The United Kingdom's Experience of Zika Virus (2016-2017)

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Introduction

- First human infection with this mosquito-borne flavivirus was identified in 1962
- Detected in Brazil for the first time in 2015; subsequently spread through the Americas in explosive outbreak
- Originally perceived to be a benign infection causing only rash, fever and arthralgia
- Now known to be a cause of severe congenital abnormalities and a trigger for Guillain Barre Syndrome
- Also now known to be capable of sexual transmission
- In the UK, NHS diagnostic testing for Zika virus (ZIKV) is performed on symptomatic individuals at RIPL, PHE Porton by RT-PCR (based on Pyke *et al*, 2014) on plasma, urine and occasionally semen and by serology (Euroimmun, Germany) on serum or plasma

Aim

Here we present the UK's experience of ZIKV during the recent epidemic. We examine the number of samples received and tested, the proportion that were positive and review their demographics, travel destination, symptoms, pregnancy status and results, and in negative cases whether an alternative diagnosis was made.

Method

A retrospective review was performed on the laboratory information management system searching by orders for ZIKV PCR and/or serology tests between 1st January 2016 and 31st December 2017. Each individual request form and result was reviewed.

Results

Figure 1 shows the number of patient requests for ZIKV testing, the number tested and the results. It also shows the way positive PCR and serology results were categorized.

Figure 1

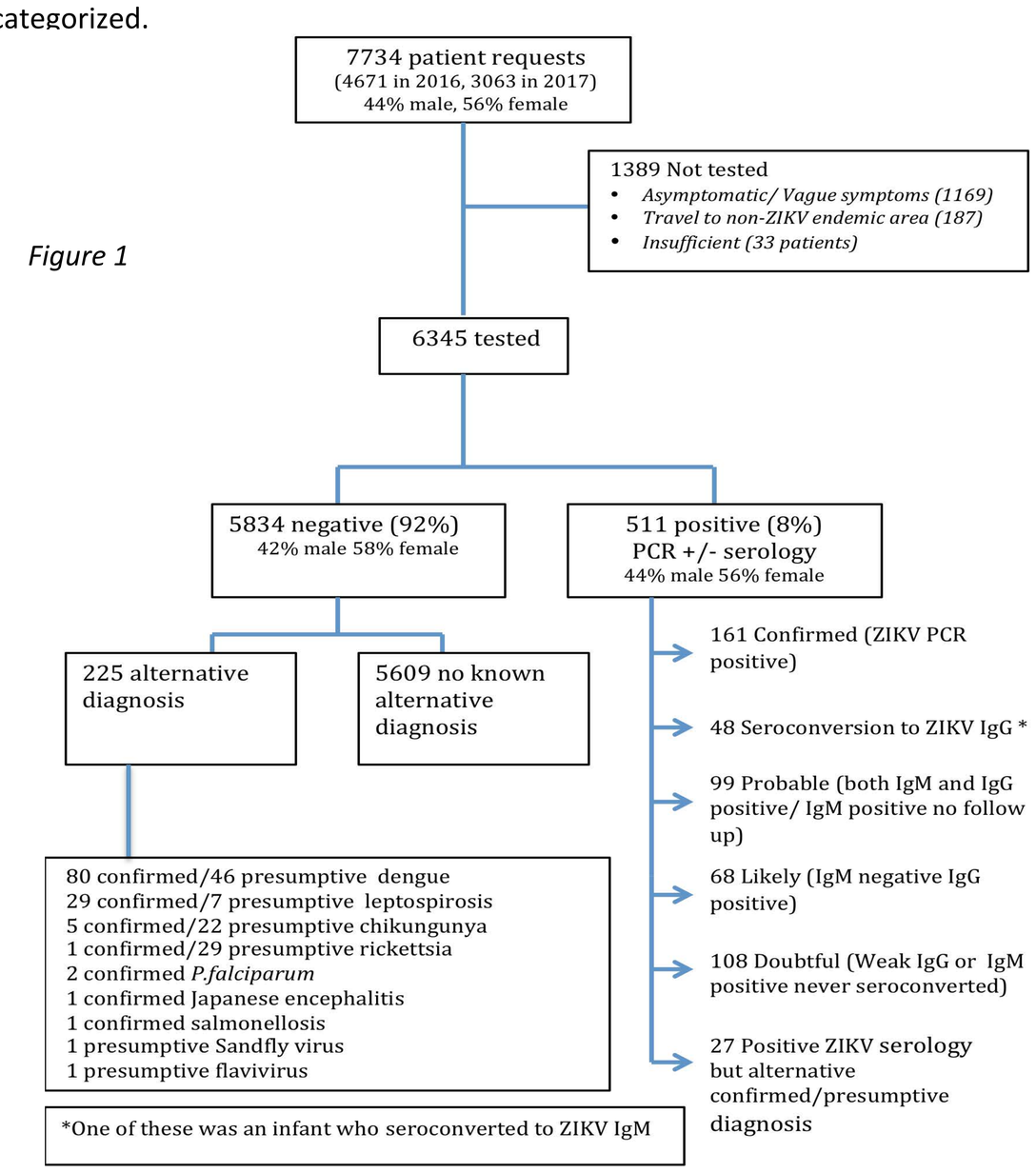

Figure 2– Number of ZIKV PCR positive results over time

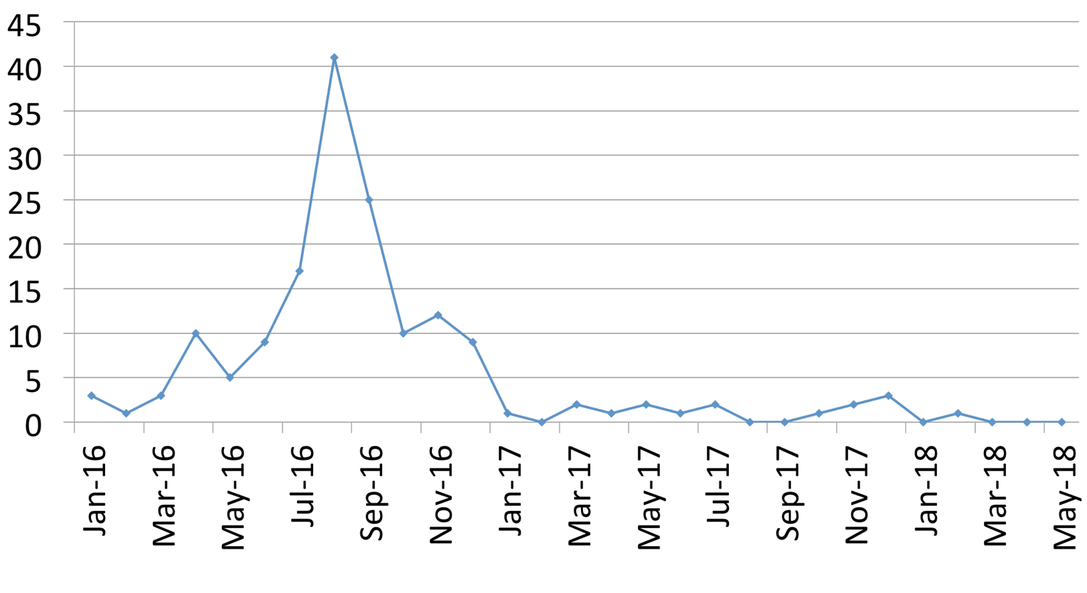

Figure 3 – Presenting clinical features of patients with positive ZIKV results

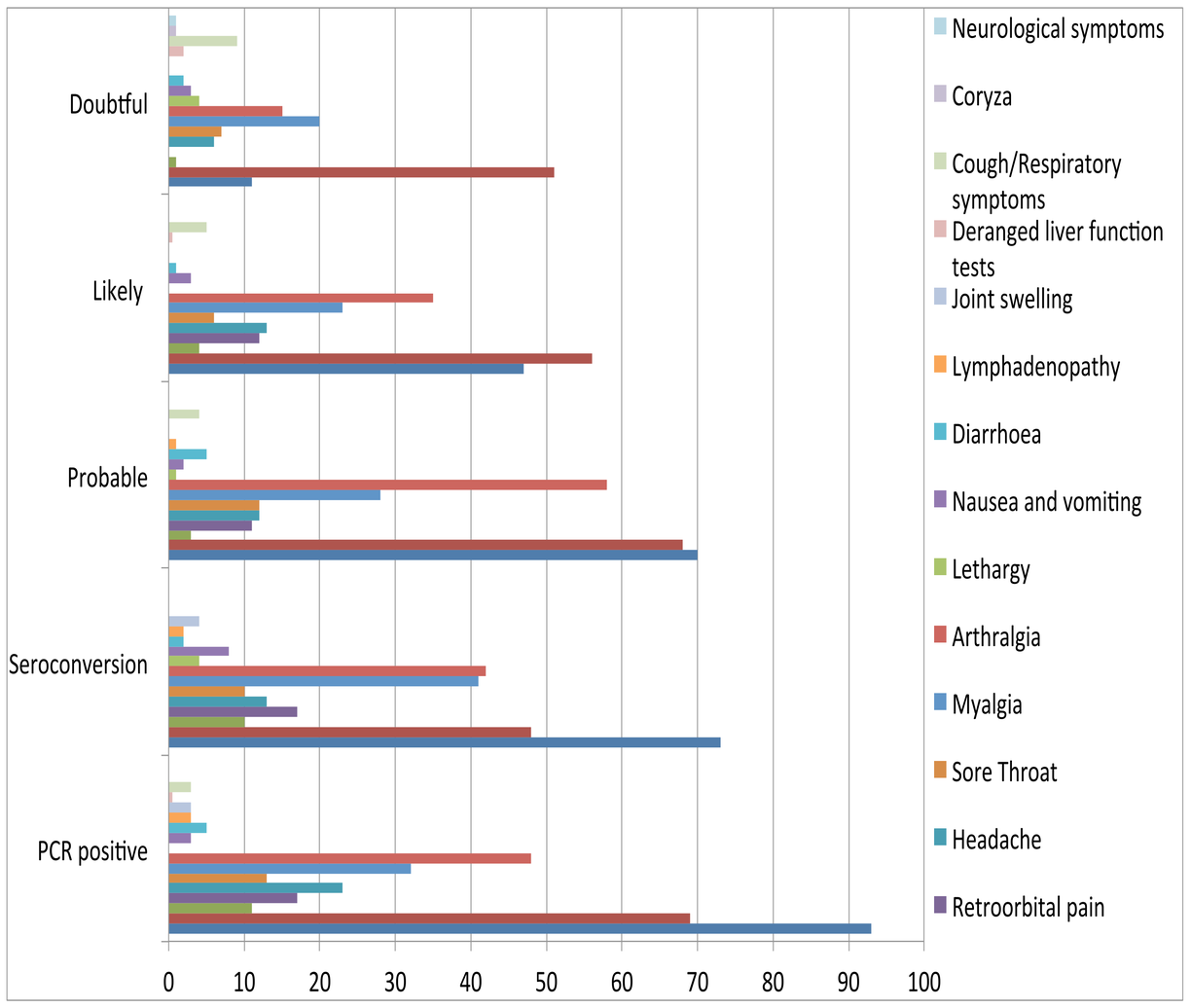

Table 1 – Countries visited by patients with positive ZIKV results

	Caribbean	Central America	S. America	SE Asia	Antipodes and Pacific Islands	USA	Africa
PCR positive	108	28	23	4	0	0	0
Seroconversion	36	6	3	1	1	1	0
Probable	64	13	19	2	0	1	0
Likely	39	10	15	4	0	0	0
Doubtful	32	11	18	38	1	3	5

- Of the 161 PCR positive patients, 70 had ZIKV RNA detected only in urine and 18 in both urine and blood. The maximum duration of detection in urine was 29 days post symptom onset
- ZIKV antibodies were detected in all PCR positive cases where follow-up sera were received
- Only 1 instance of sexual transmission of ZIKV was identified
- Only 15 pregnant women had laboratory evidence of ZIKV infection; amongst the offspring of these 15 women, one baby was found to be infected and she is progressing appropriately with her developmental milestones

Discussion

Observations regarding testing and result interpretation

•Urine is an excellent diagnostic sample; ZIKV RNA is detectable more often and for longer (up to 3 or 4 weeks) in urine as compared with serum/plasma
•ZIKV IgM (as detected by the Euroimmun assay) does not persist >6 wks post symptom onset
•ZIKV IgM (as detected by the Euroimmun assay) often does not appear in patients with previous dengue infection
•Isolated false positive ZIKV IgM results occur commonly; it is essential to obtain follow-up samples to look for ZIKV IgG seroconversion
•Isolated ZIKV IgG is hard to interpret: it can represent (i) past ZIKV infection, (ii) recent ZIKV infection in someone with previous dengue, (iii) cross reactivity, *i.e.* flavivirus antigen exposure at some time, or (iv) non-specific reactivity.

Additional conclusions and learning points from this review

•The most common symptom in PCR or seroconversion-confirmed ZIKV disease was a rash. Fever was less common. The presence of respiratory or gastrointestinal symptoms make an alternative diagnosis considerably more likely.
•The majority of returning travelers to the UK diagnosed with ZIKV had been to the Caribbean. There were only a few returning travelers with ZIKV from the Far East and none from Africa.
•Despite the understandable concern, sexual transmission and transplacental infection are uncommon phenomena. No case of Congenital Zika Syndrome has been identified in the UK
•Despite continued testing of "suspected cases", very few ZIKV infections have been diagnosed in the UK since the epidemic in the Americas and Caribbean has subsided
•Detailed travel and clinical information is required for the optimal interpretation of ZIKV serology results, especially now that the risk of ZIKV acquisition has decreased
•Medical professionals seeing patients concerned about ZIKV infection need to keep a wider differential in mind, especially outside of an epidemic when an alternative diagnosis is more much more likely

Reference: Pyke AT, Daly MT, Cameron JN et al, Imported Zika virus infection from the Cook Islands into Australia, 2014 PLOS Current Outbreaks 2014 , Edition 1