary. The destructive action of the amoebae was successfully countered for a time by reparative processes, involving fibrous encapsulation of the abscess and gradual resorption of the contents. These in turn depend on host immunity and the latter might have been enhanced by the regime of bed rest at Matlock and at Fitzroy Square, for in hepatic amoebiasis 'absolute rest in bed is necessary'. The activities associated with departure for India, followed by the two-week voyage itself, broke the nursing pattern of the previous 15 months and altered whatever factor, whether rest, diet or another, which had permitted the partial recovery. When Ramanujan disembarked at Bombay on 27 March 1919, it was clear to his family that he was a very sick man. The new symptom of productive cough, which soon developed, indicates that pleuropulmonary involvement had begun. This is usually pleurisy with effusion, often with partial collapse of the basilar lung; later the liver abscess may extend or rupture into the lung itself, leading to consolidation and abscess formation, or less often into the pleural cavity causing empyema. Fever, pain, cough, dyspnoea, weakness and extreme emaciation are the main symptoms of this terminal stage of amoebiasis.

Attempted suicide

It has become generally known that Ramanujan attempted suicide in late 1917 or early 1918 by throwing himself in front of a train at a London underground station. Fortunately, he suffered only superficial leg wounds. Since attempted suicide was then a criminal offence he was arrested, but charges were dropped after Hardy had personally intervened on his behalf. But our knowledge of that event depends entirely on the witness

of Hardy. One evening in 1936 he appeared late at dinner in Trinity bandaged, and when questioned told the following story to his fellow diners, who included the cosmologist S. Chandrasekhar. He had gone to Scotland Yard after being the victim of a road accident in London. While there he met a senior police officer, who taxed Hardy with having once given him false evidence. The officer then revealed that he had handled the arrest of Ramanujan for attempted suicide and that Hardy had intervened by telling the police that Ramanujan could not be arrested since he was an F.R.S. Ramanujan was released; but not, the officer emphasized, because the police were bluffed by Hardy's assertion, for they had known all along that Hardy was lying and 'had perjured' himself by stating that Ramanujan was an F.R.S., whereas in fact he did not become a Fellow until a month later. But the officer assured Hardy that he was not going to be arrested. Since Ramanujan's election to the Royal Society was on 28 February 1918, this apparently dates the event at the start of that month.

But why did Hardy reveal such details in this way 16 years after more, colleague's death? Much of the story is surely fanciful. Hardy would never have expected the police to believe that being an F.R.S. would confer immunity from arrest; a police officer would be most unlikely to accuse 18 years later a arrest character referee of lying in a police interview; the term perjury would have been legally incorrect and the mention of arrest was ridiculous. What was true, I believe, was that Hardy met a senior policeman, probably approaching retirement, who had been involved in the arrest and who asked about Ramanujan's subsequent history. Worried that the full story might be made public, Hardy decided out of deep concern for his friend's posthumous reputation to lessen the opprobrium associated with attempt suicide by maintaining that the police quickly released Ramanujan, without further action. Whereas, as I shall try to show, Ramanujan was conditionally discharged, the condition being his confinement under medical supervision for at least 12 months.

Nandy gives an earlier date for the event, the second half of 1917. This is much more reasonable, because by February Ramanujan's intermittent fever had become a daily occurrence and he would have been too ill to travel from Matlock to London and wander about that city in winter. The likely sequence of events is as follows. Early in October Ramanujan went to the Mendip Hills sanatorium. While there he heard of his failure to obtain a Trinity fellowship. Disappointed over this, despondent at the effect of illness on his mathematical work, and probably dissatisfied with conditions of Mendip Hills, he went to stay in London. It was probably on this occasion that, fleeing from a boarding house because he had inadvertently drunk there a beverage containing eggs, he was caught up in a heavy bombing raid. Such an air raid occurred on 19 October 1917, in which 27 people were killed. Ramanujan at the time said he regarded the raid as 'punishment meted out to him by God for having partaken of anything non-vegetarian'. This response suggests a pathological state of mind, and Hardy once said of Ramanujan 'he was (except for a period when his mental equilibrium was definitely upset by illness) a very shrewd and sensible person; further more, there are references to his fits of depression in late 1917 and early 1918. Chronic amoebiasis is an illness that upsets mental equilibrium and can give rise to depression.

It was, I suggest, at this time that Ramanujan attempted suicide. After his arrest, it would be recognized that he was physically ill and that this had contributed to, if not caused, his

depression with suicidal tendencies. Charges may well have been dropped conditionally on his entering a hospital, probably remote from London, under full-time medical supervision and his remaining there for a specified time (e.g. 12 months) or until fully recovered. Hardy may have agreed to be responsible for Ramanujan's compliance with this arrangement. It so happens there is evidence of such a commitment in a letter from A.S. Ram to Hardy, 23 June 1918. Mr Ram, who had visited Ramanujan at Matlock a week before, was worried both by his physical state and by the food provided, and also perplexed by his submissive acceptance of the situation:

Ramanujan has wrong notions of what is meant by Sanatorium and Nursing Home ... [He] seems to have been somewhat cowed down by Dr Ram, who seems to have told him 'As long as you are a patient and not well you are not free and the doctor has control over your movements'. Besides I do not know how Ramanujan got into his head the impression that Dr Ram had told him or given him to understand that Ramanujan had by some agreement to stay at Matlock sanatorium at least 12 months. Anyway before I could think of shifting Ramanujan I was advised by Ramanujan to consult both Dr Ram and Prof. Hardy (i.e. yourself)... Ramanujan is pretty keen on moving to somewhere near London but feels helpless to carry out his desire.

When Mr Ram spoke to Dr Ram, the latter made it clear that he had made no agreement whatever as to the length of time Ramanujan should stay at Matlock. Later in the same letter Mr Ram, when discussing the possibility of moving Ramanujan elsewhere in England, says: 'Do you think you can still fall on your first offer from Bournemouth? I mean the one that Ramanujan had to go to, if Dr Ram had not brought him to [Matlock].'

It is clear from this that Hardy bore the responsibility for deciding where Ramanujan stayed and that there was also a period of residency to fulfil. Hardy's response to Mr Ram's letter was to effect Ramanujan's transfer from Matlock to Fitzroy House, a hospital in London. There he stayed until November, 12 months after the move to Matlock, before going into a nursing home.

Conclusion

Two questions will inevitably arise from the suggested diagnosis of hepatic amoebiasis; namely, why the diagnosis was not made at the time and what prospect of a cure could there have been.

Hepatic amoebiasis was regarded in 1918 as a tropical disease ('tropical liver abscess'), and this would have had important implications for successful diagnosis, especially in provincial medical centres. Furthermore, the specialists called in were experts in either tuberculosis or gastric medicine. Another major difficulty is that a patient with this disease would not, unless specifically asked, recall as relevant that he had had two episodes of dysentery 11 and 8 years before. Finally, there is the very good reason that, because of the great variability in physical findings, the diagnosis was difficult in 1918 and remains so today: hepatic amoebiasis 'presents a severe challenge to the diagnostic

skills of the clinician... [and] should be considered in any patient with fever and an abnormal abdominal examination coming from an endemic area'. This same admonition was made by Savill in 1930 but not in earlier editions of his book (e.g. that of 1918).

The treatment available in 1917 was essentially the same as that in 1962, namely administration of emetine with aspiration of any detectable abscess. In recent years the use of metronidazole has been preferred, generally without the need for aspiration. Emetine alone would probably have cured Ramanujan in 1917, and perhaps as late as his departure for India. Since the abscess must have enlarged rapidly thereafter aspiration would have been essential. Pulmonary amoebiasis responds well to emetine, so that unless secondary infection or empyema had occurred, emetine and aspiration might have effected a cure as late as January 1920, when Ramanujan wrote for a last time to Hardy, full of hope, wanting to subscribe to new journals and still producing mathematics of very high quality.