

Crohn's disease and the timing of discovery

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In 1932 Drs Crohn, Ginzburg and Oppenheimer described the chronic granulomatous condition of the intestine that came to be known as Crohn's Disease. Dr Crohn was a leading gastroenterologist at the Mt Sinai Hospital in New York when he made his observation and reported the Mt Sinai experience at the American Medical Association Meeting in New Orleans in 1932. The Mt Sinai Hospital had been the professional home for the 48 year old Dr Crohn ever since he finished medical school at Columbia University. The hospital was founded in 1852 and had expanded far beyond its original intent to serve Jewish immigrants and citizens to be a powerhouse of academic medicine. In 1932 the hospital would have been in deep discussion about terrible rumors from Europe about anti-Semitism. The next year Mt. Sinai would begin resettling émigré physicians displaced by events in Europe and later would field the Mt Sinai Third General Hospital in the war in North Africa.

In this essay three questions are posed. Was 1932 a good year for discovery? Second, if Crohn's Disease is a fairly common disease why did it take so long to discover? Or was it such a tough clinical problem that its discovery even in 1932 especially prescient?

In 1932 the economy of the planet was terrible. Germany had never recovered from the First World War and after the stock market crash in the US in late October 1929

matters just seemed to slide down in ruin. By 1932 there was no recovery. In that year the unemployment rate in the US was 24.1% and the Dow Jones stock average reached its nadir of 41. There were bread lines, soup kitchens and the drought of 1930-1936 was displacing many thousands of Americans from the ruined dust bowl lands of the Midwest seeking something better in California. The nation and the world had a lot to think about in 1932 and little of it was optimistic.

New York City was a little better off. The huge number of immigrants from Eastern Europe and Italy had tapered and the terrible immigrant slums and tenements were actually getting better with an improvement in public health. Mayor Jimmy Walker resigned in the midst of a corruption scandal, but Radio City Music Hall opened in 1932 and the New York Yankees Baseball Team won the World Series. Still New York was hardly privileged and poverty was rampant with high anxiety about the future of the economy or for that matter of civilization itself. New York was home to every possible political nuance including communism. Russia was having its worst famine in history but socialism still attracted thousands.

In 1932 Romania was in the period of Greater Romania with a huge land area of almost 300,000 square km. King Carol II ruled under the 1923 constitution that assured a liberal constitutional monarchy. The journal *Chirurgia* was in its thirty-fifth year since its inception. Romania was ably represented at the 1932 Winter Olympics by four athletes in bobsled events at Lake Placid in New York. However, Romania shared the economic pain of the world with a drop in agricultural exports of 56% from 1929 to 1934 and a general moratorium on debt payments in 1932.

Geopolitics in 1932 was a dreadful matter. Japan occupied Shanghai and declared Manchuria independent. Adolph Hitler gained German citizenship through naturalization. His venomous philosophy was getting steadily stronger and would

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take the government the next year. Franklin Roosevelt was elected president in the US and began the exasperating process of trying to restart the US economy. Ramsay MacDonald was the prime minister to King George V, Joseph Stalin was in demonic control in Russia and Mussolini had embarked on empire building from Italy. This should have been a very bad year to be creative.

However arts were active. Maurice Ravel introduced his *Concerto in G* and Faulkner published "Light in August". Pearl Buck published "The Good Earth" and Broadway was lively even in making fun of the depression. Irving Berlin put out "Face the Music" while "Buddy can you spare a dime?" was another hit song. Paul Robeson starred in a revival of *Showboat* under the auspices of Ziegfeld. The Metropolitan Opera was directed by Tullio Serafin and Arturo Toscanini conducted the New York Philharmonic Symphony. George Enescu would premier "Oedipe" in 1936 and the number of composers and writers in Romania was enormous in a period of great cultural vigor. The Polaroid camera was invented as was the radiotelescope. It is actually striking how much intellectual activity goes on in terrible times. Perhaps creativity is an escape from the ugly reality of a world gone mad. The Nobel Prizes were to Werner Heisenberg for Physics (uncertainty principle) and John Galsworthy for literature (Forsyth Saga). Physiology and Medicine went to Adrian for electrophysiology.

Was 1932 a good year for discovery? No. There was no money, geopolitics was a disaster, and there were huge population shifts. There was hopelessness despair everywhere. War revolution, depression, fascism, communism, colonialism and racism were everywhere or threatened. However, such dreadful times may allow the most creative minds to take flight in escape and make the world a better place despite itself.

Let us turn to the second question. If granulomatous enteritis is so common why did it take so long to discover this entity? The simplest answer is tuberculosis. Tuberculous enteritis is a chronic granulomatous infection of the ileum and colon associated with stricture, perforation and fistula. Since 50%-90% of persons with untreated pulmonary tuberculosis will have intestinal involvement. Tuberculosis was a disease of poor housing, poor nutrition in the main although anyone could fall victim. In 199932 New York was solving its problems with bad housing in important ways. As tuberculosis declined in the city the distinct entity we now know as Crohn's was ready for an astute clinician to recognize its properties.

Tuberculosis has been recognized in bony involvement from mummies from 2400 BC. Mummies from the Paraca-Caverna Culture in Peru manifested tuberculosis as well. And yet the mycobacterium responsible for the disease was not recognized until 1882 in the work of Robert Koch. TB can be pulmonary, intestinal, osseous or military. It is usually acquired by respiratory contamination but can be transmitted by milk. Isolation of the patient was recognized in the early 20th

century leading to sanatoria in Europe and the US where fresh air, ample nutrition and rest were the mainstay. Laws against spitting were added and perhaps that helped somehow. However, after the work of Roentgen TB could be diagnosed on chest x-ray and the organism itself could be recognized as the acid fast bacillus in microscopy. The end of tuberculosis was attended by great accuracy in its recognition. However, the main deterrent was problem better ventilated housing with lower density of people who had a better diet. There was no specific treatment for tuberculosis until the development of streptomycin in 1943 followed by para-aminosalicylate in 1949 isoniazid, ethambutol, etc. in the coming years. However, the decline of TB preceded proper drug treatment by many years and cannot be truly credited to treatment. In 1850 the deaths due to TB of all deaths in Europe accounted for 500/100,000 while in 1950 accounted for only 50/100,000. From the time of identification of the tubercle bacillus until drug treatment the death rate from TB had dropped by half in England and Wales. TB mortality in New York was 338/100,000 in 1900, 149 in 1920 and 90 in 1930. I would submit that the sharp decline in tuberculosis made the enteritis that was seen occasionally at Mt Sinai stand out to the prepared clinical eye. All the patients described in the original paper had been surgical patients who had required some sort of operative intervention for resection, drainage, etc. Even with the disease identified and named there was no specific treatment and it was sadly recognized that repeated surgery might be required as the pathology skipped about the intestinal tract.

If the striking prevalence of intestinal TB explains why it took so long to recognize a common disease that might have been around as long as TB, let us probe whether or not the recognition of Crohn's Disease in 1932 represented any huge leap of logic and insightful observation. The answer to that is an emphatic "yes". Dr Crohn and his colleagues made their observations just as the conflicting diagnosis of tuberculosis was on the wane and long before effective drug therapy for the old nemesis. Their discovery was a solid piece of clinical science that changed the world of gastroenterology long before molecular medicine. It should be noted also that their observations remain unchallenged as we enter another century seeking better ways to recognize, treat, rehabilitate and perhaps even prevent this dreaded disease.

1932 was a very difficult and trying time for the world. Discovery cannot wait for peace and may even be encouraged by chaos as bright minds seek refuge. After all Beethoven wrote sublime music during a Napoleonic barrage and Ann Frank's diary is truly the story of a special young woman and not one of the horror or the war. By the way the need for clinical astuteness has not passed. Tuberculosis is of course making resurgence and the next time you see terminal ileitis with a perforation but there is a strange absence of the creeping fat, stop and think. Could this be tuberculosis?