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Mapping the methodologies of Burkitt lymphoma

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ABSTRACT

While recent accounts have emphasised the planned, large-scale and systematic character of cancer virus research in the mid-C20, I argue here that a distinctive kind of small-scale scientific research existed, and made a distinctive contribution to the development of the field as a whole. Using the case of the research carried out to understand the causes of Burkitt lymphoma in Africa during the 1960s, I highlight two distinctive practices—geographical mapping and the re-purposing of existing disease infrastructure—that played a central role in this episode. My intention here is threefold: first, I will argue that this research is unlike the research practices usually identified as typical 'big science' research concerning cancer viruses, particularly in the United States. Second, I will argue that this kind of research is also clearly distinct from the kind of research that Derek Price (Price, 1963) characterised as 'little science'. Thirdly, I will sketch a positive characterisation of this kind of research as 'small science'. I conclude by suggesting that this characterisation may be applied to other kinds of historical biomedical research, and that so doing may offer the pluralist a useful alternative way of understanding medical research in the twentieth century.

1. Introduction

Historical interest in viruses and cancer has grown steadily over the last few years. Perhaps this is unsurprising: cancer virus research played a prominent role in the development of laboratory medicine in the twentieth century. This role of cancer virus research within major biomedical research programmes (particularly in the USA) has been developed in work that tends to emphasise its planned and institutional character. For example, cancer virus research may be discussed in the context of major planned research efforts (Gaudillière, 1998; Scheffler, 2014), in the institutional interactions between biomedical research establishments and other quasi-governmental institutions, such as prisons (Stark & Campbell, 2014), or as contributor to research in other fields, such as molecular biology (Gaudillière, 1998). As John Pickstone points out, this alignment of the historiography of cancer virus research largely along institutional lines is of a piece with other social histories of medicine, where both the form of the work and the intensions of the historian have largely been imported from other contexts. Particularly important in this regard are "sociological histories of modernisation and industrialisation" (Pickstone, 2012: 239) which acted as important intellectual drivers of the development of social history of medicine in the late twentieth century (reviewed in Porter, 1995).

This is not to say that cancer virus research itself (as scientific practice) was confined to large research institutions. As the other papers in this issue also relate, the actual practices that contributed to tumour virology research in the later twentieth century were exceptionally polymorphous. This paper will sketch out one group of research that does not align with the dominant narrative of centralised science, and one that is thus not so clearly visible through the usual historiographical optics. Its aim therefore is to focus on research work occurring at a rather small scale. Important too is that this work occurred outside the United States, placing the practices reviewed here at further geographical remove from the big medicine of (for example) the National Cancer Institute.

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This paper characterises a very particular kind of research in tumour virology, and it does this via the case of Burkitt lymphoma (BL hence) in Equatorial Africa between 1950 and 1970. While many historical accounts of these events have been given before (Evans, 1993; Glemser, 1971; zur Hausen, 2006; Hutt, 1981), they are firmly aligned with a historical tradition that Stark and Campbell characterise as "organized searches for causes, therapeutics, and preventions" (2014: 218). While this paper will discuss just such a search for causes and prevention, my emphasis here is on the means by which these goals were sought, rather than the details of the causes or prevention strategies that were eventually found. I have selected two kinds of research work for special attention. First is the group of geographical research practices used to investigate the aetiology of BL during the 1960s. While these have previously been described as romantic adventure stories of derring-do in the tropics (Glemser, 1971), my intention here is to understand them more in terms of the growing interest in the history of science community of understanding the geography of the production of scientific knowledge. This alternative means of describing the role of place—described as the 'geographical turn' in the history of science by Finnegan (2008: 369)—in part consists of a greater attention to the role played by location in conditioning the character of scientific activity. In this essay, I therefore aim to pick out some of the geographical techniques employed in this case, and to demonstrate how these techniques shaped ideas about the nature and causation of BL.

Second, I have picked out a number of examples where existing research infrastructure—particularly that put in place to conduct malaria research—became reused by researchers interested in BL. Each of these two studies is intended to reflect in more detail my historiographical middle-way. In turn, this should serve as a corrective to the prevailing historical interpretation of the search for cancer viruses. While planned, managed, or centralised research was an important part of the field (see, for that, Scheffler's paper 2014), it was not constitutive of it. Epistemologically and practically distinctive things happened in the intellectual cracks and corners, and these played a key role in shaping the much more visible big science of national institutions. Yet these practices, which I refer to below as *small science*, have been poorly served by this emphasis on centralisation, planning and management.

The structure of this paper will be as follows. In Section 2, I give an outline of research conducted on Burkitt lymphoma in Africa between 1950 and 1970. I then develop two areas of this research in more detail. The first of these, discussed in Section 3, is the role of maps and mapping practices, and their interactions with other research practices, while in Section 4, I deal with the re-use of research infrastructure to investigate this disease. I then move to more conceptual territory in Section 5, where I characterise (in fairly general terms) small science, and briefly hold up certain aspects of the BL case as useful illustrations of this kind of scientific practice.

2. Burkitt lymphoma

This case deals with research conducted between 1950 and 1970 on BL, a tumour syndrome caused by infection with Epstein–Barr Virus (EBV). EBV has a world-wide distribution, and is associated with the development of a range of malignant and non-malignant conditions (Deyrup, 2008). While up to 90% of adults show evidence of prior infection (Henle et al., 1969), the development of malignant disease is rather rare in the developed world, where infection manifests most usually as infectious mononucleosis (glandular fever). However, in combination with environmental factors found in the tropics, the virus can contribute to the development of BL, which is a highly malignant and rapidly progressive extranodal B-cell lymphoma.[1] This cancer mainly affects children, and has a number of unusual clinical features, such as its predilection for anatomical sites not usually associated with malignancy, such as the bones of the jaws.

A very brief account of the clinical (rather than laboratory) research performed on this disease is as follows: the strangely high incidence of jaw tumours of atypical appearance in children was reported several times in Equatorial East Africa during the first half of the twentieth century.[2] These were usually regarded more as curiosities than viable targets of research:

> *His face was massively swollen, with bizarre lesions involving both sides of his upper and lower jaws. I had never seen anything like it. The teeth were loose and the features grossly distorted. If a single jaw quadrant had been involved, I might have considered it to be an infective process such as osteomyelitis, but not with all four quadrants affected. This unusual distribution also seemed to rule out any form of neoplasia. Results of the biopsy had suggested some form of granuloma. I was totally baffled, but photographed the child and considered this to be another of the curiosities one had to become accustomed to seeing from time to time in Africa.*
>
> (Burkitt, 1983, 1777)

However, further encounters with other children with similar symptoms rapidly changed the status of these curiosities. Not only did other children have massive, characteristic tumours in the jaws, they also had distinctive abdominal tumours. This combination of tumours in the jaws and at multiple sites in the abdomen arising simultaneously suggested the operation of some altogether unknown disease mechanism. Further research (see Burkitt, 1983; Clarke, 2011; Hutt, 1981) revealed that, far from being occasional oddities, cases of this tumour syndrome were alarmingly common in Uganda. Early descriptions of the syndrome (Burkitt, 1958; Burkitt & O'Conor, 1961; O'Conor, 1961; O'Conor & Davies, 1960) gave clinical, epidemiological, pathological and histopathological features. Of particular note was that the tumour syndrome was caused by some kind of extranodal lymphoma; that the disease was geographically confined to an East-West belt across Equatorial Africa; and that the incidence rate was extremely high in localised areas within this lymphoma belt. Rather than being an isolated oddity, it appeared instead that a very common cancer had been hidden in plain sight. As the manifestations of the disease were not subtle—instead florid, progressive, and fatal—the fact that so little attention had been paid to isolated cases of the disease was somewhat mysterious:

[1] The means by which EBV causes a range of diseases depending on context is complicated, and the technical details go far beyond the scope of this essay. In very general terms, though, it appears to be the case that infection with EBV interacts with other agents to promote the development of chromosomal abnormalities (particularly translocations), and it is these that bring about malignant disease. Unlike other tumour viruses, such as human papillomavirus, where infection with different strains of the virus manifest as different types of cancer, the link between EBV and human disease seems highly multifactorial, with different combinations of virus plus other causal factors leading to different diseases. For details of these in relation to EBV, see Thorley-Lawson & Allday (2008).

[2] Some of these reports were widely disseminated. For example, there was a clinical meeting in the Mulago hospital in Uganda in October 1955, proceedings of which were published as a short article entitled 'Tumours of the Jaw' on the 29th exists, at which Burkitt was present (Singh, 1955). In this note, the higher incidence of jaw tumours at Mulago than in either Europe or America was noted (Singh, 1955, 70). Other reports from Uganda at the turn of the century were also known (Davies et al., 1964; Hutt, 1981, 762).