



Challenge studies - introduction

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1952 - 1974



T.E. Woodward



Mrs Quailles

Photo courtesy of Prof M Levine, University of Maryland;
www.ovg.ox.ac.uk

2g NaHCO₃



3-10x10¹⁰ CFU Ty21a in milk
 x 5-8 doses



Challenge with 10⁵ CFU



87% PROTECTIVE EFFICACY

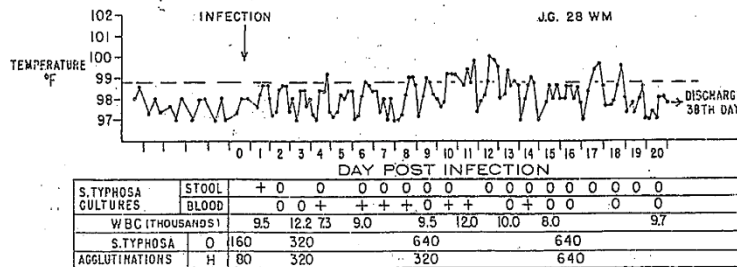


FIG. 1. Clinical summary of volunteer no. 9, J. G., after the ingestion of 10⁸ viable *Salmonella typhosa* Quailles strain. Rectal temperatures are recorded.



Waddington CS, J Infect, 2012



Oxford Challenge Model



Mrs Quiailes



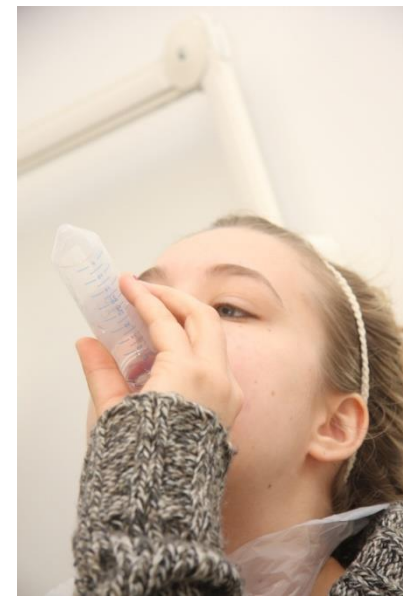
S.typhi Quiailes strain
B.N. ASS/VPU/2010/002
Oral Administration 1×10^5 cfu/ml
Volume: 1ml Vial Number: 678.
D.o.M. 12 AUG 10
Store: -65°C to -80°C
A.Pollard Tel: 01865 234226
FOR CLINICAL TRIAL USE ONLY





Primary endpoint

- Fever $>38^{\circ}\text{C}$ +/- Positive blood culture



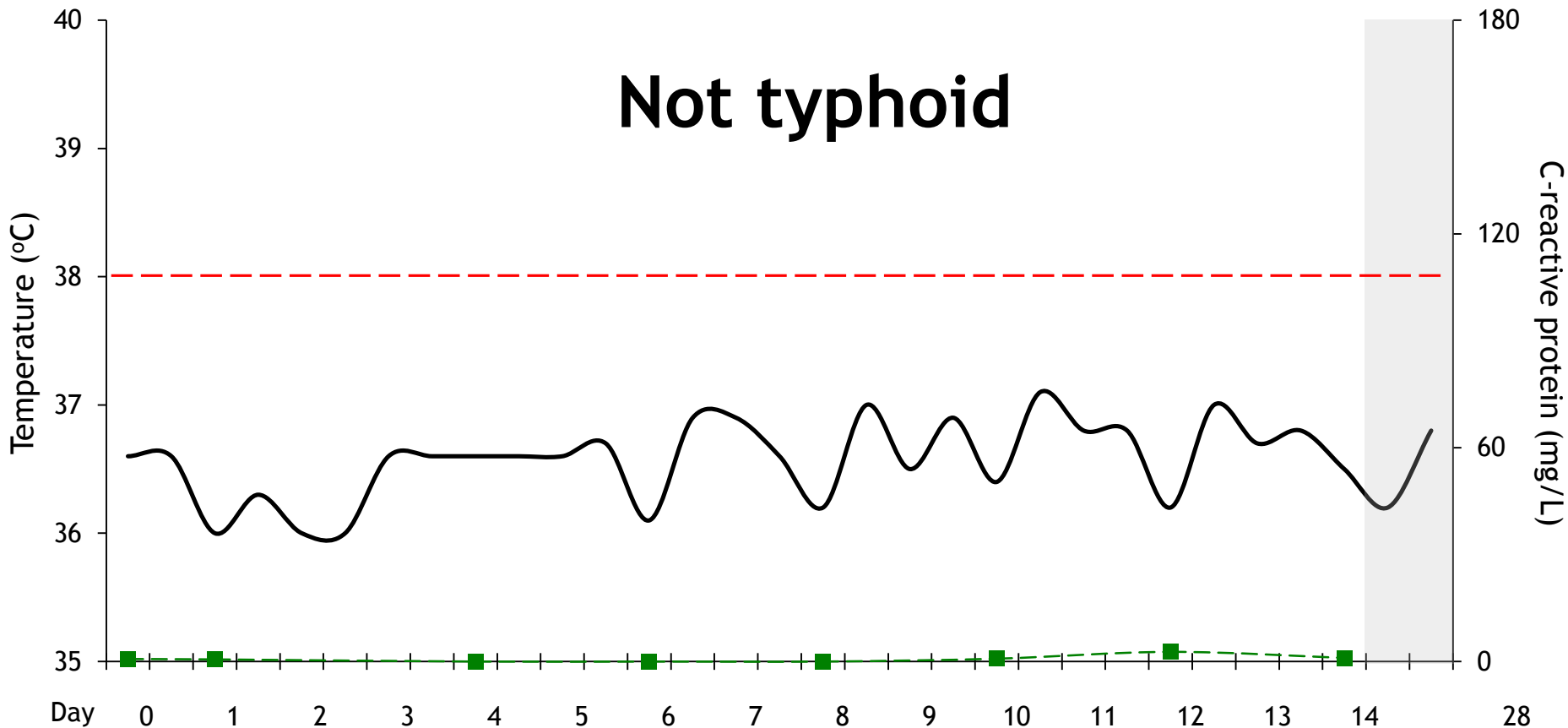
Field definition

Fever for 3 days + positive blood culture



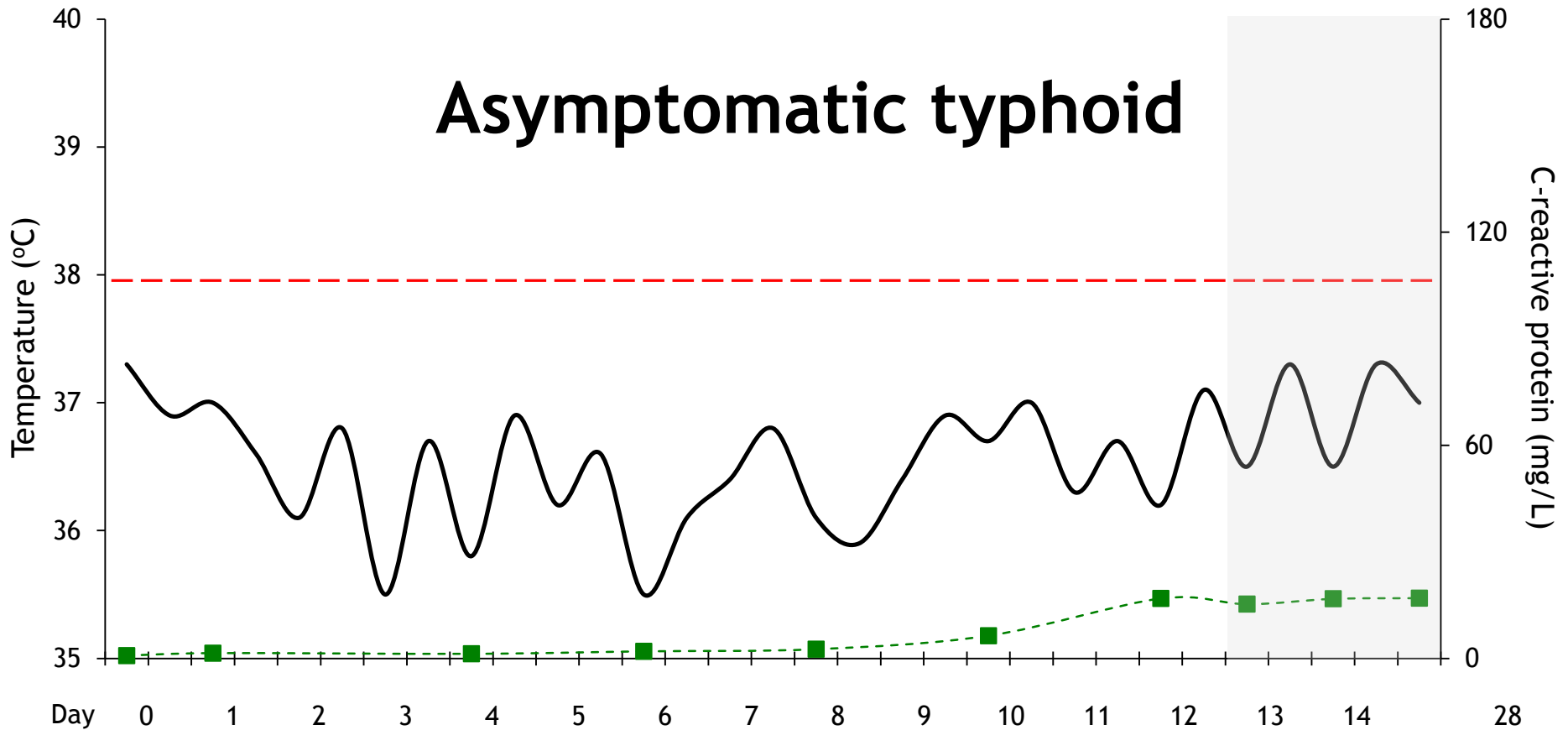
DISEASE PHENOTYPES

Not typhoid



Blood Cx	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Stool Cx	-	+	-	-	-	-	-	-	-	-	-	-	-	-	-	-
Widal O	2														4	8
Widal H	NA														NA	NA

Asymptomatic typhoid

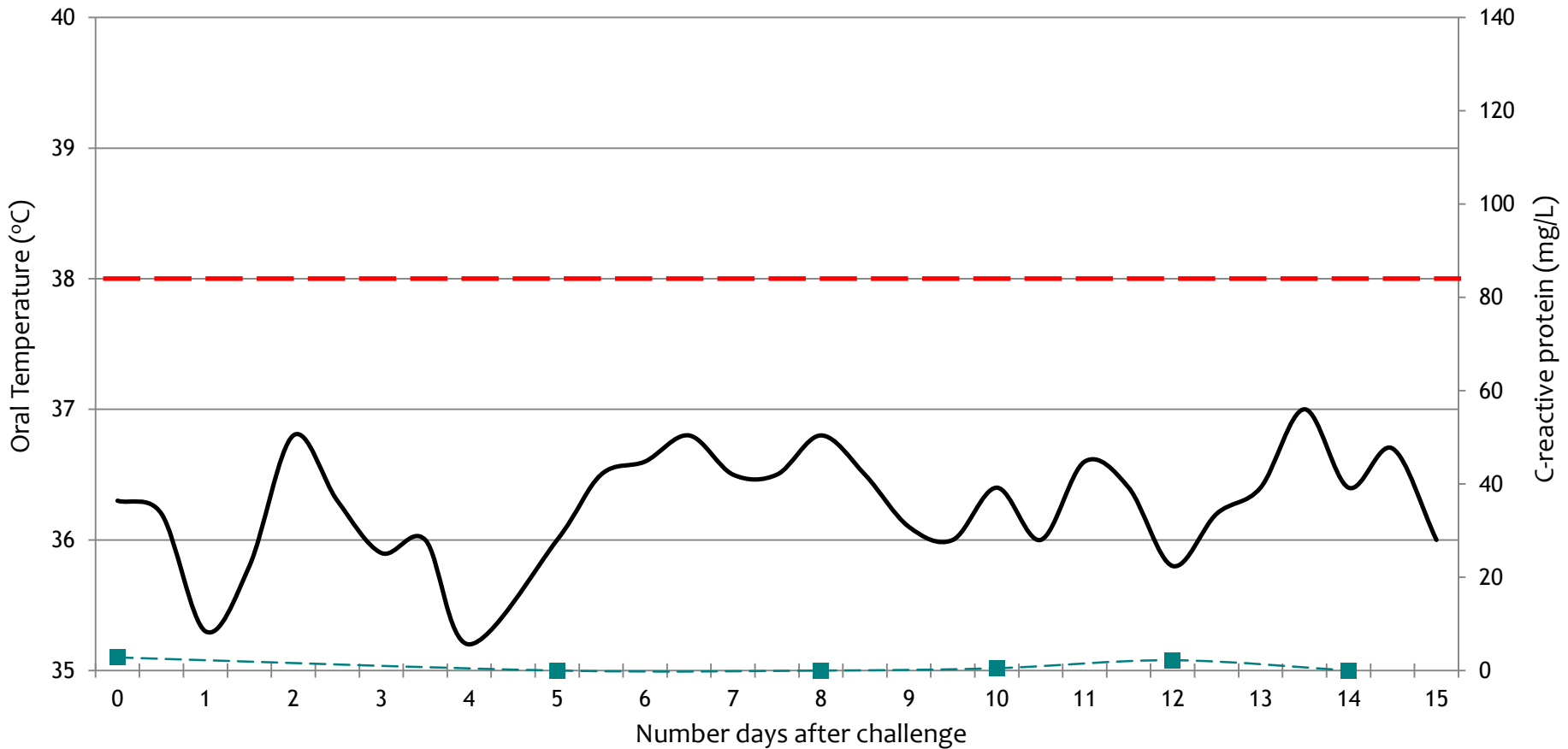


Blood Cx	-	-	-	-	-	-	-	-	-	-	-	+	-	+	-	-	-	-
Stool Cx	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-

QBC CFU/mL	0																		
Widal O	2																		32
Widal H	4																		16

Persistent shedders

Day	0	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Blood						-		-		-		-		-		-
Stool	-	+				-		-	+	+	+	+	+	+		





Oxford Typhoid Programme

N=370



- T1: typhoid dose-escalation study, $n=41$
- T2: double blind RCT (M01ZH09, Ty21a, placebo), $n=99$
- VAST: double blind RCT (Vi-TT, Vi, MenACWY) & AZ vs Cip, $n=111$
- P1: paratyphoid dose-escalation study, $n=40$
- PATCH: Paratyphoid and Typhoid challenge and rechallenge, $n=79$in progress
- Tyger: toxin- strain....in progress

