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Invasive pneumococcal disease leads to activation and hyperreactivity of platelets

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ABSTRACT

Using a novel porcine model of intravenous *Streptococcus pneumoniae* infection, we showed that invasive pneumococcal infections induce marked platelet activation and hyperreactivity. This may contribute to the vascular complications seen in pneumococcal infection.

Dear Editors,

Community acquired pneumonia (CAP) is associated with an increased short-term and long-term risk for cardiovascular events (CVE) [1]. The Gram-positive bacterium *Streptococcus pneumoniae* is a major cause of CAP and sepsis. *S. pneumoniae* is well known to interact with and activate platelets *ex vivo* [2]. Platelets play a central role in acute CVE and atherosclerosis [3], and we speculate that excessive platelet activation may also contribute to the vascular comorbidity in pneumococcal infections. However, whether systemic platelet activation and platelet hyperreactivity are prominent features of invasive pneumococcal infections *in vivo* is not well-established.

Porcine animal models are frequently used in cardiovascular research due to the similarities with humans in terms of cardiac anatomy and the hemostatic system [4]. Pigs are also a natural host of the pathogen *Streptococcus suis*, which has strong genetic similarities with *S. pneumoniae*. Using a novel porcine model of pneumococcal disease, we investigated the hypothesis that invasive pneumococcal infections are associated with pronounced platelet activation and hyperreactivity.

1. Methods

1.1. Porcine S. pneumoniae infection model

Full details of the animal experimental model are described elsewhere [5]. In short, two groups of five piglets received 1 ml intravenous injection of either a low (4.2×10^6 Colony-Forming Unit [CFU]/ml) or high dose (2.9×10^8 CFU/ml) of *S. pneumoniae* strain PBCN214, a serotype 8 invasive strain isolated from a patient with pneumonia, meningitis and sepsis. Two other groups of five piglets each received 3 ml of intranasal inoculation of a low (2.5×10^6 CFU/ml) or high dose (2.9×10^8 CFU/ml) of *S. pneumoniae* strain BHN418, a serotype 6B strain previously used in experimental human carriage models [6]. Piglets were euthanized at day seven post-inoculation, or earlier when reaching pre-defined humane end points. The animal experiment was approved by the Ethical Committee of the Central Veterinary Institute of Wageningen UR (The Netherlands), in accordance with the Dutch law on animal experiments (permit number 2014004b).

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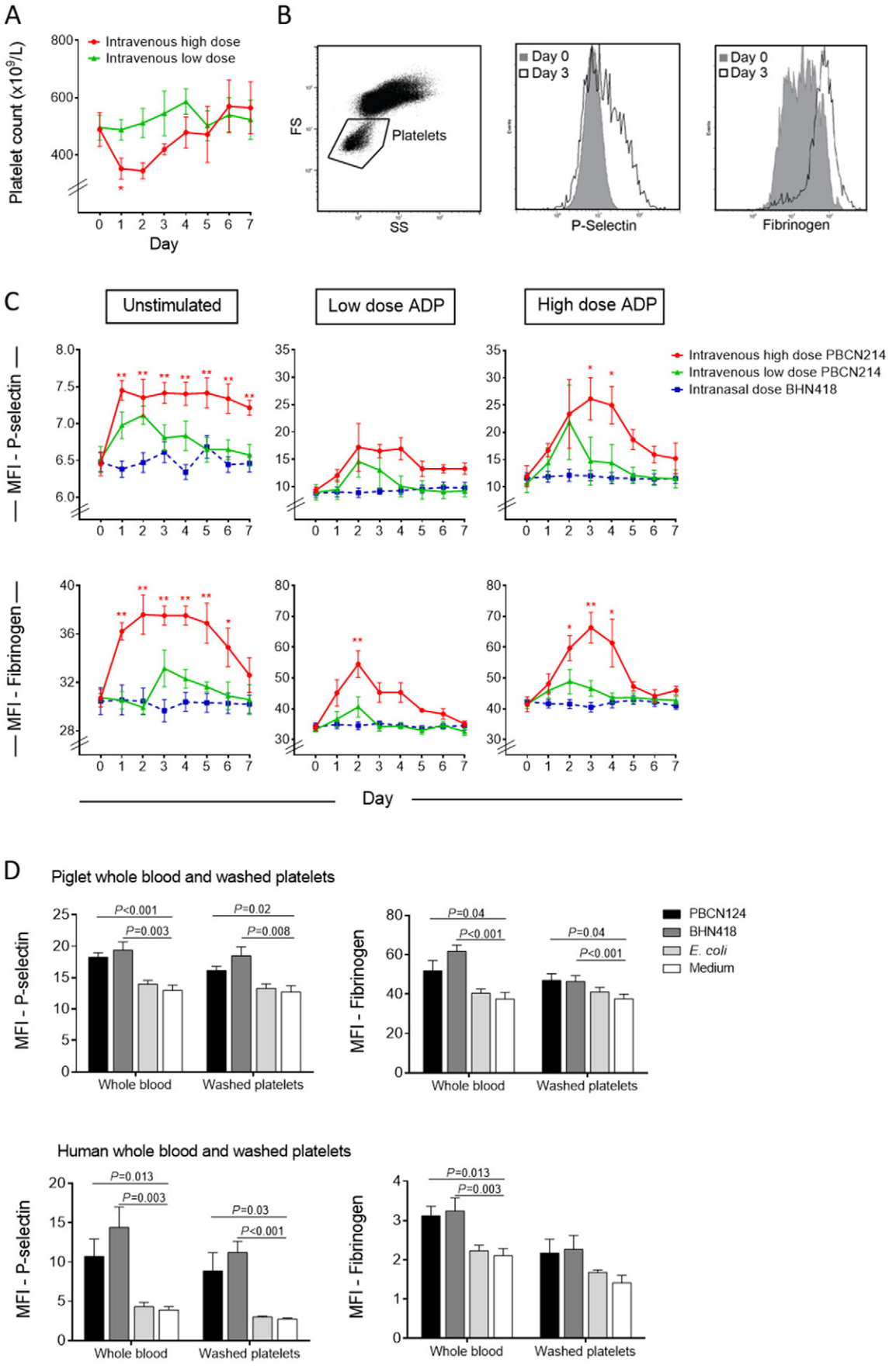
A
Platelet count (x10⁹/L)
Intravenous high dose
Intravenous low dose
Day
B
FS
SS
Platelets
Day 0
Day 3
P-Selectin
Fibrinogen
C
Unstimulated
Low dose ADP
High dose ADP
MFI - P-selectin
MFI - Fibrinogen
Intravenous high dose PBCN214
Intravenous low dose PBCN214
Intranasal dose BHN418
Day
D
Piglet whole blood and washed platelets
MFI - P-selectin
P<0.001
P=0.003
P=0.02
P=0.008
MFI - Fibrinogen
P=0.04
P<0.001
P=0.04
P<0.001
Whole blood
Washed platelets
PBCN124
BHN418
E. coli
Medium
Human whole blood and washed platelets
P=0.013
P=0.003
P=0.03
P<0.001
P=0.013
P=0.003