NOTES AND RECORDS

THE ROYAL SOCIETY JOURNAL OF THE HISTORY OF SCIENCE

The Forgotten Typers – The rise and fall of Weimar bacteriophage-typing (1921-1935)

Journal:	<i>Notes and Records: the Royal Society journal of the history of science</i>
Manuscript ID	RSNR-2019-0020.R2
Article Type:	Research
Subject:	20th Century science < HISTORY OF SCIENCE, History of medical sciences < HISTORY OF SCIENCE, History of biology < HISTORY OF SCIENCE
Keywords:	Bacteriophage-typing, Bacteriophages, Epidemiology, Bacteriology, Weimar, Experimental System

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**The Forgotten Typers – The rise and fall of Weimar bacteriophage typing
(1921-1935)**

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14 **Acknowledgements**

15 I would like to thank Ton van Helvoort, Dmitry Myelnikov, and Neeraja Sankaran for
16 comments on the manuscript; the two anonymous reviewers of this paper for their
17 insightful remarks on experimental systems; Malte Müller for obtaining relevant articles
18 from German collections; and Charlotte Kirchhelle for producing Figure One.

For Review Only

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21 **Abstract**
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23 Using bacteriophages to type – identify – bacteria was one of the most important tools of
24 20th century epidemiology. Challenging existing accounts’ focus on Anglophone research,
25 this paper shows that modern phage-typing arose in German-speaking continental
26 laboratories from 1921 onwards. Several factors contributed to this rise: the limitations of
27 existing phenotypic systems; demobilised German bacteriologists’ interwar engagement
28 with phages as a means to explore bacterial type variation; the existence of well-stocked
29 and well-defined microbial culture collections with a strong focus on typhoid and
30 paratyphoid; the standardisation, free provision, and calibration of phage diagnostic
31 systems by a centralised laboratory network; and phage-typers’ implicit agreement to
32 blackbox ontological controversies about phages’ nature in favour of a mission-oriented
33 focus on practical epidemiological applications. The result was an experimental system
34 which simultaneously treated phages as technical objects and epistemic things. Although
35 the human network supporting phage-typing collapsed after the Nazi rise to power,
36 Weimar-era phage researchers laid the foundation for modern phage-based diagnostics and
37 epidemiology.
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39 **Keywords:** Bacteriophage-typing; Bacteriophages; Epidemiology; Bacteriology; Weimar
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1. Introduction

Bacteriophages – ‘bacteria devourers’ – have played an important yet frequently overlooked role in the history of modern epidemiology. First isolated during World War One,¹ phages were at the centre of heated debates about ‘viral nature’, became important experimental molecular tools and commodities, and experienced repeated booms and busts as antibacterials.² However, interwar bacteriophage research also laid the foundation for a new mode of bacterial identification: phage-typing makes use of the specificity of bacteria-phage interactions to identify and differentiate bacterial strains. This specificity results from the evolutionary cycle in which bacteria and phages are locked: bacteria develop resistance against phages and phages overcome this resistance via mutation. Over millennia, this cycle has not only given rise to a large number of different phage entities – the number of which is currently estimated at 10^{31} – but has also selected for highly specialised phages, which

¹ Germans laid claim to discovering lysogenic ‘Flatterformen’, which were described by Eugen Gildemeister in 1917 and confirmed as bacteriophages in 1921; C. Sonnenschein, ‘Die Herkunft der Bakteriophagen im Menschen und im tierischen Organismus’, *Giornale di Batteriologia e Immunologia* **2**, 1-32 (1927), p. 2; K. Lüdtke, *Zur Geschichte der frühen Virusforschung. Wie sich mit technischen Fortschritten bei der Untersuchung ‘filtrierbarer’ infektiöser Agenzien das Verständnis der Virusnatur entwickelt hatte* (Max-Planck-Institut Für Wissenschaftsgeschichte, Berlin, 1999), pp. 24-25.

² K. Lüdtke, op. cit. (note 1); W. C. Summers, *Félix d’Herelle and the Origins of Molecular Biology* (Yale University Press, New Haven, 1999); T. Van Helvoort, ‘The Construction of Bacteriophage as Bacterial Virus: Linking Endogenous and Exogenous Thought Styles’, *Journal of the history of Biology* **27**, 91-139 (1994); W. C. Summers, ‘How Bacteriophage Came to Be Used by the Phage Group’, *Journal of the History of Biology* **26**, 255-267 (1993); A. N. Creager, *The Life of a Virus. Tobacco Mosaic Virus as an Experimental Model, 1930-1965* (University of Chicago Press, Chicago, 2002); A. N. Creager, ‘The Paradox of the Phage Group: Essay Review’, *Journal of the History of Biology*, 183-193 (2010); D. Myelnikov, ‘An Alternative Cure: The Adoption and Survival of Bacteriophage Therapy in the USSR, 1922–1955’, *Journal of the History of Medicine and Allied Sciences* **73**, 385-411 (2018); T. Häusler, *Viruses vs. Superbugs. A Solution To The Antibiotics Crisis* (Macmillan, London, 2006); N. Sankaran, *Frank Macfarlane Burnet and the nature of the bacteriophage, 1924-1937* PhD thesis, Yale University, (2006).

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3 54 only attack a limited number of bacteria species or strains.³ By isolating phages with a
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6 55 narrow lytic spectrum – causing lysis (destruction) of a bacterial cell – and further adapting
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8 56 them to only lyse one or very few bacteria types, it is possible to create a standardised set
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11 57 of specialised typing phages with differentiated targets. Infecting a plated bacterial culture
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13 58 with this typing set ideally results in a pattern of lytic clearings – *tâches vierges* – on the
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15 59 bacterial lawn, which enables researchers to identify the respective species/strain.⁴
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20 61 **Figure One: Bacterial type assignation via lysis by a set of standardised typing phages**
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24 63 Over the past 80 years, phage-typing has profoundly shaped public health,
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26 64 epidemiology, and microbiology. In contrast to claims according to which phages lost
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28 65 medical relevance after the 1920s,⁵ the rapid 1930s/1940s expansion of phage-typing
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30 66 networks made bacteriophages take centre stage in epidemiological endeavours to map
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32 67 bacterial prevalence and account for variations of type and virulence. Phage-typing data on
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34 68 nosocomial, food-, and waterborne infections as well as on antimicrobial resistant bacteria
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36 69 inspired changes in hospital design, expanded the clinical gaze beyond the hospital, and
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50 ³ A. Jurczak-Kurek, et al. 'Biodiversity of bacteriophages: morphological and biological
51 properties of a large group of phages isolated from urban sewage', *Scientific reports* **6**,
52 34338 (2016); S. T. Abedon, 'Phages', in *Bacteriophages in Health and Disease* (eds Stephen
53 T. Abedon & Paul Hyman), 1-5 (CABI, Wallingford and Cambridge, 2012).
54 ⁴ M. L. Williams & J. T. LeJeune, 'Phages and Bacterial Epidemiology', in *Bacteriophages in*
55 *Health and Disease* (eds Paul Hyman & Stephen T. Abedon), 76-85 (CABI, Wallingford and
56 Cambridge, 2012); S. S. Kasatiya & P. Nicolle, 'Phage-Typing', in *Practical Handbook of*
57 *Microbiology* (ed William O'Leary), 279-295, (CRC Press, Boca Raton, 1989).
58 ⁵ N. Sankaran, 'Mutant Bacteriophages, Frank Macfarlane Burnet, and the Changing Nature
59 of "Genespeak" in the 1930s', *Journal of the History of Biology* **43**, 571-599 (2010), p. 594.
60

70 influenced drug regulations and food supply chains.⁶ To this day, many microbial
71 taxonomies bear the imprint of decades of phage-typing efforts.

72 This paper reconstructs the beginnings of phage-typing. Challenging some historians'
73 claim that phage-typing originated in Canada (1936/38) and Britain (1940),⁷ it shows that
74 phage-typing was first conceived of and employed as a diagnostic and epidemiological
75 technology in German-speaking laboratories of the Weimar period. What emerges is a
76 complicated story of phages' gradual repurposing amidst microbiological and political
77 upheaval. Every typing system has to fulfil five epidemiological criteria: it has to be stable
78 over time (stability); reliably assign a subtype to the general organism being tested
79 (typeability); differentiate between strains (discriminatory power), group related isolates
80 similarly (concordance), and create reproducible results (reproducibility).⁸ To generate
81 taxonomic data that is meaningful to the biomedical community, a typing system also has to
82 offer advantages over other systems and be used in a standardised way by a large network
83 of researchers.

84 Using bacteriophages to achieve these criteria was not easy. One of the main
85 challenges for Weimar-era phage typers lay in fostering trust in data being produced by

⁶ G. A. J. Ayliffe & M. P. English, *Hospital Infection. From Miasmas to MRSA* (Cambridge University Press, Cambridge, 2003); K. Hillier, 'Babies and Bacteria: Phage Typing Bacteriologists, and the Birth of Infection Control', *Bulletin of the History of Medicine* **80**, 733-761 (2006); F. Condrau & R. G. W. Kirk, 'Negotiating hospital infections: The debate between ecological balance and eradication strategies in British hospitals, 1947-1969', *Dynamis* **31**, 385-404 (2011); A. Hardy, *Salmonella Infections, Networks of Knowledge, and Public Health in Britain 1880-1975* (Oxford University Press, Oxford, 2015); C. Kirchhelle, 'Swann Song. British antibiotic regulation in livestock production (1953-2006)', *Bulletin of the History of Medicine* **92**, 317-350 (2018).

⁷ Ayliffe, op. cit. (note 6), pp. 154-155; Hillier, op. cit. (note 6); Hardy, op. cit. (note 6), pp. 129-131; Wall, R. *Bacteria in Britain, 1880-1939* (Pickering and Chatto, London, 2013), pp. 4-5, 155, 157.

⁸ M. J. Struelens, 'Consensus guidelines for appropriate use and evaluation of microbial epidemiologic typing systems', *Clinical Microbiology and Infection* **2**, 2-11 (1996).

86 enigmatic components. Lack of agreement on phages' basic nature meant that interwar
87 researchers did not know why or how typing sets were able to discriminate between
88 bacteria. Another challenge lay in standardising typing protocols across different
89 laboratories. In contrast to genotypic systems' focus on genetic sequences, bacteriophage-
90 typing is phenotypic. Phages 'identify' bacteria via antigenic surface components of the cell
91 wall. Many of the 10^{31} phage entities will identify different surface components. To produce
92 concordant results, phage-typers thus have to use only one of innumerable potential sets of
93 typing phages. This standardised set has to be centrally curated and regularly checked for
94 corruption as a result of bacterial co-passaging, phage mutation, or other factors.⁹

95 As will be shown, Weimar researchers overcame these challenges by: (1)
96 transforming phages from unknowable "epistemic things" into semi-reliably functioning
97 "technical objects";¹⁰ (2) leveraging existing laboratory networks to propagate and
98 collectively evolve typing systems; (3) focusing on prominent but difficult to culture bacteria
99 with extensive well-defined microbial culture collections, which could be used to fine tune
100 typing sets and create trust in results.

101 In a crucial first ontological step, early typers implicitly agreed to 'blackbox'¹¹
102 ongoing controversies about bacteriophages' biological nature. Similar to Norbert Wiener's
103 description of early cybernetic systems, standardised collections of typing phages were

⁹ Williams & Lejeune, op. cit. (note 4); H. Brandis, 'Die Anwendung von Phagen in der bakteriologischen Diagnostik mit besonderer Berücksichtigung der Typisierung von Typhus- und Paratyphus B Bakterien sowie Staphylokokken', in *Ergebnisse der Mikrobiologie Immunitätsforschung und Experimentellen Therapie* (eds W. Kikuth et al.), 96-159 (Springer Verlag, Berlin, 1957).

¹⁰ H. J. Rheinberger, *Toward a History of Epistemic Things. Synthesizing Proteins in the Test Tube* (Stanford University Press, Stanford, 1997), pp. 28-31.

¹¹ M. Callon, 'The sociology of an actor-network: The case of the electric vehicle', in *Mapping the Dynamics of Science and Technology: Sociology of Science in the Real World* (eds M. Callon, J. Law, & A. Rip), 19-34 (Palgrave Macmillan, London, 1986).

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3 104 ontological black boxes designed to reliably perform a function before one knew how they
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6 105 functioned.¹² Applying what Olga Amsterdamska has called a “mission-oriented”¹³ medical
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8 106 gaze, researchers deliberately ignored whether phages were viruses, enzymes, or infectious
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11 107 hereditary material and instead focused on *using* phages’ effects on bacteria to solve readily
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13 108 identifiable epidemiological challenges – first as an extension of existing serological
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15 109 techniques and then as a typing system *sui generis*.

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18 110 This did not mean that they abandoned basic research on phages’ nature.
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20 111 Complicating Hans-Jörg Rheinberger’s functional division of experimental systems into a
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22 112 part that is under investigation (epistemic thing) and a part that provides a stable context
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24 113 for experimentation (technical object(s)),¹⁴ the rise of phages as epistemic things and
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26 114 technical objects occurred in parallel. In a significant blurring of lines between ‘basic’ and
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28 115 ‘applied’ research, Weimar phage-typers simultaneously studied phages as intriguing
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30 116 unknowable and unstable entities whilst also harnessing them as technical objects to
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32 117 produce semi-reproducible statements about the microbial world. The result was a
33
34 118 profoundly messy and unruly experimental system with competing theories repeatedly
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36 119 destabilising research trajectories. It was also a system that was difficult to monopolize by
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38 120 one discipline. From the mid-1920s onwards, emerging collections of typing phages served
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40 121 as a resource not only for epidemiologists studying disease ecologies but also for
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42 122 microbiologists interested in bacterial type variability and practitioners trialling new phage-
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55 ¹² P. Galison, 'The ontology of the enemy: Norbert Wiener and the cybernetic vision', *Critical*
56 *inquiry* **21**, 228-266 (1994), p. 246.

57 ¹³ O. Amsterdamska, 'Medical and Biological Constraints: Early Research on Variation in
58 Bacteriology', *Social Studies of Science* **17**, 657-687 (1987), p. 662.

59 ¹⁴ Rheinberger, op. cit. (note 10).
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123 based therapies. Intriguingly, these disciplines could be represented by one and the same
124 person working with different 'hats'.

125 Despite its instability, this unruly research system remained viable because of the
126 centralised provision of two core typing phages, a collectively evolved set of laboratory
127 techniques, and a focus on two prominent organisms – *Salmonella enterica* Seroovar Typhi/
128 typhoid and *Salmonella enterica* Seroovar Paratyphi B/ paratyphoid B. In the case of these
129 two pathogens, long-standing diagnostic problems created a perfect market niche for a new
130 typing system to show its worth by outcompeting existing techniques. Typhoidal infections'
131 status as *Leitkrankheiten* (lead infections) for Kochian bacteriologists also meant that it was
132 relatively easy for phage-typers to justify broader research on bacteriophages' role in
133 bacterial type variation within the practically orientated public health laboratories they
134 often worked in.¹⁵ These laboratories in turn gave typers access to a continuous stream of
135 patients, pathogens, and phages, which could be used to establish dedicated phage
136 collections, as well as to well-described bacterial culture collections, which could be used to
137 calibrate protocols and create trust in type assignments. Throughout the period analysed, a
138 bare minimum of cohesion between emerging typing sets was maintained by the use of two
139 standardised "reference" phages. Provided by Cologne's Institute of Hygiene, these phages

¹⁵ For the broader context of interwar research on type variation and epidemiology see: W. Anderson, 'Natural Histories of Infectious Disease: Ecological Vision in Twentieth-Century Biomedical Science', *Osiris* **19**, 39-61 (2004); J. A. Mendelsohn, 'From Eradication to Equilibrium: How Epidemics Became Complex after World War I, in *Greater Than The Parts. Holism in Biomedicine 1920-1950* (ed Christopher; Weisz Lawrence, George), 303-331 (Oxford University Press, Oxford, 1998); P.-O. Méthot, 'Bacterial Transformation and the Origins of Epidemics in the Interwar Period: The Epidemiological Significance of Fred Griffith's 'Transforming Experiment', *Journal of the history of Biology* **49**, 311-358.

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3 140 allowed researchers to compare typing sets' efficacy and enabled Cologne to emerge as a
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6 141 clearing house or nodal hub for the collective evolution of phage-typing techniques.¹⁶
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8 142 The volatile and comparatively small Weimar-era phage-typing network did not
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10 143 survive the disruption of the German microbiologist community under National Socialism.

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13 144 As the last part of this article reconstructs, German Jewish typers were sacked, imprisoned,
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15 145 or fled the country. Remaining researchers rallied to the Nazi cause and refocused on more
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18 146 urgent therapeutic challenges in tropical and military medicine. Cut off from the human and
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20 147 physical networks underpinning its 1920s rise, German phage-typing crumbled while more
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23 148 robust and fine-grained typing systems evolved abroad.
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¹⁶ B. Latour, *Science in Action* (Harvard University Press, Boston, 1987), chapter 6.

2. A competitive environment: alternative phenotypic systems

Bacteriophage-typing originated in a highly competitive environment of different phenotypic modes of bacterial diagnosis and classification.

Interwar microbiologists were already employing various optical, chemical, culturing, and serological technologies to differentiate between bacteria via phenotypic characteristics. Microscopy and selective chemical staining allowed them to identify distinctive colony shapes. Characteristic chemical reactions offered a further way of classification. In 1900, Fred Neufeld's observation that Ox gall dissolved *Streptococcus pneumonia* provided a new rapid chemical test for pneumococci. Researchers could also use standardised media like MacConkey, brilliant green, or methylene blue to selectively culture bacteria. Serological methods offered a further way of differentiating between microorganisms. Following the discovery of the diphtheria antigen (toxin) and antitoxins in 1888 and 1890, researchers began to use antibody-antigen reactions as diagnostics.¹⁷ In 1896, Ferdinand Widal developed an agglutination test for typhoid after observing that blood serum from a typhoid carrier caused *Salmonella enterica* serovar Typhi cultures to clump (agglutinate). Ten years later, August Paul von Wasserman, Julius Citron, and Albert Neisser developed the first complement-fixation test for syphilis, which used standardised amounts of antigens and complements to test whether antibodies had formed in a patient's serum in response to an infection.

The Widal and Wassermann tests were soon joined by further tests like the tuberculin-based Mantoux test for tuberculosis (1907/08) and the Schick test for diphtheria (1910/11). The new set of phenotypic diagnostics played an important role in facilitating the

¹⁷ S. Podolsky, *Pneumonia Before Antibiotics: Therapeutic Evolution and Evaluation in Twentieth-Century America*. (Johns Hopkins University Press, Baltimore, 2010).

172 almost missionary spread of lab-based bacteriology from European hubs to other industrial
 173 nations and colonies.¹⁸ Around the world, laboratory-based diagnosis illuminated previously
 174 unknown pathways and reservoirs of infection – as in the case of asymptomatic carriers of
 175 pathogens – and seemed to legitimise new forms of centralised ‘microbe hunting’ and state
 176 intervention into the lives of individuals.¹⁹ By World War One, all combatants were making
 177 extensive use of serological diagnosis to identify and combat diseases like syphilis, typhoid,
 178 typhus, and dysentery in humans and the non-human environment.²⁰

179 However, existing typing technologies remained far from perfect. Despite
 180 contemporary enthusiasm and standardisation efforts, interwar bacteriological diagnosis
 181 was hampered by significant variations of assay specificity, culturing material, laboratory
 182 practice, and competing taxonomic systems.²¹ In the case of Wassermann testing for
 183 syphilis, bacteriologist Ludwik Fleck already noted in 1935 that early specificity had
 184 fluctuated between 15-20% before gradually rising to 70-90% as a result of reciprocal

¹⁸ Amsterdamska, op. cit. (note 13), p. 671; P. Chakrabarti, *Bacteriology in British India; Laboratory Medicine and the Tropics* (University of Rochester Press, Rochester, 2012).

¹⁹ S. Berger, *Bakterien in Krieg und Frieden: Eine Geschichte der medizinischen Bakteriologie in Deutschland, 1890-1933*. (Wallstein Verlag, 2009); Wall, op. cit. (note 7); Hardy, op. cit. (note 6); C. Gradmann, M. Harrison & A. Rasmussen, 'Typhoid and the Military', *Clinical Infectious Diseases* **Forthcoming** (2019).

²⁰ J. A. Mendelsohn, *Cultures of Bacteriology: Formation and Transformation of a Science in France and Germany, 1870-1914* PhD thesis, Princeton, (1996); S. Berger, "Die Jagd auf Mikroben hat erheblich an Reiz verloren". Der sinkende Stern der Bakteriologie in Medizin und Gesundheitspolitik der Weimarer Republik', in *Das präventive Selbst. Eine Kulturgeschichte moderner Gesundheitspolitik*, (eds Martin Lengwiler and Jeannette Madarász), 87-114 (transcript, Bielefeld 2010).

²¹ Mendelsohn, op. cit. (note 20); P. M. H. Mazumdar, P. M. H., 'The Silence of the Laboratory: the League of Nations standardizes syphilis tests', *Social History of Medicine* **16**, 437-459 (2003); P. M. H. Mazumdar, 'The State, the Serum Institutes and the League of Nations', in *Evaluating and Standardizing Therapeutic Agents, 1890-1950* (eds Christoph Gradmann & Jonathan Simon), 118-138 (Palgrave Macmillan, London, 2010); A. Hardy, 'Questions of Quality: The Danish State Serum Institute, Thorvald Madsen and Biological Standardisation', in *Evaluating and Standardizing Therapeutic Agents, 1890-1950* (eds Christoph Gradmann & Jonathan Simon), 139-152 (Palgrave Macmillan, London, 2010).

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3 185 finetuning of reagents and researchers.²² To this day, the Widal test for typhoid has no
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6 186 universal standards that define the cut-off dilution of agglutinating antibodies, suffers from
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8 187 low specificity (50-70%), and is unable to discern active infections from previous infections
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11 188 or vaccination.²³

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13 189 There were other limitations. Existing technologies were often too slow to inform
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15 190 clinical practice and the expense of producing or purchasing media, antibodies,
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18 191 complements, and antigens limited the number of laboratories capable of typing isolates.
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20 192 Another important limitation was that tests did not always differentiate between bacterial
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23 193 types. By the 1920s, the observation that bacteria genera are composed of multiple species
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25 194 and types was no longer new. In 1909, Fred Neufeld had distinguished three *Streptococcus*
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27 195 *pneumonia* types using antisera. Between 1913 and 1915, further research by Oswald Avery
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30 196 led to the discovery of a fourth antigenic group and a formalized system of antigenic type
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33 197 identification.²⁴

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35 198 **Table One: Taxonomic Table for *S. Typhi***

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Taxon	Example
Kingdom	Eubacteria
Phylum	Proteobacteria
Order	Enterobacteriales
Family	Enterobacteriaceae
Genus	Salmonella
Species	<i>Salmonella typhi</i>
Type	<i>S. typhi</i> T 4904

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²² L. Fleck, *Genesis and Development of a Scientific Fact*. 2012 edn, (University of Chicago Press, Chicago, 1935), p. 78.

²³ J. B. Harris & E. T. Ryan, 'Enteric Fever and Other Causes of Fever and Abdominal Symptoms', in *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases* Vol. 1 (eds John E. Bennett, Raphael Dolin, & Martin J. Blaser), 1270-1282 (Elsevier, Philadelphia, 2015).

²⁴ K. Eichfeld & R. M. Krause, 'Fred Neufeld and pneumococcal serotypes: foundations for the discovery of the transforming principle', *Cellular and Molecular Life Sciences* **70**, 2225–2236 (2013), pp. 2225-2226; Podolsky, op. cit. (note 17).

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210 More fine-grained knowledge of bacterial types was not only important for medical
211 practice but was also needed to make sense of epidemiological data on virulence changes of
212 bacterial disease and Joseph Arkwrights's 1921 observation of smooth (virulent)-rough
213 (avirulent) transitions of dysentery and enteric bacteria. Type and virulence shifts
214 challenged the Kochian dogmas of species stability and one microbe one disease and
215 triggered taxonomic controversies about how stable bacterial variations had to be to
216 constitute distinct types.²⁵ After an era of growing confidence in bacteriological capabilities,
217 the microbial world appeared vaster and more fluid than previously thought. New tools
218 were required to map and navigate it.

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²⁵ Mendelsohn, op. cit. (note 15), pp. 303-331; Méthot, op. cit. (note 15); O. Amsterdamska, 'Demarcating Epidemiology', *Science, Technology, & Human Values* **30**, 17-51 (2005), pp. 35-42; C. Gradmann, 'A spirit of scientific rigour: Koch's postulates in twentieth-century medicine', *Microbes and Infection* **16**, 885-892 (2014).

3. A need for precision: from antilysins to phage typing

The 1915/1917 discovery of bacteriophages offered a solution. Despite arguing over phages' viral, enzymatic, or hereditary nature, interwar microbiologists wasted little time in searching for practical applications of the new phenomenon. Rather than being one or the other, researchers simultaneously treated phages as "epistemic things"²⁶ with a fluid identity that had to be defined and as technical objects whose effects could be put to use. In the former territories of Imperial Germany and Austro-Hungary, one group of researchers became particularly interested in the specificity with which certain phages attacked only few bacteria species and types – first as an extension of existing serological tests and then as a diagnostic technology *sui generis*.

In 1921, Oskar Bail, Chair of Hygiene and Bacteriology at the German University of Prague in Czechoslovakia, first suggested using phages to differentiate between bacteria. Described as a "glowing German patriot"²⁷, Bail had studied biology and medicine and become interested in bacteriology as a doctoral student of Max von Gruber in Vienna. His previous research had focused on cholera, serum therapy, public health, and military and racial hygiene.²⁸ After World War One, Bail became interested in the prominent issue of bacterial type changes and bacteriophages' role in inducing them. Whilst analysing phages' effectiveness against Flexner (*Shigella*) and Coli bacteria,²⁹ he was struck by the "sharp

²⁶ Rheinberger, op. cit. (note 10), pp. 27-31.

²⁷ H. Braun, 'Oskar Bail', *Klinische Wochenschrift* **7**, 719 (1928).

²⁸ O. Bail, *Der Krieg in seiner rassenhygienischen Bedeutung* (Deutscher Verein zur Verbreitung gemeinnütziger Kenntnisse, Prag, 1915); O. Bail, *Kriegshygienische Fragen* (Calve, Prag, 1915).

²⁹ Bacteriological taxonomies have changed significantly since the interwar period and historical definitions are not always adequately captured by modern definitions. Throughout this article, I have provided the terminology used by contemporaries in the main text and provided the most likely though by no means definite corresponding modern taxonomic assignments in brackets.

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3 238 specificity of phage action" (*scharfe Spezifität*), which could potentially be used as a new
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6 239 "differentiation and research tool for closely related bacteria".³⁰ One year later, British
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8 240 researcher Bessie Callow reported encouraging host-range differences in staphylococcal
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10 241 bacteriophages whilst working at Columbia University. Isolated from New York patients,
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13 242 Callow's phages would only lyse a limited number of staphylococcal cultures despite
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15 243 repeated co-passaging.³¹

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18 244 Bail's suggestion of phage-based diagnostics and Callow's report of host-range
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20 245 specificity struck a chord amongst German-speaking researchers, who were adapting to
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22 246 bacteriology's changed interwar status. In Imperial Germany and Austro-Hungary,
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24 247 bacteriologists had profited from close associations with the military and played a
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26 248 prominent role as often draconian microbe hunters.³² Described by Silvia Berger, this role
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28 249 came back to haunt them after 1918. Not only were left-leaning policy-makers sceptical of
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30 250 old imperial elites, Kochian bacteriologists' helplessness during the 'Spanish Flu', inability to
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32 251 explain bacterial type and virulence changes, and the absence of epidemics following the
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34 252 breakdown of wartime bacteriological controls damaged their standing vis-à-vis a new
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36 253 generation of public health experts emphasizing preventive health.³³ With their old
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38 254 certainties in flux, demobilised bacteriologists were open to exploring the mysterious
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40 255 'd'Hérelle principle' in relation to emerging questions of bacterial variability but also
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42 256 recognized phages' diagnostic potential as a means to shore up their crumbling authority. In
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54 ³⁰ O. Bail, 'Bakteriophage Wirkungen gegen Flexner- und Koli-Bakterien', *Wiener klinische*
55 *Wochenschrift* **34**, 447-449 (1921), p. 447.

56 ³¹ B. R. Callow, 'Bacteriophage Phenomena with Staphylococcus Aureus', *Journal of*
57 *Infectious Diseases* **30**, 643-650 (1922), p. 648.

58 ³² Mendelsohn, op. cit. (note 20), p. 567.

59 ³³ Berger, op. cit. (note 20), pp. 87-114; Berger, op. cit. (note 19), pp. 292-294.
60

257 contrast to orthodox microbe hunting bastions like the *Reichsgesundheitsamt*,³⁴ the
258 integration of phages as new research tools occurred particularly rapidly in university-
259 affiliated institutes of hygiene, which often had close ties to local public health authorities.

260 Within two years of the 1918 armistice, Prague-based researchers under Oskar Bail
261 were optimising phage production and using phages to study bacterial proliferation, type
262 changes, and infectivity.³⁵ In contrast to existing theories of bacteriophages as universally
263 adaptive ultramicrobes or as destructive bacterial enzymes, Bail viewed phages as self-
264 propagating filterable splinters (*Splitter*) of bacterial chromatin (hereditary material). The
265 splinters hijacked bacterial cells undergoing cell division. Some splinters absorbed so much
266 chromatin that cell division turned into lysis culminating in the release of new chromatin
267 splinters: “not the bacteriophage divides itself (...), but the new phage forces a bacterium in
268 the process of multiplication to become a phage.”³⁶ In other cases, the presence of
269 sufficient bacterial chromatin allowed splinters to be reabsorbed and induce hereditary
270 changes in cells – including resistance to other splinters by eliminating part of the cell’s
271 chromatin (a gene in Bail’s terminology).³⁷ Bail’s concept of infectious hereditary not only
272 enabled him to reconcile observations of rapid lytic and delayed lysogenic phage action, it

³⁴ Berger, op. cit. (note 19), pp. 322-324.

³⁵ O. Bail, 'Das bakterioophage Virus von d'Herelle', *Wiener Klinische Wochenschrift* **34**, 237-238 (1921); O. Bail, 'Versuche über die Vielheit von Bakteriophagen', *Zeitschrift für Immunitätsforschung und experimentelle Therapie*. Originale. **38**, 57-164 (1923/24); T. Kigasawa, 'Bakteriophagenvermehrung bei höheren Temperaturen', *Zeitschrift für Hygiene und Infektionskrankheiten* **108**, 508-521 (1928); T. Watanabe, 'Serologische Untersuchungen an Shigabakteriophagen', *Zeitschrift für Immunitätsforschung und experimentelle Therapie*. Originale. **37**, 106-147 (1923); O. Bail, 'Versuche an Bakterienpopulationen', *Deutsche Medizinische Wochenschrift* **50**, 1289-1290 (1924).

³⁶ O. Bail, 'Der Stand und die Ergebnisse der Bakteriophagenforschung', *Deutsche Medizinische Wochenschrift* **51**, 13-16 (1925), p. 15.

³⁷ The focus on phages as hereditary principles later influenced the US Phage Group's concept of a phage as a 'naked gene', see forthcoming research by Ton van Helvoort.

273 also convinced him that individual phages could be type specific to certain bacteria – and
 274 thus useful for type assignments of both phages and bacteria strains.³⁸

275 The problem was knowing which phage one was dealing with. Eager to avoid the
 276 ontological “confusions”³⁹ of early bacteriology, Bail re-emphasized the Kochian dogma of
 277 only conducting research with clearly defined pure phages (*Reinzucht*). Using natural
 278 filtrates often entailed working with an unreliable phage mix (*bunte Mischung*). However,
 279 guaranteeing a *Reinzucht* – especially of polyvalent phages lysing multiple bacteria –
 280 remained difficult. What was required was a more reliable classification tool than merely
 281 classifying phages according to the bacteria they lysed. While Bail began using bacterial
 282 cultures with known phage resistance to differentiate amongst phages,⁴⁰ using serological
 283 tools also seemed promising.⁴¹

284 In 1921, several researchers had described the antigenicity of phages after observing
 285 that animals injected with phages produced sera suppressing the activity of these phages.⁴²
 286 Similar serum reactions with phages and the bacteria they lysed prompted Bail to describe
 287 his chromatin splinters as antigens sharing many components of bacterial antigens.⁴³ In
 288 1923, Richard Otto and Russian researcher N. Sukiennikowa at the Robert Koch Institute
 289 suggested that phages and antibodies might bind to similar components of the bacterial

³⁸ Bail, op. cit. (notes 30; 35, p. 238; & 36, p. 14).

³⁹ Bail, op. cit. (note 36), p. 13.

⁴⁰ Bail, op. cit. (note 35 [1923/1924])

⁴¹ Bail’s laboratory was a hotspot of serological expertise. After Austro-Hungary’s defeat, Bail retained his post at the German University (Charles University) of Prague in the new Republic of Czechoslovakia and worked alongside leading serologists like Edmund Weil and Arthur Felix; P. J. Weindling, *Epidemics and Genocide in Eastern Europe, 1890-1945* (Oxford University Press, 2000), 209; J. Craigie, 'Arthur Felix 1887-1956', *Biographical Memoirs of Fellows of the Royal Society* **3**, 52-79 (1957), 55.

⁴² E. Weiss & L. A. Arnold, 'Study of Antigenic Properties of Bacteriophage', *The Journal of Infectious Diseases* **34**, 317-327 (1924).

⁴³ Bail, op. cit. (note 30), p. 212.

cell.⁴⁴ In the same year, Prague-based Tai Watanabe found that serological characterisation and Bail's technique of cross-resistance tests led to similar groupings of shigella phages.⁴⁵ Finding striking parallels in bacterial phage susceptibility and agglutination patterns, Berlin-based researcher Kurt Marcuse proposed that phages had specific antigenic points of attack on the bacterial surface in 1925.⁴⁶ In 1926, Philip Hadley and Eugenia Dabney reported that the antigenic similarity of *B. typhosus* (*S. [Eberthella] Typhi*) and fowl typhoid (*S. Gallinarum*) organisms was reflected in their susceptibility to the same phages.⁴⁷

If phages were antigenic, it was possible to identify and differentiate between them via well-known agglutination reactions. Well-versed in serological diagnosis, the mid-1920s thus saw former microbe hunters begin to use 'antilynsins' (phage-specific antibodies) to taxonomize and isolate specialised phages. Building on contemporary ideas of phages' as part of a body's natural recovery from bacterial infection,⁴⁸ researchers theorised that convalescents' sera contained antilynsins against the bacteriophages that had lysed bacterial pathogens. Isolating these antilynsins would allow them to identify therapeutically useful type-specific bacteriophages via agglutination. It might also help disease diagnosis. Should a patient's serum reduce the lytic action of a known therapeutic phage, this could indicate the presence of an infection.⁴⁹

⁴⁴ R. Otto & N. Sukiennikowa, Bakteriophages Lysin und Paragglutination. *Zeitschrift für Hygiene und Infektionskrankheiten* **101**, 119-124 (1923), pp. 119 & 124.

⁴⁵ Watanabe, op. cit. (note 35).

⁴⁶ K. Marcuse, 'Untersuchungen über das d'Herellesche Phänomen. III. Mitteilung. Beziehungen zwischen Bakteriophagie und Agglutination (Rezeptorenstudien)', *Zeitschrift für Hygiene und Infektionskrankheiten* **105**, 2-26 (1925), pp. 20-21; 24-25.

⁴⁷ P. Hadley & E. Dabney, 'The Bacteriophagic Relationships Between *B. Coli*, *S. Fecalis* and *S. Lacticus*', *Proceedings of the Society for Experimental Biology and Medicine* **XXIV**, 13-18 (1926/1927).

⁴⁸ Summers, op. cit. (note 2).

⁴⁹ S. Katsu, 'Antibakteriophage Wirkungen im Menschenserum', *Deutsche Medizinische Wochenschrift* **51**, 1896-1897 (1925).

307 In 1924/25, two researchers embarked on the hunt for human antilysins. Working in
 308 Bail's Prague Department, Japanese researcher Schokitschi Katsu identified antilysins in sera
 309 from local typhoid and dysentery patients. Katsu's antilysins not only inhibited the action of
 310 Flexner-dysenteriae (*Shigella flexneri*) and typhoid (*S. Typhi*) phages but also revealed
 311 previously undetected infections.⁵⁰ However, Katsu was scooped. Speaking at the July 1925
 312 meeting of the University of Cologne's Scientific-Medical Association, an ambitious young
 313 German researcher called Curt Sonnenschein reported three breakthroughs: not only had
 314 he found effective antilysins in human sera (Sonnenschein called them 'antiphagins'), he
 315 also reported the successful use of specialised phages to rapidly diagnose paratyphoid and
 316 elucidate relatedness amongst supposedly distinct *Pseudomonas aeruginosa* isolates.⁵¹

317 Sonnenschein was a medically-trained bacteriologist, who had studied in Gießen and
 318 Freiburg prior to commencing his *Habilitation* at Cologne's Institute of Hygiene. Despite
 319 simultaneously engaging in basic research on bacterial type variation and trialling phages for
 320 therapeutic purposes,⁵² Sonnenschein criticised that "9/10s of early research had focused
 321 on the nearly purely theoretical and most difficult aspects of bacteriophages' effects"⁵³ with
 322 the remaining 1/10 focusing on phage therapy. Questions of practical use in epidemiology
 323 had been neglected despite the clear need for improved diagnostics for the bacterial causes
 324 of typhoid, paratyphoid, typhus, and dysentery.

⁵⁰ Ibid.

⁵¹ C. Sonnenschein, 'Der Nachweis antibakteriophager Serumwirkung. Eine neue serologische Reaktion bei Infektionskrankheiten', *Deutsche Medizinische Wochenschrift* **51**, 1434-1336 (1925).

⁵² C. Sonnenschein, 'Die Mucosus-Form des Pyocyaneus-Bakteriums, Bacterium pyocyaneum mucosum', *Zentralblatt für Bakteriologie, Parasitenkunde und Infektionskrankheiten - Erste Abteilung* **104**, 365-373 (1927), p. 367; C. Sonnenschein & F. E. Koch, 'Bakteriophagenbehandlung bei Paratyphus', *Münchener Medizinische Wochenschrift* **77**, 1901 (1930).

⁵³ Sonnenschein, op. cit. (note 51), 1434.

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3 325 The combined use of antiphagins and diagnostic phages seemed particularly
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6 326 promising. On March 20th, 1925, Sonnenschein had detected antiphagin in the serum of a
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8 327 paratyphoid B patient. The antiphagin was capable of reducing the action of a powerful lytic
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10 328 paratyphoid B phage that Sonnenschein had isolated from a cholecystectomy and tested on
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13 329 Cologne's culture collection of enteric bacteria, which had already been well-described with
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15 330 other typing methods.⁵⁴ Because phages and the bacteria they lysed formed a serologically
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18 331 related system (*bakteriophages System*), antiphagins could be used to diagnose previously
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20 332 untypable lysogenic bacteria strains and aid the collection and characterization of further
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23 333 type-specific bacteriophages. These phage *Reinzuchten* should be archived alongside
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25 334 corresponding bacterial strains in dedicated culture collections and could serve as
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28 335 therapeutics, tools for basic research, and bacterial diagnostics: if bacteriophages could be
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30 336 identified via testing on known bacterial laboratory strains, known laboratory phages could
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33 337 also be used to identify bacteria.⁵⁵

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35 338 The antiphagin-aided identification of monovalent phages that would attack ideally
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38 339 all members (*artumfassend*) of one bacterial species ("*homoiologue*" phages) was
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40 340 particularly desirable.⁵⁶ According to Sonnenschein, monovalent phages could be screened
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43 341 for in patients or created via repeated co-passaging of polyvalent 'heterophages' on one
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45 342 bacterial species. His research showed that these phages offered a powerful new way to
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48 343 rapidly identify pathogens. In the case of the typhoid-dysentery-coli group, monovalent
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50 344 phages distinguished between bacteria that were either difficult or impossible to

54 Ibid.

55 C. Sonnenschein, 'Über Paratyphus-Bakteriophagen und -Antiphagine (Beiträge zur angewandten Bakteriophagie)' *Zentralblatt für Bakteriologie, Parasitenkunde und Infektionskrankheiten - Erste Abteilung* **97**, 312-317 (1926), pp. 314-316.

56 C. Sonnenschein, 'Die Verwendbarkeit der Bakteriophagie für die bakteriologische Diagnose', *Münchener Medizinische Wochenschrift* **72**, 1443-1444 (1925).

differentiate serologically. Monovalent bacteriophages isolated by Sonnenschein clearly distinguished between paratyphoid-B and Breslau-Aertrycke (*S. Typhimurium*) strains with similar agglutination reactions.⁵⁷ Sonnenschein had also used monovalent phages to distinguish between typhoid (*S. typhi*) and the Gärtner bacillus (*S. enteritidis*) and had used three polyvalent phages to distinguish between Flexner (*Shigella Flexneri*), Shiga (*Shigella dysenteriae*), and Y-types (*Shigella Flexneri*).⁵⁸ The isolation or cultivation of pure phage cultures via co-passaging was a “new, simple, auxiliary tool in the bacteriological laboratory technique.”⁵⁹ In the case of paratyphoid B, which was causing increasing concern among 1920s public health authorities, Sonnenschein’s monovalent phage had been able to produce positive diagnostic results within 5-6 hours – much faster than selective culturing (‘bunte Reihe’) or agglutination methods.⁶⁰

While there were clear applications of typing phages as practical diagnostics to hunt for and confirm carriage of enteric bacteria, they could also be simultaneously used as technical objects and epistemic things to explore bacterial variation and relatedness (*Verwandtschaftsbeziehungen*) – both of which were emerging as key areas of interest for interwar bacteriologists and epidemiologists.⁶¹ Using type-specific phages, Sonnenschein and his superior Karl Ludwig Pesch had shown that the pseudo *B. Pyoceaneus* (*Pseudomonas aeruginosa*) fluorescence group did not constitute a unique bacterial type.⁶² Sonnenschein also used phages to study the relatedness of capsulated (*Wallform*/ smooth)

⁵⁷ Anne Hardy has highlighted the difficulties of existing serological systems for these bacteria, op. cit. (note 6), pp. 119-120.

⁵⁸ The Y-Type subdivision of *Shigella Flexneri* was held to be an atypical laboratory strain.

⁵⁹ Sonnenschein, op. cit. (note 56), p. 1444.

⁶⁰ Sonnenschein, op. cit. (note 55), pp. 313-315; Sonnenschein, C. Typhus und Paratyphus in Köln im Jahre 1926. *Munchener medizinische Wochenschrift*, 475 (1927).

⁶¹ Anderson, op. cit. (note 15); Mendelsohn, op. cit. (note 15); Méthot, op. cit. (note 15).

⁶² Sonnenschein, op. cit. (note 56).

364 and non-capsulated (*wallfreie*/rough) paratyphoid B forms via the *in vitro* creation of
365 mucoid-producing phage-infected forms.⁶³ The latter were not agglutinable and could also
366 be isolated from allegedly cured chronic carriers.⁶⁴

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368 **Figure Two: Sonnenschein 1926 phage dripping method paratyphoid B phage;**

369 **Figure Legend: Source – C. Sonnenschein, 'Atypische Wuchsformen von Bakterien als**

370 **Krankheitserreger. Mucosus-Form von B. paratyphi im Blut eines Paratyphuskranken',**

371 ***Zentralblatt für Bakteriologie, Parasitenkunde und Infektionskrankheiten - Erste Abteilung***

372 **100, 11-19 (1926); reproduced with permission of Elsevier STM Journals.**

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374 Figure Two illustrates Sonnenschein's method of allowing drips of phage solution to spread

375 over agar plates. *Picture 17* (bottom right) shows his paratyphoid B phage's lysis of a

376 capsulated (smooth) paratyphoid B variant (*Wallform*). White spots in the two phage drip

377 areas are phage resistant *Flatterformen*. *Pictures 18 and 19* show the effect of the same

378 phage on a non-capsulated paratyphoid B variant (*wallfreie* rough Form) and the resulting

379 growth of phage-resistant mucoid-producing paratyphoid B variants in lysed (dark) areas.

380 Sonnenschein claimed to be able to return the mucoid-producing form into a non-

381 capsulated (rough) form by eliminating the infective phage via passage in bile and to turn

382 the mucoid producing colony into a capsulated (smooth) strain by using another mucoid-

383 type specific phage.⁶⁵ His findings highlighted both the usefulness of typing phages as

⁶³ C. Sonnenschein, 'Atypische Wuchsformen von Bakterien als Krankheitserreger. Mucosus-Form von B. paratyphi im Blut eines Paratyphuskranken', *Zentralblatt für Bakteriologie, Parasitenkunde und Infektionskrankheiten - Erste Abteilung* **100**, 11-19 (1926).

⁶⁴ Sonnenschein, op. cit. (note 55).

⁶⁵ Sonnenschein, op. cit. (note 63).

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3 384 diagnostics but also indicated that these same phages could produce bacterial type
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6 385 variations, whose reversibility indicated ongoing relatedness⁶⁶ – thereby undermining
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8 386 contemporary notions of mucoid-producing strains as a distinct type of capsoid bacteria.⁶⁷
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10 387 In Sonnenschein's hands, one and the same bacteriophage was simultaneously a
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13 388 technical objects for elucidating clinical riddles but also a mysterious epistemic thing that
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15 389 could induce type variation and differentiate between types. The experimental system
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18 390 arising out of Sonnenschein's work would remain characterized by this unruly parallelism.
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58 ⁶⁶ Sonnenschein did not reflect in detail about potential genetic interpretations of phages'
59 potential to induce type changes.

60 ⁶⁷ Sonnenschein, op. cit. (note 52), p. 367.

4. Building a typing system: Sonnenschein's Weimar phage network

Sonnenschein's publications laid the foundation for a new era of phage-typing: from 1925 onwards, German-speaking researchers would screen for, classify, and adapt useful bacteriophages, which would be stored in microbial culture collections alongside corresponding bacterial strains for later use as diagnostics, therapeutics, and research tools. By 1930, bacteriological centres in Saxony, Prussia, Baden, and Hungary were phage-typing. Facilitated by the demise of Prague phage research after Oskar Bail's death in 1927,⁶⁸ Cologne's type culture collection emerged as the authoritative German-speaking source of *Reinzuchten* of diagnostic phages. It was this provision of reference phages by one 'centre of calculation'⁶⁹ that not only enabled a collective evolution of methodologies but also guaranteed a minimum of translatability between different typing sets and resulting phenotypic statements about the microbial world.

In 1928, Sonnenschein announced the isolation of a new diagnostic phage for typhoid. Similar to his earlier focus on paratyphoid B, this discovery was not entirely serendipitous but the result of targeted screening.⁷⁰ From 1902 onwards, campaigns against typhoid carriers had formed a core legitimization narrative for Kochian microbe hunters. However, typhoid cleansing had proven less straightforward than planned. During the First World War, military bacteriologists and clinicians increasingly complained that existing bacteriological tests provided too little clarity for the diagnosis of enteric infections. This criticism intensified during the 1920s and created a large and prestigious bacteriological

⁶⁸ Braun, op. cit. (note 27); Katsu, op. cit. (note 49).

⁶⁹ Latour, op. cit. (note 16), chapter 6.

⁷⁰ C. Sonnenschein, 'Bakteriendiagnose mit Bakteriophagen. Beschleunigung der bakteriologischen Typhusdiagnose', *Deutsche Medizinische Wochenschrift* **54**, 1034-1036 (1928).

market niche in which Sonnenschein's new phage-based diagnostics could outcompete other phenotypic methods.⁷¹

There were already a range of tests for *S. Typhi* including selective culturing, motility tests, gram staining, testing for indol production, lactose, and sugar processing, agglutination reactions, and feed experiments on mice. However, differentiating between typhoid and related bacteria like paratyphoid A, B, and enteritis bacteria remained difficult. Of 120 typhoid-similar (*typhusähnlich*) bacteria, only few could be definitely classified using existing serological methods. Things were further complicated by spontaneous bacterial variation and phage-induced virulence changes. Standard bacteriological confirmation of typhoid thus consisted of time-consuming test rows: 24 hours for selective culturing, 2-3 hours for agglutination tests, and 4-5 days for the formation of distinctive button head colonies on rhamnose agar. Sonnenschein's phage offered the potential to revolutionise this time-consuming process. In the case of positive lysis, the new *S. Typhi* phage could reduce confirmation to a 4 ½-10 ½ hour process.

The impressive host range of the *S. Typhi* phage was another major advantage.

According to Sonnenschein, every diagnostic phage had to fulfil three criteria:

1. They had to reliably attack only one bacteria species such as *S. typhi* in cultures that might contain several very similar bacteria species.
2. They should be effective against a high percentage of known types of a bacteria species.
3. They should be consistent in the strength and variability of their attack on the bacteria species.⁷²

Although the 1925 paratyphoid B phage already fulfilled the first criterion, its host range was not very broad and lysis patterns varied in their consistency. Isolated from a typhoid patient's faeces in early 1927, Sonnenschein's new phage had lysed 101 of 109 available *S.*

⁷¹ Berger, op. cit. (note 19), 299 & 329.

⁷² Sonnenschein, op. cit. (note 70), 1035.

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3 437 *typhi* strains (92.7% host range) in Cologne's culture collection but had not lysed 403
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6 438 cultures of *pseudomonas*, *coli* bacteria, paratyphoid A-B, and related strains such as
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8 439 Enteritidis Gärtner (*S. enteritidis*), Breslau (*S. typhimurium*), abortus ovis (*S. abortus ovis*),
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10 440 Freiburg (*S. typhimurium*), *Pyocyaneum* (*P. aeruginosa*), as well as organisms of the *Proteus*
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13 441 genus. Lytic action against *S. typhi* had not varied in 15 weeks of use and the phage had
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15 442 even lysed cultures from patients that had not been identified as typhoid via serological
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18 443 tests and selective culturing. Adopting a technique already popular for phage therapy,
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20 444 Sonnenschein had subsequently used repeated co-passaging to further adapt his phage to
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23 445 lyse *S. typhi* strains that initially only showed weak lytic reactions.⁷³

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25 446 The alleged speed and host-range of Sonnenschein's typhoid phage fulfilled a major
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28 447 bacteriological desideratum. However, by themselves, these two factors would not
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30 448 necessarily outcompete already existing phenotypic classification systems. To become
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32 449 established as a routine phenotypic diagnostic, Sonnenschein's phages had to spread to
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35 450 other laboratories with sufficiently large numbers of bacterial samples to showcase their
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37 451 usefulness. Sonnenschein actively fostered the creation of such a network. In Cologne, his
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40 452 phages were stored in sealed glass vials and regularly re-propagated on corresponding
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42 453 bacterial strains. When other laboratories requested them, typing phages were sent free of
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45 454 charge in heat sealed capillary vials (*Capillarröhrchen*) alongside their propagating cultures
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47 455 and detailed instructions on how to use them. Sonnenschein not only provided further
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50 456 instructions via mail but also pooled published and unpublished efficacy reports in
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52 457 Cologne.⁷⁴

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58 ⁷³ Ibid., pp. 1035-1036.

59 ⁷⁴ G. Elkeles, *Paratyphus, Fleischvergiftung und ihre Beziehungen zueinander* (Springer,
60 Berlin, 1930), pp. 104-105.

Responses from the medical community were favourable. In 1929, Prague-based Friedrich Hoder and Liane Heller reviewed the efficacy of Sonnenschein's phages. Hoder and Heller tested the paratyphoid B phage on nine paratyphoid B and 41 samples of closely related Paratyphoid A and C, typhoid, Gärtner (*S. enteritidis*), Meißelbeck (unknown member of the *Fleischvergifter* group), Breslau-Aertryck (*S. typhimurium*), coli, as well as Flexner and Dysentery (*Shigella*) organisms from various environmental sources. All nine paratyphoid B – and one *S. Typhi* – cultures were lysed. The phage even identified an unknown atypical paratyphoid B strain.

Figure Three: Hoder & Heller 1929 phage mixing method

Figure Legend: Hoder and Heller divided an agarplate into 6 sections and inoculated each section with bacteria and bacteriophages. After 24 hours, one sector was completely lysed indicating susceptibility to one of Sonnenschein's phages; Source – F. Hoder & L. Heller, 'Beitrag zur Diagnose von Paratyphus B mittels Bakteriophagen', *Münchener Medizinische Wochenschrift* 76, 489-490 (1929); Reproduced with permission of SpringerMedizin.

Hoder and Heller concluded that phages were a valuable new diagnostic method that should, however, still be used in conjunction with other tests because of occasionally phage-resistant bacteria strains.⁷⁵ Further positive reviews were published by Sonnenschein's superior at Cologne's Institute of Hygiene, Karl Ludwig Pesch, and by Gerhard Elekes, the head of Berlin's Charlottenburg (Westend) bacteriology institute.⁷⁶ At Budapest's Stephanie

⁷⁵ Hoder, F. & Heller, L. Beitrag zur Diagnose von Paratyphus B mittels Bakteriophagen. *Munchener medizinische Wochenschrift* 76, 489-490 (1929).

⁷⁶ Pesch, K. L. Das Paratyphus-Problem. *Klinische Wochenschrift* 10, 145-149 (1931), 148; Elekes, op. cit. (note 74).

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3 479 children's clinic, bacteriologist Zoltán Teveli also reported achieving a 91.4% diagnostic
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6 480 specificity when working with Sonnenschein's typhoid phage.⁷⁷
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8 481 Increasing use of Sonnenschein's phages led to a refinement of typing techniques. In
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10 482 a manner similar to what Ludwik Fleck described regarding the collective calibration of the
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13 483 Wassermann test,⁷⁸ the Weimar phage-typing network engaged in a reciprocal self-
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15 484 calibration of techniques. Over time, tinkering with phages resulted in a set of mutually
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18 485 evolving laboratory practices, which can be interpreted as a collective experimental system.
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20 486 Despite significant variation in the constitution of individual typing sets and a resulting
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23 487 increase of incommensurable type assignments, this phenotypic system remained loosely
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25 488 tied together by a centralised supply of core typing phages from Cologne and a shared
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28 489 'language' of common laboratory techniques.
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30 490 From the late 1920s onwards, limited supplies prompted researchers outside of
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33 491 Cologne to repropagate diagnostic phages and modify Sonnenschein's dripping technique.
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35 492 In Prague, Hoder and Heller used sterilised loops to mix a small amount of phage with a
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38 493 solution containing bacteria, which was then applied to a larger plate (see Figure 3). The
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40 494 method was quickly adopted by other laboratories like that of Elkeles in Berlin.⁷⁹
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42 495 Researchers also tried to find diagnostic phages for other organisms. Mirroring
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45 496 Sonnenschein's initial preoccupation with enteric organisms, the isolation of phages for the
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47 497 Dysentery/Ruhr (*Shigella*) group was seen as particularly important. In contrast to typhoid
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50 498 and paratyphoid A, which were deemed exclusive to humans, there was significant
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52 499 controversy about the alleged role of paratyphoid B in causing food poisoning as well as its
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56 ⁷⁷ Teveli, Z. Die bazilläre Diagnose des Typhus abdominalis mittels Bakteriophagen. *Jahrbuch*
57 *für Kinderheilung und Physische Erziehung* **80**, 114-116 (1931).

58 ⁷⁸ Fleck, op. cit. (note 22).

59 ⁷⁹ Elkeles, op. cit. (note 74), 105.
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3 500 bacteriological differentiation from other food poisoning (*Fleischvergifter*) organisms.
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6 501 Within the so-called 'pseudo-Ruhr' group ('weaker' dysentery bacilli like *Shigella flexneri*),
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8 502 further confusion was caused by the lack of common international taxonomies and a
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10 503 reliable way to differentiate so-called Y- and Strong types of Flexner-Dysentery Bacilli
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12 504 (*Shigella flexneri*).⁸⁰
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15 505 In 1928, veterinary researchers R. Standfuß and E. Lehr from Potsdam's State
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17 506 Veterinary Investigation Office used Sonnenschein's paratyphoid B phage as part of a wider
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19 507 diagnostic review designed to show that paratyphoid B was not a cause of food poisoning.
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21 508 Testing 540 strains of the coli-typhoid group with an array of serological, selective culturing,
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23 509 and chemical techniques, they found that Sonnenschein's phage reliably lysed all 50
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25 510 confirmed human paratyphoid B cultures but left salmonella (*S. typhimurium*) cultures from
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27 511 food poisoning outbreaks unharmed.⁸¹ In 1931, Prague-based researcher Minoru Toyoda
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29 512 reported the isolation of an effective diagnostic bacteriophage from poultry faeces.
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31 513 According to Minoru, the polyvalent phage only attacked organisms of the Shiga (*Shigella*
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33 514 *dysenteriae*), Flexner (*Shigella flexneri*) and Y (*Shigella flexneri* Y-Type) group but did not
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35 515 attack members of the typhoid-paratyphoid-coli group. Phage specificity had been tested on
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37 516 110 strains from Prague's culture collection and on stools obtained from hospitals around
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39 517 Bohemia. Results could be obtained within 12-24 hours, a period of time at the end of which
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53 ⁸⁰ Ibid., pp. 69-84; 'Aussprache - 11. Tagung der Deutschen Vereinigung für Mikrobiologie in
54 Frankfurt a.M. 1925', *Zentralblatt für Bakteriologie, Parasitenkunde und*
55 *Infektionskrankheiten* - Erste Abteilung **97**, 316-333 (1926); D. S. Linton, "'War Dysentery"
56 and the Limitations of German Military Hygiene during World War I', *Bulletin of the History*
57 *of Medicine* **84**, 607-639 (2010), p. 612.

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59 ⁸¹ R. Standfuß & E. Lehr, 'Zur Erkennung und Unterscheidung der Keime der Paratyphus-
60 Enteritis-Gruppe', *Berliner Tierärztliche Wochenschrift* **44**, 533-542 (1928), pp. 541-542.

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3 518 “standard [serological] analysis usually only began”.⁸² In the same year, Friedrich Sartorius
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6 519 and Heinrich Reploh from Münster’s Institute of Hygiene also reported using phages to
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8 520 distinguish between organisms of the ‘pseudo-Ruhr’ group. Comparing international typing
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10 521 systems and employing bacterial cultures obtained from the Lister Institute, Japan, British
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12 522 India, West Africa, and Leipzig, Sartorius and Reploh were looking for new confirmatory
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14 523 reactions to accompany serological analyses. In the case of Ruhr (shigella) strains growing
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16 524 on Mannitol agar, they reported that a combination of saccharose media and the gradated
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18 525 effects (weak/ strong lysis) of Ruhr bacteriophages isolated from poultry faeces allowed
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23 526 them to differentiate between all tested strains.⁸³

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25 527 Rather than isolate new diagnostic phages, Adam Schmidt, head of the pathological
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28 528 institute of Saxony’s State Hospital in Zwickau, decided to modify existing ones. In 1932,
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30 529 Schmidt reported that he had created effective adaptations of Sonnenschein’s original
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32 530 paratyphoid B phage. According to Schmidt, it would have been time consuming to repeat
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34 531 Sonnenschein’s mass screening of patient faeces and hospital sewage to find new
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37 532 monovalent phages. Instead, he had tried to change the valency (*Valenz*) of Sonnenschein’s
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40 533 phage via co-passage so that it no longer attacked paratyphoid B but other bacteria such as
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42 534 the Breslau bacilli (*S. typhimurium*). This was possible because of the phage’s alleged latent
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44 535 valency for all bacteria within the wider *Fleischvergifter*/paratyphoid group. After 16 co-
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47 536 passages – the first 9 with a combination of paratyphoid B and Breslau organisms, the next
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50 537 seven with only Breslau organisms – , Schmidt claimed to have achieved such a

55 ⁸² M. Toyoda, 'Verwendung eines Dysenterie Bakteriophagen in der bakteriologischen
56 Diagnostik', *Deutsche Medizinische Wochenschrift* **57**, 451 (1931).

57 ⁸³ F. Sartorius & H. Reploh, 'Neue Ergebnisse der praktischen Differenzierung der
58 Ruhrtypen', *Zentralblatt für Bakteriologie, Parasitenkunde und Infektionskrankheiten - Erste*
59 *Abteilung* **122**, 135-139 (1931).
60

modification. 50 further co-passages had supposedly resulted in a phage specific enough to only attack Breslau and not Aertrycke or Typhimurium bacteria (all now classified as *S. typhimurium*). The phage had then been modified further to leave Breslau strains unharmed and lyse Gärtner (*S. enteritidis*), Pullorum (*S. pullorum*), Gallinarum, (*S. gallinarum*), Ratin (*S. enteritidis*), Suipestifer (*S. typhimurium/ typhi-suis/ cholerae-suis*), Kunzendorf (*Salmonella choleraesuis* var. Kunzendorf), Glässer-Voldagsen (*S. typhi-suis*), Orient (paratyphoid C), and Amerika (*S. cholerae-suis*) strains. Ultimately, three phage adaptations had been sufficiently stable for clinical diagnosis of Breslau, Suipestifer, and Gärtner-Suipestifer organisms.⁸⁴

Since 1930, Schmidt's institute had also used the original Sonnenschein paratyphoid B and typhoid phages to test fresh clinical cultures as well as Zwickau's extensive collection of archived strains, many of which had been cultured from strains stored at the State Hygiene Institute of Sombor, Yugoslavia. Of 177 analysed *S. Typhi* strains, Sonnenschein's typhoid phage lysed 162 (91.5%) – despite slight lysis variations on xylosepositive and -negative strains. The typhoid phage did not attack 147 samples of the paratyphoid-coli-dysentery group and had often enabled Schmidt's institute to speed up typhoid diagnosis by 24 hours.⁸⁵ In the case of Sonnenschein's original paratyphoid B phage, Schmidt reported that clinical tests had lysed 88.5% of confirmed paratyphoid B strains. Similar to other researchers, he also discussed a case where the phage had revealed an atypical paratyphoid B strain. A provisional phage-based paratyphoid B diagnosis only took eight hours whereas it had previously taken 14-16 days to differentiate between paratyphoid B and related

⁸⁴ A. Schmidt, 'Gewinnung spezifisch eingestellter Diagnostikphagen durch Umzüchtung', *Zentralblatt für Bakteriologie, Parasitenkunde und Infektionskrankheiten - Erste Abteilung* **123**, 202-206 (1932); for nomenclature see: R. St John-Brooks, 'The Genus *Salmonella* Ligneries, 1900: Issued by the *Salmonella* Subcommittee of the Nomenclature Committee of the International Society for Microbiology', *Journal of Hygiene* **34**, 333-350 (1934).

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bacteria. In Zwickau’s state hospital, petri dishes with enteric bacteria samples were now divided into five sections, which were each inoculated with a different diagnostic phage (typhoid, paratyphoid B, Breslau, Suipestifer, and Gärtner). In combination with confirmatory selective culturing (*Kleine Bunte Reihe*) and agglutination tests, phage-typing often enabled clinicians to make a reliable diagnosis within 24 hours of receiving a specimen. However, the “scientifically and epidemiological extremely important” identification of bacterial types below the species level still depended on other “long and laborious examination methods”.⁸⁵

⁸⁵ A. Schmidt, 'Über die Verwendung des Bakteriophagen in der Typhus- und Paratyphusdiagnose', *Zentralblatt für Bakteriologie, Parasitenkunde und Infektionskrankheiten - Erste Abteilung* **123**, 207-212 (1932), 212.

5. Below the species level: Kurt Marcuse's differentiation of typhoid types

Achieving such a phage-based differentiation below the bacterial species level was the aim of Kurt Marcuse at the *Hauptgesundheitsamt* in Berlin. In 1927, Marcuse had joined the hunt for diagnostic phages whilst working under Gerhard Elkeles at the Diagnostic Institute Charlottenburg-Westend. Conducting experiments on Ruhr (shigella) bacteria, Marcuse noted that serologically related bacteria were lysed by the same phages. He next tried to differentiate five strains of E-pseudo-Ruhr (likely *Shigella sonnei*) bacteria by subjecting them to 46 phages of different providence and found that phage susceptibility correlated with epidemiological relatedness. According to Marcuse, phages might be used to “discover and prove epidemiologically related cases.”⁸⁶

However, work on expanding phage-typing proved less straightforward than expected. Having obtained Sonnenschein's phages, Marcuse not only confirmed their efficacy in 1931 but also reported that the paratyphoid B phage lysed other Ruhr bacteria like E-Ruhr (*Shigella sonnei*) and Flexner (*Shigella flexneri*) strains whilst leaving Y- (*Shigella flexneri* type Y) and Shiga (*Shigella dysenteriae*) strains unharmed. When testing the paratyphoid B phage on archived strains, he also found that lysis depended on the specific type of E-Ruhr (*Shigella sonnei*): if colonies had a smooth shape, they were not lysed, if they had a flat (rough) shape, the colonies were lysed and also failed to develop phage resistance. According to Marcuse, lysis by Sonnenschein's paratyphoid B phage was nonetheless gradated and consistent enough to aid E-Ruhr (*Shigella sonnei*) diagnosis.⁸⁷

⁸⁶ K. Marcuse, 'Untersuchungen über das d'Herellesche Phänomen. IV. Mitteilung. Studien über die 'Strukturanalyse' bei Lysinen', *Zeitschrift für Hygiene und Infektionskrankheiten* **107**, 563-570 (1927), p. 570.

⁸⁷ K. Marcuse, 'Zur Bakteriophagen-Diagnostik der E-Ruhr', *Klinische Wochenschrift* **10**, 732-734 (1931).

Figure Four: Marcuse's 1931 trial of different paratyphoid B phage application methods

Figure Legend: Controls in columns 1 & 3; top row inoculation with a loop; second row Hoder and Heller's mixing technique; fourth row preapplication of phage; Source – K. Marcuse, 'Zur Bakteriophagen-Diagnostik der E-Ruhr', *Klinische Wochenschrift* 10, 732-734 (1931); Reproduced with permission of SpringerOnline.

Marcuse's initial optimism about new typing applications proved too hasty. Within a year of publishing his 1931 paper, he was not only forced to report that he had been unable to replicate his own results with the paratyphoid B phage on Flexner (*Shigella flexneri*) strains but that he had also been unable to confirm the specificity of other newly isolated diagnostic Ruhr-phages (Toyoda; Sartorius and Reploh (1931)). Six years after its isolation, Sonnenschein's paratyphoid B phage remained the only phage to offer moderate specificity for Ruhr bacilli by lysing Shiga E as opposed to Y strains (*sonnei/flexneri* type Y).⁸⁸

Still convinced of phages' epidemiological value, Marcuse embarked on a wider review of phage-typing. In 1934, he published two papers in the *Zentralblatt für Bakteriologie*. For his first paper, he used the extensive bacterial culture collections of the *Hauptgesundheitsamt* to reevaluate the efficacy of Sonnenschein's paratyphoid B phage. Since 1931, Marcuse had tested the phage on 1,500 bacteria strains of which 601 belonged to the paratyphoid group (220 Schottmüller (paratyphoid B), 200 Breslau (*S. typhimurium*), 17 other paratyphoid B group, 9 paratyphoid A group, 62 paratyphoid C group, and 93 Enteritis-Gärtner (*S. enteritidis*)). 452 typhoid, 7 cholera-, 313 Ruhr (*Shigella*), and 177 Coli and Paracoli (*Blaustämme*) strains were used as controls. Sonnenschein's paratyphoid B

⁸⁸ K. W. Clauberg & K. Marcuse, 'Über die Bakteriophagendiagnostik als Hilfsmittel für die Typendifferenzierung innerhalb der Ruhrbazillengruppe', *Zentralblatt für Bakteriologie, Parasitenkunde und Infektionskrankheiten - Erste Abteilung* 124, 29-32 (1932).

phage again proved its effectiveness – albeit with a reduced success rate: 154 of 220 paratyphoid B strains were lysed with 4 giving weak reactions (ca. 70-72% host range). With the exception of a typhoid, Breslau, and four paracoli strains, the paratyphoid B phage had not lysed any other bacteria types. However, in separate tests it once again lysed 97% of rough E-Ruhr (*Shigella sonnei*) strains. Referencing Schmidt's Zwickau work, Marcuse tried to increase the paratyphoid B phage's diagnostic specificity via co-passaging with the 55 resistant paratyphoid B strains. Weak lysis was detected on 11 of these strains, of which the seven strongest reacting strains were chosen for further co-passaging with Sonnenschein's phage. However, three of the new phage strains also attacked Gärtner (*S. enteritidis*) organisms and lysis patterns of the four other strains were uneven. Marcuse therefore decided to boost the four strains' potency via a fourth co-passage with sensitive paratyphoid B strains. One of the resulting phages not only consistently lysed sensitive strains but also lysed the previously resistant paratyphoid B samples. Used in combination, the original Sonnenschein phage and Marcuse's PIV188/BSo phage lysed 100% of paratyphoid B strains in Berlin's culture collection.⁸⁹

Marcuse's second paper focused on Sonnenschein's *S. Typhi* phage. Since 1931, Marcuse had used this phage to test over 1,567 bacterial isolates from patients and Berlin type collections (469 typhoid, 601 paratyphoid-enteritis, 7 cholera, 313 Ruhr, and 177 Coli and Paracoli (*Blaustämme*) cultures). Although it did not lyse non-typhoid cultures, Sonnenschein's phage surprisingly lysed only 30% (138) of serologically confirmed typhoid cultures. Once again, Marcuse attempted to improve its diagnostic value via co-passaging

⁸⁹ K. Marcuse, 'Über Phagendiagnostik innerhalb der Paratyphusgruppe', *Zentralblatt für Bakteriologie, Parasitenkunde und Infektionskrankheiten - Erste Abteilung* **131**, 49-53 (1934).

with seemingly insensitive typhoid strains. In nine cases, this procedure resulted in phages, which would strongly and reliably lyse previously resistant *S. Typhi* strains. In total, 100 of 138 previously resistant strains were lysed by the new phages – the remaining 38 strains formed a group of their own.⁹⁰

Significantly, the modified typhoid phages each only attacked a limited number of *S. Typhi* cultures and could thus be used to establish individual typhoid types. To improve the consistency of lysis patterns, Marcuse next co-passaged modified phages and Sonnenschein’s original phage on susceptible *S. Typhi* strains. This resulted in the discovery of two new phages, which lysed some previously resistant *S. Typhi* strains. By 1934, Marcuse had developed a typing set of five typhoid phages, which lysed 99% of tested *S. Typhi* cultures – including lysogenised *Flatterformen* – and could be used to differentiate between six typhoid groups despite occasional type changes of some strains from H to c group.

Table Two: Marcuse’s 1934 *S. Typhi* phage type assignments

Group	Original (Sonnenschein) lysin FoSoTy	FP II V 121	FP II V 18	FP II Ty 26758	FP II Ty 6576	Results (Befunde)
H sensitive main group	++++	++++	++++	++++	++++	331
a-group	-	++++	- ¹⁾	- bis +	+ bis +++++	69

⁹⁰ K. Marcuse, 'Über Typhusdiagnostik mit spezifischen Bakteriophagen (nach Sonnenschein)', *Zentralblatt für Bakteriologie, Parasitenkunde und Infektionskrankheiten - Erste Abteilung* **131**, 206-211 (1934).

b-group	-	- ¹⁾	++++	- bis +	++++	31
c-group	-	-	-	++++	- bis +	10
d-group	-	-	-	-	++++	23
Resistant strains	-	-	-	-	-	5
						469

1) occasional weak reactions in the form of Taches vierges.

Source: K. Marcuse, 'Über Typhusdiagnostik mit spezifischen Bakteriophagen (nach Sonnenschein)', *Zentralblatt für Bakteriologie, Parasitenkunde und Infektionskrankheiten - Erste Abteilung* 131, 206-211 (1934), p. 208.

Marcuse was well-aware of his findings' implications: in addition to highlighting phages' value as diagnostics, he stressed that standardised typing sets could be used to investigate bacterial type differences and for epidemiological purposes. In 31 of 33 cases, Marcuse's typhoid phage set had assigned the same type to infected material (faeces, urine, blood) from the same source. Typing phages had also assigned the same type to multiple samples taken from chronic carriers (26 of 30 cases). The same *S. Typhi* phage type had moreover been detected in all patients from 8 of 9 large-scale typhoid outbreaks – with one patient in the ninth outbreak testing positive for two phage types.⁹¹

Thirteen years after Oskar Bail's initial phage-typing proposal, German-speaking bacteriologists had evolved an experimental system, which had turned phages into technical objects making increasingly sophisticated statements about the microbial environment. Drawing on a centralised network providing monovalent phages to speed up clinical typhoid and paratyphoid B diagnosis, different laboratories had subsequently used their extensive

⁹¹ Ibid.

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3 662 culture collections to develop fine-tuned phage sets for type assignments below the species
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6 663 level. Calibrating typing sets against well-defined bacterial culture collections also served as
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8 664 a means to create trust in typing results. What had started as a phenotypic assistant
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10 665 technique for bacterial diagnosis had turned into an innovative research and
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13 666 epidemiological tool *sui generis*. Although phenotypic results generated by adapted or
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15 667 newly isolated phages were frequently incommensurable with data generated in other labs,
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18 668 the shared supply of baseline phages, common language resulting from collectively evolved
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20 669 laboratory practices, and calibration of phages on culture collections, which had been typed
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23 670 using other methods, provided a minimum of trust and experimental stability.
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6. An epistemic blackbox – typing with an unknown entity

But what were interwar researchers talking about when they referenced phages? With the exception of Neeraja Sankaran, Karlheinz Lüdtke, and Ton van Helvoort,⁹² few scholars have addressed early German understandings of bacteriophages.

In the case of the phage-typers featured in this paper, interpretations differed widely. Far from following a quasi-dialectic process whereby the successful proliferation of experimental systems depends on a minimum of ontological stabilization, typing phages' transformation into exportable technical objects preceded any kind of consensus on phages' nature. In 1927, Curt Sonnenschein, published a lengthy tract in which he claimed that phages were external entities, which attacked bacteria and did not generate spontaneously.⁹³ Although he initially refused to comment on whether phages were alive or dead, he explicitly referred to them as viruses in 1938.⁹⁴ In Heidelberg, Friedrich Hoder interpreted phages as a non-living type-specific hereditary principle or product of bacterial decay and described the release of new phages by lysogenic bacterial cultures as akin to asymptomatic disease carriage.⁹⁵ In Zwickau, Adam Schmidt viewed bacteriophages as theoretically endlessly adaptable chemical lysins (*Lysine*).⁹⁶ Meanwhile, Kurt Marcuse favoured Oskar Bail's 1921 interpretation of phages as infective hereditary splinters and

⁹² Sankaran, op. cit. (note 2); Lüdtke, op. cit. (note 1), and T. van Helvoort, 'History of Virus Research in the Twentieth Century: The Problem of Conceptual Continuity', *History of Science* **32**, 185-235 (1994).

⁹³ Sonnenschein, op. cit. (note 1), pp. 1-3, 20, 29-31.

⁹⁴ C. Sonnenschein, 'Weitere Erfahrungen mit der Bakteriophagenbehandlung', *Zentralblatt für Innere Medizin* **59**, 537-538 (1938), p. 538.

⁹⁵ F. Hoder, 'Der gegenwärtige Stand der Bakteriophagenforschung', *Archiv für Mikrobiologie* **4**, 589-635 (1933), 598-599, 630.

⁹⁶ Schmidt, op. cit. (note 84), 202.

689 conducted experiments to elucidate whether other lysis inducing substances affected or
690 produced phages.⁹⁷

691 It was nonetheless surprisingly rare for such ontological disagreements to affect
692 phages' actual use as technical objects. In the German-speaking world, sustained principled
693 opposition to phage-typing on ontological grounds mostly came from researchers working
694 under Walter Seiffert at Freiburg's Institute of Hygiene. Convinced that phages were
695 endogenous autolytic intermediary protein synthesis products, Seiffert and his co-workers
696 used deductive reasoning to deny that there could be sufficient overlap between phage and
697 bacterial specificity for epidemiological or therapeutic applications.⁹⁸ After personally
698 testing Sonnenschein's phages in 1929, Seiffert tasked his assistant, Mario Massa, with a
699 systematic review. Massa's 1931 review was scathing: neither the original diagnostic phages
700 obtained from Sonnenschein in 1929 nor subsequent phages sent in 1931 had produced
701 reliable results on Freiburg strains. According to Massa, Sonnenschein's typhoid phage had
702 lysed only 5 of 13 serologically confirmed typhoid strains while his paratyphoid B phage had
703 lysed only 5 of 11 paratyphoid B strains. Even more worrying was phages' lack of specificity.
704 According to Massa, the paratyphoid B phage had also lysed 4 of 13 typhoid strains while
705 the typhoid phage had lysed one paratyphoid B strain. In the case of Ruhr Flexner (*Shigella*

⁹⁷ Marcuse, op. cit. (note 86), p. 565; K. Marcuse, 'Untersuchungen über das d'Herellesche Phänomen. II. Mitteilung. Untersuchungen über die Bedeutung der Leukocyten für das d'Herellesche Phänomen', *Zeitschrift für Hygiene und Infektionskrankheiten* **102**, 206-209 (1924); K. Marcuse, 'Untersuchungen über das d'Herellesche Phänomen. V. Mitteilung. Beziehungen des d'Herelleschen Phänomens zur Phagocytose, geprüft an Amöben', *Zeitschrift für Hygiene und Infektionskrankheiten* **108**, 308-314 (1928); K. Marcuse, 'Untersuchungen über das d'Herellesche Phänomen. VI Mitteilung. Einfluß der fermentativen Lyse auf das d'Herellesche Phänomen', *Zeitschrift für Hygiene und Infektionskrankheiten* **109**, 434-442 (1929).

⁹⁸ W. Seiffert, 'Die Bewertung des d'Herellschen Phänomens', *Seuchenbekämpfung*, 234 (1926).

706 *flexneri*), Y, and Shiga (*Shigella dysenteriae*) strains, cultures had been lysed not only by
 707 Sonnenschein's 1925 Flexner phage and an unspecified Kruse-Shiga-phage but also by the
 708 two other diagnostic phages. One could "not speak of specificity of these lysates in
 709 accordance with bacterial specificity (...) even if the Sonnenschein phages similar to many
 710 others prefer one species for lysis."⁹⁹ Creating wider phage-based taxonomies was "of
 711 course completely impossible"¹⁰⁰ because of phages' 'nature'.

712 Most researchers, however, refused to let ongoing ontological disagreements over
 713 phages' identity get in the way of practical applications. Similar to what Olga Amsterdamska
 714 has described for pre-war controversies about bacterial mono- or pleomorphism, the
 715 "matter in which a given phenomenon [was] deemed theoretically relevant [was]
 716 constrained by the context of research".¹⁰¹ In the case of phages, this context was shaped
 717 by societal hopes for targeted antibacterials – as evidenced by the contemporary success of
 718 Sinclair Lewis' *Arrowsmith* – and the epidemiological need for more fine-grained and quicker
 719 diagnostics. The result was a "mission-oriented"¹⁰² ontological pragmatism. Regardless of
 720 what they thought the vials they received from Cologne contained, early phage-typers were
 721 happy to side-line ontological questions as long as diagnostic phages produced reliable
 722 results. In laboratories from Cologne to Budapest, bacteriophages thus transitioned from
 723 unknowable epistemic things into useful technical objects.¹⁰³ In 1925, Sonnenschein himself
 724 noted:

⁹⁹ M. Massa, 'Untersuchungen über die Spezifität der sogenannten Diagnostik-Bakteriophagen', *Zeitschrift für Immunitätsforschung und experimentelle Therapie – Originale* **70**, 525-536 (1931), p. 534.

¹⁰⁰ Ibid., p. 535.

¹⁰¹ Amsterdamska, op. cit. (note 13), 680.

¹⁰² Ibid., 658-659, 662.

¹⁰³ Rheinberger, op. cit. (note 10).

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3 725 If I now work with a theoretically unexplained, perhaps living perhaps non-living, questionable
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5 726 ‘unknown entity’, I can only say that other proven diagnostic reactions [like the Weil-Felix and
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7 727 Wassermann reactions] are not completely explained either.¹⁰⁴
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9 728 To function as an epidemiological technology, phage-typing only required researchers to
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11 729 trust that their diagnostic black boxes were relatively similar, stable, and type specific –
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14 730 what they contained was of secondary importance. This ontological pragmatism cannot be
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17 731 explained by disciplinary priorities alone most discussed researchers were simultaneously
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19 732 active as clinicians, epidemiologists, and microbiologists. Grounded in a shared culture of
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22 733 techniques, it also carried over into basic research on phages as epistemic things. In 1933,
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24 734 Australian researcher Frank Macfarlane Burnet noted that phages were treated identically –
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26 735 “as if it were an extrinsic virus in laboratories”¹⁰⁵— regardless of whether experimenters
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29 736 thought phages were viruses, lysates, or hereditary matter. Rather than being distinct,
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31 737 technical objects and epistemic things could be the same thing.
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58 ¹⁰⁴ Sonnenschein, op. cit. (note 51), 1435.
59 ¹⁰⁵ F. M. Burnet, 'Recent work on the biological nature of bacteriophages', *Transactions of*
60 *the Royal Society of Tropical Medicine and Hygiene* **26**, 409-416 (1933), 424.

7. Epilogue: ruptured networks and foreign reinvention

Whether Weimar phage-typing was effective is impossible to say in hindsight. In addition to the problematic retrospective diagnosis of bacteriological data and translation of historical taxonomies into modern terms,¹⁰⁶ the main reason for this is that the highpoint of Weimar-era phage-typing research occurred just before the shattering of corresponding microbiological networks under National Socialism. Embracing the racialised Nazi ideology, most German phage-typers and the tropical medicine community more widely supported the new regime and refocused on military medicine, racial hygiene, phage therapy, and vaccine development in preparation for future conflicts.¹⁰⁷ By contrast, their German-Jewish colleagues were sacked and either emigrated or were imprisoned.¹⁰⁸ Without a human network to sustain and evolve it, the techniques and infrastructure of Weimar-era phage-typing disintegrated.

One year after publishing his 1934 typing paper, Jewish researcher Kurt Marcuse was sacked from Berlin's *Hauptgesundheitsamt* by the Nazis. Temporarily finding employment at the University of Basel between 1937 and 1938, Marcuse returned to Berlin where he worked for the *Poliklinik* on Alexanderplatz prior to losing his medical approbation as a result of a directive from July 25th, 1938 and being arrested and imprisoned in the KZ Sachsenhausen in November 1938. Due to his service in the First World War, Marcuse was released in December 1938. From 1939 onwards, he worked for Berlin's Jewish medical services as a *Krankenbehandler* and under increasingly horrific circumstances as director of

¹⁰⁶ A. Cunningham, 'Identifying Disease In The Past: Cutting The Gordian Knot', *Asclepio* **LVI**, 13-34 (2002).

¹⁰⁷ T. Werther, *Fleckfieberforschung im Deutschen Reich 1914-1945. Untersuchungen zur Beziehung zwischen Wissenschaft, Industrie und Politik unter besonderer Berücksichtigung der IG Farben* PhD thesis, Philipps-Universität Marburg, (2004), p. 56.

¹⁰⁸ See also work by Berger, op. cit. (note 19), pp. 363-364.

759 the bacteriological division in Berlin's Jewish Hospital. Surviving the Second World War,
 760 Marcuse took over as acting director of West Berlin's renamed *Landesgesundheitsamt* in
 761 1945.¹⁰⁹ Marcuse's former superior Gerhard Elkeles was also forced from his post and
 762 emigrated to South America via the Netherlands. Both did not publish on phages again.¹¹⁰

763 By contrast, Curt Sonnenschein's career flourished under National Socialism.
 764 Mirroring a wider refocusing of German microbiologists away from-Weimar era concerns
 765 about bacterial virulence, variation, and epidemiological holism,¹¹¹ Sonnenschein had
 766 concentrated on lucrative applications of phage therapy from 1928 onwards.¹¹² After
 767 transferring to Hamburg's Institute for Ships and Tropical diseases in 1930, he tested phage
 768 treatments on crews suffering from enteric disease. Two years later, he obtained an
 769 extraordinary professorship at the *Hamburger Tropeninstitut* (Hamburg Institute for Tropical
 770 Medicine). While his use of monovalent phages to treat chronic carriers remained
 771 disappointing,¹¹³ his newly isolated polyvalent phages for typhoid, paratyphoid A/B, and
 772 dysentery were being commercially manufacturing by IG Farben's Behringwerke by 1935.¹¹⁴
 773 As one of the signatories of the *Bekanntnis der deutschen Professoren zu Adolf Hitler* in
 774 November 1933, Sonnenschein was promoted to director of the bacteriological-serological

¹⁰⁹ R. Elkin, *Das Jüdische Krankenhaus muß erhalten bleiben! Das Jüdische Krankenhaus in Berlin zwischen 1938 und 1945*. (Edition Hentrich, Berlin, 1993), 106; 'Kurt Marcuse', *Verfolgte Ärzte* (Institut für Geschichte der Medizin Charité, Berlin 2013).

¹¹⁰ 'Gerhard Elkeles', *Verfolgte Ärzte* (Institut für Geschichte der Medizin Charité, Berlin 2013).

¹¹¹ Berger, op. cit. (note 19), 363-365.

¹¹² Hoder, op. cit. (note 95), 618.

¹¹³ Sonnenschein was following d'Herelle's prescriptions for context specific mono- and polyvalent phage therapy, see Ton Van Helvoort's paper in this issue.

¹¹⁴ Sonnenschein, op. cit. (note 94); C. Sonnenschein, 'Eigene Erfahrungen mit der Bakteriophagentherapie bakterieller Infektionskrankheiten, insbesondere des Typhus', *Zentralblatt für Bakteriologie, Parasitenkunde und Infektionskrankheiten - Erste Abteilung* **135**, 171-177 (1935); C. Sonnenschein, 'Therapeutische Anwendung von Bakteriophagen, insbesondere beim Typhus', *Klinische Wochenschrift* **12**, 685-686 (1933).

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3 775 division of the *Tropeninstitut* in 1936 and became a council member of the *Deutsche*
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6 776 *Tropenmedizinische Gesellschaft* where he systematically expelled Jewish members.
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8 777 Following the death of Karl Ludwig Pesch – his ardently National Socialist former superior –,
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11 778 Sonnenschein obtained Pesch's recently awarded post as professor for hygiene and
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13 779 bacteriology at the 'front university' (German University) of Prague in 1941. In Prague, he
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16 780 transitioned from working on tropical medicine to military hygiene – both as a researcher
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18 781 and Wehrmacht medical officer. After a brief post-1945 professional hiatus, Sonnenschein
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21 782 became *Ordinarius* of hygiene and bacteriology at the University of Würzburg, director of
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23 783 Würzburg's State Institute for Medical-Technical Assistants, and rector of the University of
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25 784 Würzburg (1958/59).¹¹⁵ He also ceased publishing on phages.
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28 785 Marcuse's 1932 co-author Karl Wilhelm Clauberg experienced a similar career hike
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30 786 and became director of the *Hauptgesundheitsamt's* hygiene institute in Berlin in 1933. From
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33 787 1935, he was director of bacteriology at the renamed Horst-Wessel-hospital (*Klinikum*
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35 788 *Friedrichshain*), extra ordinary lecturer at the Technical University and University of Berlin,
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37 789 and doctor of the prisoner-of-war camp *Stalag IIIa* (Sept-Dec 1939). Working directly
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40 790 opposite the SS Hygiene Institute and experimenting on human diphtheria convalescents
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43 791 with type toxins, Clauberg was dismissed in 1945 and founded a private diagnostic institute
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53 ¹¹⁵ E. Klee, *Das Personenlexikon zum Dritten Reich: Wer war was vor und nach 1945*.
54 (Fischer Taschenbuch Verlag, Frankfurt a. M., 2015), p. 454; P. Svobodny, P., 'Wanderungen
55 und Wandlungen: Die medizinische Fakultät der Deutschen Universität Prag und ihre
56 Beziehungen zur deutschen und österreichischen Universitäten in den Jahren 1882-1945', in
57 *Zehn Jahre Universitätspartnerschaft. Univerzita Karlova v Praze - Universität zu Köln*.
58 *Kolloquium zur Universitäts- und Fachgeschichte* (ed Walter Pape), 15-30 (Universitäts- und
59 Stadtbibliothek zu Köln, Köln, 2011), p. 25.
60

792 before returning to head Berlin's Behring hospital.¹¹⁶ He also abandoned phage-typing
793 research.

794 Other Weimar-era phage researchers like Friedrich Sartorius, Richard Standfuß,
795 Heinrich Reploh, and Friedrich Hoder also rose through the academic ranks: Hoder headed
796 Bremen's Hygiene Institute after temporarily directing the *Forschungsinstitut für Hygiene*
797 *und Immunitätslehre* in Berlin-Dahlem in 1933, Standfuß became director of the newly
798 created veterinary medicine faculty at Gießen in 1935, Reploh obtained a permanent post in
799 Münster and actively supported his superior Karl Jötten's work on eugenics. Friedrich
800 Sartorius also professed party loyalty to gain promotion at Münster, which was, however,
801 denied after it was found that his wife was Jewish according to Nazi ancestry rules.¹¹⁷
802 Although Cologne's Institute of Hygiene continued to propagate and distribute vials of
803 Sonnenscheins' typhoid, paratyphoid, and dysentery phages until at least 1949,¹¹⁸ none of
804 the featured Weimar-era phage-typers pursued research in this area again.

805 Fortunately, the implosion of phage research was limited to Germany. During the
806 late 1930s, phage-typing was reinvented abroad. Serological research on antigenic relations
807 between phages and host bacteria was crucial for this reinvention. Between 1933 and 1936,
808 American and Australian researchers showed that aqueous bacteria extracts neutralized the

¹¹⁶ Klee, op. cit. (note 115), p. 94; J. Hahn, U. Gaida, M. Hulverscheidt, *125 Jahre Hygieneinstitute an Berliner Universitäten. Eine Festschrift*. (Charité, Berlin, 2010), p. 29.

¹¹⁷ E. Seidler, *Die Medizinische Fakultät der Albert-Ludwigs Universität Freiburg im Breisgau. Grundlagen und Entwicklungen*. 1993 edn, (Springer Verlag, Berlin, 1991), p. 331; J. Hamdorf, 'Zum Gedenken an Friedrich Sartorius', *Flurgespräche* (2017); G. Möllers, *Jüdische Tierärzte im Deutschen Reich in der Zeit von 1918 bis 1945*, Dr. med. vet. thesis, Tierärztliche Hochschule Hannover, (2002), p. 265; W. Schauder, 'Nachruf auf Richard Standfuß', *Nachrichten der Giessener Hochschulgesellschaft* **29**, 126-127 (1960); J. N. Dicke, *Eugenik und Rassenhygiene in Münster*. (Weißensee Verlag, Münster, 2004).

¹¹⁸ O. Seifert, *Untersuchungen über die Verwendbarkeit spezifischer Bakteriophagen zur Diagnose von Salmonellakeimen*, Dr Med thesis, Johann-Wolfgang Goethe Universität Frankfurt a. M., (1949).

809 phages to which these bacteria had been susceptible but did not affect non-type specific
 810 phages. This not only confirmed phages' antigenic specificity but also led to the realization
 811 that the phage-binding unit was determined by a cell wall polysaccharide.¹¹⁹ Findings of
 812 phages' antigenic specificity coincided with the 1934 antigenic reordering of salmonella
 813 taxonomies (Kauffmann-White system)¹²⁰ and the discovery of the Vi-antigen in the capsule
 814 of virulent *S. Typhi* by Margaret Pitt and Arthur Felix— the latter, a former co-worker of
 815 Oskar Bail and co-discoverer of the O- and H-antigens.¹²¹

816 The isolation of the Vi-antigen triggered an international hunt for Vi-specific phages.
 817 In 1935/36, three groups in Canada, the Netherlands, and France reported isolating phages
 818 that would only lyse Vi *S. typhi* strains.¹²² In Canada, researchers headed by Scottish born
 819 James Craigie went on to systematically develop a next-generation typhoid Vi-phage-typing
 820 set via phage adaptation.¹²³ Published in 1938, the new typing set surpassed both

¹¹⁹ P. Levine; A. W. Frisch & E. V. Cohen, 'On Absorption of Phage by Bacilli', *Journal of Immunology* **26**, 321-325 (1934); P. Levine & A. W. Frisch, 'On Differentiation in the *Suipestifer* Group and on Resistance to Phage', *Journal of Immunology* **30**, 63-88 (1936); F. M. Burnet, 'The Phage-Inactivating Agent of Bacterial Extracts' *Journal of Pathology and Bacteriology* **38**, 285-299 (1936).

¹²⁰ The system was based on Bruce White's 1929 theory that *Salmonella* were enmeshed in a web of antigenic ancestral affinities and that individual types did not transmute; Hardy, op. cit. (note 6), pp. 121-124.

¹²¹ Craigie, op. cit. (note 41).

¹²² J. A. Craigie, 'Bacteriophage for the V Form of Salmonella Typhi. Abstract of 37th Meeting of American Bacteriologists', *Journal of Bacteriology* **31**, 56 (1936); R. T. Scholtens, 'The Resistance Developed against Bacteriophage', *Journal of Hygiene* **36**, 452-455 (1936); V. Sertic & N.-A. Boulgakov, 'Sur La Sensibilité Des Souches D'Eberthella typhi Au Bactériophage, En Relation Avec Les Caractères Antigéniques', *Comptes Rendus Hebdomadaires des Séances et Mémoires de la Société de Biologie* **88**, 35-37 (1936).

¹²³ J. A. Craigie & K. F. Brandon, 'Bacteriophage Specific for the O-Resistant V Form of B. Typhosus', *The Journal of Pathology and Bacteriology* **XLIII**, 233-248 (1936); J. A. Craigie & K. F. Brandon, 'The Identification of the V and W Forms of B. Typhosus and the Occurrence of the V Form in Cases of Typhoid Fever and in Carriers', *Journal of Pathology and Bacteriology* **XLIII**, 249-260 (1936); J. A. Craigie & C. H. Yen, 'The Demonstration of Types of B Typhosus by Means of Preparations of Type II Vi Phage: I. Principles and Technique', *Canadian Public Health Journal* **29**, 448-463 (1938); J. A. Craigie & C. H. Yen, 'The Demonstration of Types of

821 Sonnenschein's phages and Marcuse's typing system via its high specificity for a known
 822 antigen, stability, and phenotypic differentiation of *S. Typhi* into eight types.¹²⁴ Facilitated by
 823 wartime needs for fine-grained surveillance technologies, the set's rapid uptake across the
 824 English-speaking world ended any remaining aspirations Weimar phage typers' may have
 825 had for an international spread of their own system.¹²⁵ The Canadian team's failure to cite
 826 any preceding Weimar research was also a clear indication of German microbiology's
 827 increasing isolation following the Nazi rise to power. Outside of Germany, this loss of
 828 memory often carried over into the post-war era. In 1954, US researchers' promoting the
 829 use of the O-1 Phage (isolated by Felix & Callow in 1941) for rapid laboratory diagnosis of
 830 the wider salmonella genus mentioned neither Bail, Sonnenschein, or Marcuse.¹²⁶ A similar
 831 loss of memory regarding non-English speaking labscapes has carried over into phage
 832 historiography.¹²⁷

833 In the case of phage-typing, this paper has shown that it did not originate as an
 834 Anglophone wartime technology but as a technology that was deeply rooted in German-
 835 speaking microbe hunters' interwar attempts to reconcile bacteriological diagnosis with a
 836 new politically charged world of bacterial type variation and ecological complexity. The

B Typhosus by Means of Preparations of Type II Vi Phage', *Canadian Public Health Journal* **29**, 484-496 (1938).

¹²⁴ French and Dutch researchers developed competing typing systems; V. Sertic & N-A. Boulgakov, 'Groupement Des Souches d'Escherichia coli A L'Aide Des Lysines B Sécrétées Par Les Bactériophages', *Comptes Rendus Hebdomadaires des Séances et Mémoires de la Société de Biologie* **91**, 444-446 (1939); R. T. Scholtens, 'Phage typing of Salmonella Typhi in the Netherlands', *Antonie Van Leeuwenhoek* **16**, 245-255 (1950).

¹²⁵ Seifert, op. cit. (note 118).

¹²⁶ W. B. Cherry, B. R. Davis, P. R. Edwards & R. B. Hogan, 'A simple procedure for the identification of the genus Salmonella by means of a specific bacteriophage', *Journal of Laboratory and Clinical Medicine* **44**, 51-55 (1954).

¹²⁷ Ayliffe, op. cit. (note 6), Hillier, op. cit. (note 6), Condrau and Kirk, op. cit. (note 6), Hardy, op. cit. (note 6), Wall, op. cit. (note 7).

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3 837 1930s fall of Weimar phage typing occurred just as quickly as its 1920s rise. Within less than
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6 838 a decade of Sonnenschein's 1925 paper, German-speaking researchers had developed a
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8 839 sophisticated phenotypic system based on a small corpus of ontologically unstable entities.
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11 840 Although type changes, resistance, and cross lysis prevented their standalone use in German
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13 841 *Untersuchungsämter*,¹²⁸ most published contemporary accounts confirmed the usefulness
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15 842 of Sonnenschein's diagnostic phages. Marcuse's evolved 1934 typing system was also
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17 843 allegedly stable, could reliably differentiate between and assign types below the species
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20 844 level, and group epidemiologically related isolates. It not only fulfilled current
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22 845 epidemiological criteria but also foreshadowed what would become a global system of
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24 846 phage-based pathogen surveillance after 1945. The brief rise of both typing systems rested
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26 847 on a multitude of factors: demobilised microbe hunters' post-war engagement with phages
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28 848 and bacterial type variation; the existence of well-stocked and well-defined microbial
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30 849 culture collections with a strong focus on typhoid and paratyphoid; the standardisation, free
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32 850 provision, and calibration of phage diagnostic systems by Cologne's Institute of Hygiene;
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34 851 and phage-typers' implicit agreement to blackbox ontological controversies about phages'
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36 852 nature in favour of a mission-oriented focus on epidemiological applications. This mission-
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38 853 oriented blackboxing resulted in situations where phages simultaneously functioned as
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40 854 semi-reliable technical objects to differentiate bacteria and as mysterious epistemic things
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42 855 involved in bacterial variation. It was the self-implosion of the human networks supporting
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44 856 it that led to the demise of phage-typing's Weimar phenotype.
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¹²⁸ Seifert, op. cit. (note 118).

Figure & Tables: Titles and Legends:

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Figure One: Bacterial type assignation via lysis by a set of standardised typing phages

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Table One: Taxonomic Table for *S. Typhi*

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Figure Two: Sonnenschein 1926 phage dripping method paratyphoid B phage; Source: C.

Sonnenschein, 'Atypische Wuchsformen von Bakterien als Krankheitserreger. Mucosus-

Form von *B. paratyphi* im Blut eines Paratyphuskranken', *Zentralblatt für Bakteriologie,*

***Parasitenkunde und Infektionskrankheiten* - Erste Abteilung 100, 11-19 (1926).**

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Figure Three: Hoder & Heller 1929 phage mixing method

Legend: Hoder and Heller divided an agarplate into 6 sections and inoculated each section with bacteria and

bacteriophages. After 24 hours, one sector was completely lysed indicating susceptibility to one of

Sonnenschein's phages; Source: F. Hoder & L. Heller, 'Beitrag zur Diagnose von Paratyphus B mittels

Bakteriophagen', *Münchener Medizinische Wochenschrift* 76, 489-490 (1929).

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Figure Four: Marcuse 1931 trial of different paratyphoid B phage application methods

Legend: Controls in columns 1 & 3; top row inoculation with a loop; second row Hoder and Heller's mixing

technique; fourth row preapplication of phage; Source: K. Marcuse, 'Zur Bakteriophagen-Diagnostik der E-

Ruhr', *Klinische Wochenschrift* 10, 732-734 (1931).

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Table Two: Marcuse's 1934 *S. Typhi* phage type assignations; Source: K. Marcuse, 'Über

Typhusdiagnostik mit spezifischen Bakteriophagen (nach Sonnenschein)', *Zentralblatt für*

882 ***Bakteriologie, Parasitenkunde und Infektionskrankheiten* - Erste Abteilung 131, 206-211**

883 **(1934).**

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Abb. 1.