

Aberdeen Medical Microbiology: Post War History

After the Second World War Dr John Smith who as sole Consultant in charge of the City Hospital Laboratory since its foundation in 1920 cemented the formidable reputation for the service provided to General Practitioners and clinicians alike in the face of an ever-increasing workload. The Laboratory continued to punch above its weight in the quality of its research. Dr Smith's pioneering work notably into the causation of puerperal sepsis, the role of specific strains of *E coli* in gastroenteritis in children and his meticulous studies on the role of rats in the transmission of leptospirosis in fish workers established an international reputation for the City Hospital Laboratory and for him personally which was recognised in various awards. In particular, his pioneering and comprehensive study of the pathogenic role and taxonomic identification of enteropathogenic *E.coli* that caused an outbreak of infantile gastroenteritis in Aberdeen in 1947 with 219 cases, 99 fatal yielded six quality publications, including:

J Smith (1949) The association of certain types (a and b) of Bact. coli with infantile gastroenteritis. *Journal of Hygiene*, 47:221-226

C Giles, G Sangster & J Smith (1949) Epidemic gastroenteritis of Infants in Aberdeen during 1947, *Archives of Disease in Childhood*, 24:45-53

J Smith (1955) The Aetiology of Epidemic Infantile Gastro-enteritis. The Royal College of Physicians, Edinburgh

Little did Dr James Brodie who succeeded Dr Smith in 1958 imagine that some 6 years later he and his staff would be largely unsung heroes in the investigation of the Aberdeen Typhoid Outbreak of 1964. Despite the unprecedented increase in workload Dr Brodie was able to document and subsequently publish in forensic detail the evolution of the outbreak and its ultimate resolution. The Typhoid Outbreak came at a time when brucellosis was rife in N E Scotland and Orkney and Shetland. Dr Brodie had applied his investigative powers to elucidate the epidemiology of the disease. The City Hospital Laboratory provided information on the prevalence of the disease in human and cattle population and the role of unpasteurised milk in its transmission to humans prior to and following the National Eradication Campaign to rid cattle of brucellosis. In recognition of this sterling work the City Hospital Laboratory was designated as the Scottish National Reference Laboratory for Brucellosis in 1973.

Dr Ian Porter joined the City Laboratory in 1968 and together with Dr Brodie published a seminal paper on the use of Boric acid in the preservation of urine samples. Boric Acid Preservation of Urine Samples I. A. PORTER, J. BRODIE *British Medical Journal*, 1969, 2, 353-355. Subsequently this became established practice for the many labs worldwide who were in receipt of samples from a disparate area where postal or transport delays were inevitable. Dr Porter had a lifelong interest in medical history and during his time in charge he compiled a huge amount of material which with the assistance of Dr Michael Williams he published as the definitive History of the City Hospital and the Laboratory in 2001.

When Dr Brodie retired in 1981, Dr Tom Reid who had trained in Microbiology and Immunology was appointed. He set about the task of modernising the service to make it more clinically orientated while maintaining the established high standards. New techniques

such as radioimmunoassay and Elisa [Enzyme linked immunoassay] were introduced which greatly improved the sensitivity and speed of serological tests. A hot lab manned by trained medical laboratory scientific officers was established at the Genitourinary Medicine Clinic at Woolmanhill to provide rapid confirmation and treatment. The City Laboratory was simultaneously installing its first laboratory computing system designed to greatly facilitate specimen recording and result retrieval. The close working relationship with the indomitable Dr C C Smith and the Infection Unit was reinforced leading to the publication of an array of joint scientific papers.

Dr Reid's arrival coincided with the boom in North Sea oil and gas exploration and subsequent development of oil platforms. These unprecedented developments resulted not only in new diagnostic challenges e.g. cases of malaria in oil workers, problems with *Pseudomonas* infection in the ears of saturation divers but also a huge increase in public health samples requiring to be tested for potability and screened for newly recognised pathogens such as *Legionella* species. The City Hospital Laboratory met the challenge head on and provided an excellent real time service to the Oil industry despite the North Sea weather frequently delaying helicopter deliveries.

Dr Reid was acutely aware that in the investigation and resolution of outbreaks of infection offshore and onshore a close working relationship with the Director of Public Health and local environmental health departments was critical. Over the years these links resulted in the successful resolution of many outbreaks which, in keeping with the Laboratory's tradition generated scientific publications, including one of the best studies to date of an outbreak caused by a very common but up-until-then epidemiologically elusive food-borne pathogen. It also pioneered the first effective culture method for the organism which had only been published 18 months before. Loss of the electricity supply to a Kincardineshire dairy on the night of 13-14 January 1979 caused a pasteurizer failure. Unpasteurized milk was distributed on 15 January. 347 received the milk; 148 had symptoms and had *Campylobacter* in their stools, as did 57 who had no illness. One out of sixteen milk socks grew *Campylobacter*. I A Porter, T M S Reid (1980) A milk-borne outbreak of *Campylobacter* infection. *Journal of Hygiene*, 84: 415-418.

Meanwhile the University department, under the leadership of Professor Hugh Pennington were also doing great work, including vigorous and exhaustive investigations of the big human B5 parvovirus outbreak at Findochty at the end of 1983 and the beginning of 1984 which led to the discovery that human parvovirus can cause hydrops fetalis associated with mid-trimester abortions. Key publication: T Brown, A Anand, L D Ritchie, J P Clewley, T M S Reid, (1984), Intrauterine parvovirus infection associated with hydrops fetalis, *Lancet*, 1984:1033-4. Also see A Anand, E S Gray, T Brown, J P Clewley, B J Cohen (1987) Human Parvovirus Infection in Pregnancy and Hydrops Fetalis, *New England Journal of Medicine*, 316:183-186. Studies during the outbreak also generated an early report of parvovirus -induced bone-marrow aplasia, see R J Davidson, T Brown D Wiseman, (1984) Human parvovirus infection and aplastic crisis in hereditary spherocytosis, *Journal of Infection*, 9:298-300

The juxtaposition of clinical microbiology and the food water and environmental investigations proved invaluable. When *E. coli* O157 emerged as a new pathogen the City Hospital Laboratory became a recognised centre of expertise. This was acknowledged when all the food samples from the butcher's shop implicated in the large outbreak in 1996 were transported to Aberdeen for analysis. By then the City Hospital laboratory had been amalgamated with the University lab at Forresterhill and Professor Pennington chaired the Expert Group on this outbreak set up by the Secretary of State for Scotland in November 1996 to "Report on the circumstances leading to the 1996 outbreak of infection with *E. coli* O157 in Central Scotland, the implications for food safety, and the lessons to be learned." The expert group report was published in April 1997, was debated in Parliament, and led to butchers licensing as a step towards the full implementation of HACCP.

Before Pennington's appointment the Foresterhill laboratory had been designated as the Scottish *E. coli* O157 reference laboratory.

Before then the University laboratory had been active in applying state-of-the-art molecular biology techniques to type medically important bacteria, including *E. coli*, *Haemophilus influenzae*, and *Streptococcus pyogenes*.

Y Tzabar, T H Pennington (1991) The population structure and transmission of *Escherichia coli* in an isolated human community: studies on an Antarctic base. *Epidemiology and Infection* 107:537-542. T H Pennington (1993) *Haemophilus* species and clones. *Reviews in Medical Microbiology*, 4:50-58. M Upton, P E Carter, M Morgan, G F Edwards, T H Pennington (1995) Clonal structure of invasive *Streptococcus pyogenes* in Northern Scotland. *Epidemiology and Infection*, 115:231-241

In the interim the City Lab had become the first in Scotland to hold dual accreditation for its Clinical Microbiology [CPA] and food and water microbiology [UCAS] services. With the creation of the Food Standards Agency and ever-increasing EU legislation the latter became an essential prerequisite for supermarkets, their suppliers and other food producers who required formal testing. The City Lab in consequence built a portfolio of commercial contracts in addition to its routine clinical workload.

As a result of the emergence of antimicrobial resistant (AMR) strains of bacteria such as MRSA, the City Laboratory was increasingly asked to provide Infection Control advice and investigative support. Dr Ian Gould was appointed in 1986 to replace Dr Porter and strengthen the clinical liaison and antimicrobial use aspects of this support. Ian was jointly trained in clinical microbiology and infectious disease in the United Kingdom, Canada and Africa and quickly developed clinical and laboratory investigation of AMR and its control with antibiotic policies, maintaining the academic discipline of his predecessors. Soon after his appointment he introduced the term Antimicrobial Stewardship (AMS) in Europe and was an early recipient of European Commission Framework grants in this area. He went on to chair numerous national and international working parties and advisory boards on AMS and AMR and was the first to robustly show not only that antimicrobial use was driving the MRSA epidemic: Monnet, D., MacKenzie, F.M., Lopez-Lozano, J.M., Beyaert, A., Camacho, M., Wilson, R., Stuart, D., & Gould, I.M. (2004). Antimicrobial drug use and Methicillin-resistant *Staphylococcus aureus*, Aberdeen 1996-2000. *Emerging Infectious Diseases* 10 1432-1441, Lawes T, Edwards B, López-Lozano

JM, Gould IM. Trends in Staphylococcal aureus bacteraemia and impacts of infection control practices including universal MRSA admission screening in a hospital in Scotland, 2006-2010 retrospective cohort study and time-series intervention analysis. (2012) *BMJ Open* 2 doi:p11 e000797, Lawes T, López-Lozano JM, Nebot C, Macartney G, Subbarao-Sharma R, Dare CR, Edwards GF, Gould IM. (2015) Turning the tide or riding the waves? Impacts of antibiotic stewardship and infection control on MRSA strain dynamics in a Scottish region over 16 years: non-linear time series analysis. *BMJ Open*. 26;5(3):e006596. doi: 10.1136/bmjopen-2014-006596, but that restriction of use of key antibiotics could control and even end the epidemic: Lawes T, Lopez-Lozano JM, Nebot CA, Macartney G, Subbarao-Sharma R, Dare CR, Wares KD, Gould IM. (2015) Effects of national antibiotic stewardship and infection control strategies on hospital-associated and community-associated methicillin-resistant Staphylococcus aureus infections across a region of Scotland: a non-linear time-series study. *Lancet Infect Dis*. Dec;15(12):1438-49. doi: 10.1016/S1473-3099(15)00315-1.

He went on to found the first UK, European and World-wide study groups on AMS and become President of the International Society of Chemotherapy in 2013. He was appointed Honorary Professor in the Medical School in 2016 and co-founded the Journal of Global Antibiotic Resistance and has taught in over 60 countries world-wide. Lately his collaboration with a pan-European study group was the first to demonstrate the non-linear emergence of antibiotic resistant bacteria to antibiotic use, suggesting it may be possible to control AMR by setting antibiotic use thresholds (or limits) at a population level and allow a quantitative approach to AMS for the first time ever: Lawes, T., Lopez-Lozano, J.-M., Nebot, C.A., Macartney, G., Subbarao-Sharma, R., Wares, K.D., Sinclair, C., Gould, I.M.(2017) Effect of a national 4C antibiotic stewardship intervention on the clinical and molecular epidemiology of Clostridium difficile infections in a region of Scotland: a non-linear time-series analysis *The Lancet Infectious Diseases*, 17 (2), pp. 194-206, López-Lozano JM, Lawes T, Nebot C, Beyaert A, Bertrand X, Hocquet D, Aldeyab M, Scott M, Conlon-Bingham G, Farren D, Kardos G, Fésús A, Rodríguez-Baño J, Retamar P, Gonzalo-Jiménez N, Gould IM; THRESHOLDS study group. A nonlinear time-series analysis approach to identify thresholds in associations between population antibiotic use and rates of resistance. *Nature Microbiol*. (2019) 4(7):1160-1172. More recently Ian has been studying the need for biocide stewardship to control AMR: Zamudio R, Oggioni MR, Gould IM, Hijazi K. Time for biocide stewardship? (2019) *Nature Microbiol* 4 732-733.

IM Gould, TMS Reid, TH Pennington