humans in Vietnam and Thailand [1]. Most infected individuals usually developed progressive pneumonia with acute respiratory distress syndrome and consequently died. Hemostatic disorders could also be seen in those infected cases [1]. Many laboratory aberrations are noted in the cases with bird flu. Thrombocytopenia is usually noted in the severe bird flu infection [2].

Here, the author performed this mini study in order to document the impact of bird flu infection on prothrombin time (PT) among reported Thai patients. A literature review on the papers concerning human bird flu in Thailand was performed. The author performed the literature review on human bird flu infection reports in Thailand from the database of published works cited in the Index Medicus and Science Citation Index. The author also reviewed the published works in all 256 local Thai journals, which is not included in the international citation index, for the report of human bird flu infection in Thailand. The reports that contained no complete data were excluded for further analysis.

According to this review, there are six reports [3–8] covering 12 Thai patients with confirmed diagnosis of bird flu. Of interest, prolonged PT is reported in no case. Although some researchers proposed that the prolonged PT should be a common finding in the patients with bird flu [9], the finding in this study argued against that proposal. The bleeding presentation in the patients with bird flu should relate to the pathology of platelet rather than prolonged PT.

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The development of atypical hemolytic uremic syndrome is not influenced by thrombophilia susceptibility factors

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Hemolytic uremic syndrome (HUS) is characterized by the triad of thrombocytopenia, Coomb's test negative microangiopathic hemolytic anemia and acute renal failure. HUS is classified as either (D+) when it is associated with a preceding diarrheal illness which in most is due to infection with *Escherichia coli* O157 or less commonly non-diarrheal associated (D−) (also called 'atypical'). Atypical HUS (aHUS) may be sporadic or familial. In both, mutations have been reported in regulators of the complement pathway including factor H (CFH), membrane cofactor protein (MCP) and the serine protease factor I (IF). Such mutations result in impaired protection of host surfaces against complement activation. A characteristic feature of both MCP, CFH and IF-associated aHUS is variable penetrance. One possible explanation for this is that functional variants in complement regulators act as modifiers. In support of this are reports of an association between *CFH* and *MCP* SNPs and aHUS [1]. In addition, other factors outside of the complement system may act as modifiers. In this study, we have examined the hypothesis that the three common inherited thrombophilia factors (factor V, F5 c.1691G > A; methylenetetrahydrofolate reductase, MTHFR c.677 C > T and prothrombin, F2 c.20210 G > A) are susceptibility factors for the development of aHUS.

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Table 1 Genotype and allele frequency

	Controls						HUS						
	Genotypes				Allele frequency		Genotypes				Allele frequency		
	1/1	1/2	2/2	n	1	2	1/1	1/2	2/2	n	1	2	p
F5 c.1691G > A	93	3	0	96	98.4	1.6	92	5	0	97	97.4	2.6	0.48
MTHFR c.677 C > T	42	42	10	94	67	33	44	40	9	93	68.8	31.2	0.71
F2 c.20210 G > A	97	1	0	98	99.5	0.5	90	6	0	96	97	3	0.048

A total of 97 aHUS patients and 100 normal controls were studied. Ethics approval was given by the Northern and Yorkshire Multi-Centre Research Ethics Committee. Out of the 97 aHUS patients, there were four families in which more than one family member was included in the cohort. In three families, there were two sibs included and in one three sibs. In the cohort, 20 had a *CFH* mutation, five had an *MCP* mutation and one an *IF* mutation.

The aHUS patients and the control subjects were predominantly Caucasian (aHUS 86/97; controls 100/100). DNA was extracted from peripheral blood according to standard procedures.

Regions of DNA containing the SNPs of interest were amplified by PCR. Genotyping was performed via a primer extension reaction, using the ABI PRISM SNaPshot ddNTP Primer Extension Kit (Applied Biosystems, Foster City, CA, USA) and subsequent detection was performed with an ABI PRISM 3100 Genetic Analyzer (Applied Biosystems). SNaPshot reactions were performed on pooled PCR products according to the manufacturer's instructions using pooled SNaPshot primers. Ambiguous SNPs were verified by direct sequencing using DYEnamic ET Dye Terminator Cycle Sequencing (Amersham, Little Chalfont, UK) as described by the manufacturer. The differences in genotype frequency between HUS patients and control individuals were evaluated by means of the chi-squared test. A Bonferroni correction of (0.05/3) was applied giving a significance value of 0.017.

The genotype and allele frequency for patients and controls is shown in Table 1. There was no significant association between any of the three thrombophilia alleles and aHUS. Neither was there any association when those patients known to have a *CFH*, *MCP* or *IF* mutation were analyzed independently. Thus, we have found no evidence that these three commonly inherited thrombophilia factors are acting as susceptibility factors for the development of aHUS. The rationale for testing this hypothesis was based on two observations. Firstly, the renal pathological findings in aHUS are those of a thrombotic microangiopathy affecting both arterioles and arteries. Thus, thrombophilia in association with other predisposing factors such as a *CFH*, *MCP* or *IF* mutation may increase the risk of platelet-rich microthrombi developing in the renal microvasculature. Secondly, HUS has been described in association with Cobalamin C (Cbl-C) disease which is characterized by methylmalonic aciduria and hyperhomocysteinemia. [2]. Moderate or mild hyperhomocysteinemia is an independent risk factor for vascular disease and thrombosis. MTHFR c.677 C > T results in an alanine to valine change in the catalytic domain and decreases the activity of MTHFR. MTHFR is required for the generation of methyltetrahydrofolate, the co-substrate required for remethylation of homocysteine to methionine. Decreased activity of MTHFR therefore results in hyperhomocysteinemia.

The allele frequency for the HUS patients and controls in this study is similar to that reported in large population studies for similar ethnic groups. F5 c.1691A allele frequency ranges from 1% to 7% in Caucasian populations [3], it is much less frequent in black and Asian populations. The frequencies in our HUS (2.6%) and control (1.6%) populations are compatible with the predominantly Caucasian population that we were studying. MTHFR c.677T allele frequency ranges from 25% to 40% in Europe [4]. The frequencies in our two populations lie in the middle of this range (HUS 31.2% and controls 33%). F2 c.20210A allele frequency ranges from 1.7% in Northern Europe to 3% in Southern Europe [5]. Although not significantly different, the allele frequency in our control population (0.5%) was both lower than previously reported and also lower than the HUS patients (3%).

This lack of association is in keeping with a previous report in patients with D + HUS [6] but is in contrast to findings from four independent cohorts, including our own, which show an association between *CFH* and *MCP* alleles and aHUS. Therefore, present evidence would suggest that complement regulators are the major susceptibility factors for aHUS.

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Did Jesus Christ die of pulmonary embolism?

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The life and teachings of Jesus Christ have attracted enormous attention throughout the past 2 millennia. His agony and death was the subject for numerous religious scholar and artistic creations. While the common views describe the death of Jesus on the cross as a result of bleeding, the following thesis will present another, yet unreported cause for his death.

A number of medical articles dealt with Jesus' suffering and death [1–3]. In an elaborate medical paper on the physical death of Jesus Christ published almost 20 years ago in *JAMA* [4], the authors carefully addressed potential causes of Jesus' death. After analyzing detailed descriptions from the *New Testament* [5] and contemporary Christian, Jewish and Roman sources, Edwards *et al.* [4] give the following description of events.

Before crucifixion Jesus remained for at least 12 h without food and water since the last supper. During that time, from Thursday 9 PM to Friday 9 AM, Jesus was under great emotional stress, endured beating and had to walk 4 km to and from the sites of various Jewish and Roman trials [6]. It is therefore clear that even before scourging and crucifixion, Jesus was in a state of dehydration.

Before crucifixion Jesus underwent scourging, which was a legal preliminary to every Roman execution. Scourging of the back, buttocks and legs leads to significant tissue damage and actually represents multi-trauma. This procedure caused pain and blood loss leading to a preshock state. However, the amount of blood loss by itself could not result in circulatory failure [4]. It is now clear that multiple trauma is associated with significant activation of the coagulation system, mainly by tissue factor [7,8].

After scourging, Jesus was forced to carry on his shoulders the patibulum of the cross, which weighted 34–57 kg for 600 m to the site of crucifixion [6]. This led to further dehydration and exhaustion.

At crucifixion, nailing of the wrists and ankles to the cross led to further release of tissue factor and increased procoagulant activity [9,10]. A crucified individual could not move his ankles and this prolonged immobilization in the upright position resulted in increase of the prothrombotic risk. While on the cross, a victim experienced severe stress, prolonged sun exposure and developed rapid shallow breathing, which dramatically intensified dehydration [11]. Moreover, Jesus was also given wine for pain relief, probably causing increased diuresis.

It is mentioned that crucified victims could survive on the cross between 3–4 h and 3–4 days [4]. Jesus was put on the cross on Friday before noontime and died at 3 PM, i.e. only 3–6 h after the start of crucifixion. It is clear that his death was sudden [5] and that a Roman soldier made the stabbing in his right chest after his death [5].

Edwards *et al.* [4] discuss the sudden death of Jesus and suggest a number of potential causes, including coronary thrombosis from thrombotic vegetations found on the aortic or mitral valves. While the medical evidence for this hypothesis is elusive, it is known that the common cause of death in the setting of multiple trauma, immobilization and dehydration is pulmonary embolism.

This fits well with Jesus' condition and actually was in all likelihood the major cause of death by crucifixion. It is stated that in order to expedite the death of crucified victims, the Romans fractured their legs and this resulted in death from asphyxia within minutes, probably due to embolization of thrombi or fat. This procedure was performed to the two thieves but not to Jesus.

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