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A century of *Toxoplasma* research

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One hundred years ago Charles Nicolle and Louis Manceaux published the definitive description of the protozoan parasite *Toxoplasma gondii* (Nicolle and Manceaux, 1909). Although this publication represents the authoritative definition of *T. gondii*, it was founded on their earlier attempts, and those of Alfonso Splendore, to classify this parasite (Nicolle, 1907; Nicolle and Manceaux, 1908). This initial difficulty in describing *T. gondii* foreshadows the many years following, where it remained a parasite of “doubtful nature” (Wenyon, 1926). *Toxoplasma* research has experienced periods of relatively slow progress since 1909, but the times during which work on the parasite appears to have languished are punctuated by technical developments and biological discoveries. During the past 25 years, our understanding of *T. gondii* and its impact on other infectious diseases has accelerated to a point where apparent fallow periods of research may be measured in weeks or months rather than years or decades. Historical perspective allows us to consider the context in which the seminal work and discoveries were made. Each of the historical reviews in this collection provides such a framework for a key area of study, in some cases with first-hand accounts of how timing, personality and serendipity all played a role in advancing investigations.

In 1908, Splendore insightfully (and optimistically) wrote “I think that it is impossible to determine a specific classification of this new protozoa[n] before elucidation of the whole life cycle, and I hope to discover this in my future research....” (Splendore, 1908). He was indeed correct: definition of the entire life cycle was essential to establish that *Toxoplasma* is a coccidian parasite, but sadly, he was not able to clarify the process during his research career. Nevertheless, Splendore's vision captures the essence of subsequent *Toxoplasma* research. In this issue of the International Journal for Parasitology, we reproduce translations of the original articles of Splendore, Nicolle and Manceaux which were published in 1978 in a collection entitled ‘Tropical Medicine and Parasitology: Classic Investigations’ edited by B. H. Kean and others (Kean et al., 1978). To set the stage for other reviews presented here, a discussion focused on the circumstances of the discovery of *Toxoplasma* and other early investigations of parasite behavior, provides context for the questions and problems that were to be solved over the ensuing decades (Morrisette and Ajioka, 2009). This is followed by articles by David Ferguson and by J. P. Dubey (Ferguson, 2009; Dubey, 2009) that describe discovery of the *Toxoplasma* sexual cycle which took place approximately 60 years after Splendore's prophetic words. Technical advances in microscopy promoted the ultrastructural studies that defined

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many of the organelles that are characteristic of this phylum, and these descriptions were key to grouping *Toxoplasma* with other apicomplexan parasites (Dubremetz and Ferguson, 2009). The medical history of *Toxoplasma* really began 20 years after the parasite was first observed as an infection in rabbits and gundis and another 50 years passed before *Toxoplasma* took on an unexpected and dangerously widespread role as an opportunistic infection in AIDS patients (Weiss and Dubey, 2009). To document our ever-increasing knowledge of the components that drive pathogenesis, the next articles in this special issue detail the relationship between *Toxoplasma* and its host (Boyle and Radke, 2009), the development of genetic methods to study these parasites (Sibley, 2009), and genetic diversity of *Toxoplasma* strains (Grigg and Sundar, 2009). As a coda for this collection of articles, John Boothroyd provides a perspective on the most surprising and illuminating discoveries in the last 25 years of research on *Toxoplasma*, with a look to the questions that will occupy *Toxoplasma* researchers in the next century (Boothroyd, 2009).

Ironically, none of the original pioneering scientists lived long enough to enjoy the real fruits of their discovery, but would undoubtedly be pleased to see the contribution of *T. gondii* research on our current understanding of infectious disease. If Charles Nicolle were alive today, he would likely consider the discovery of *T. gondii* on par with his Nobel prize-winning work on the transmission of typhus (Nicolle et al., 1909). The articles here pay homage to all of the scientists that have contributed to *Toxoplasma* research over the past 100 years and are dedicated to those that will continue this legacy.

References

- Boothroyd JC. *Toxoplasma gondii*: 25 years and 25 major advances for the field. Int J Parasitol. 2009in this issue
- Boyle JP, Radke JR. A history of studies that examine the interactions of *Toxoplasma* with its host cell: Emphasis on in vitro models. Int J Parasitol. 2009in this issue
- Dubremetz JF, Ferguson DJP. The role played by electron microscopy in advancing our understanding of *Toxoplasma gondii* and other apicomplexans. Int J Parasitol. 2009in this issue
- Dubey JP. History of the discovery of the life cycle of *Toxoplasma gondii*. Int J Parasitol. 2009in this issue
- Ferguson DJP. Identification of faecal transmission of *Toxoplasma gondii*: Small science, large characters. Int J Parasitol. 2009in this issue
- Grigg ME, Sundar N. Sexual recombination punctuated by outbreaks and clonal expansions predicts *Toxoplasma gondii* population genetics. Int J Parasitol. 2009in this issue
- Kean, BH.; Mott, E.; Russell, A., editors. Tropical medicine & parasitology: Classic investigations. Cornell University Press; New York: 1978.
- Morrisette NS, Ajioka JW. The early years of *Toxoplasma* research: What's past is prologue. Int J Parasitol. 2009in this issue
- Nicolle C. Sur une piroplasmose nouvelle d'un rongeur. CR Soc Biol 1907;63:213–216.
- Nicolle CM. Recherches expérimentales sur le Typhus exanthématique. Annales de L'Institute Pasteur 1909;24:243–275.
- Nicolle C, Manceaux L. Sur une infection á corps de Leishman (ou organismes voisins) du gondi. CR Acad Sci 1908;147:763.
- Nicolle C, Manceaux L. Sur un protozoaire nouveau du gondi. CR Acad Sci 1909;148:369.
- Sibley LD. Development of Forward Genetics in *Toxoplasma gondii*. Int J Parasitol. 2009in this issue
- Splendore A. Un nuovo protozoa parassita de' conigli. incontrato nelle lesioni anatomiche d'une malattia che ricorda in molti punti il Kala-azar dell' uomo. Nota preliminare pel. Rev Soc Scient Sao Paulo 1908;3:109–112.
- Weiss LM, Dubey JP. Toxoplasmosis: a history of clinical observations. Int J Parasitol. 2009in this issue
- Wenyon, CM. Protozoology, a manual for medical men, veterinarians and zoologists. Baillière, Tinadall and Cox; London, UK: 1926. Parasites of doubtful nature; p. 1041-1047.