mortality showed the same trends as mortality from myocardial infarction and stroke.

Implications

Our results add prospective evidence for the role of triggering factors, including mental and emotional stress, in cardiovascular deaths in men. We also observed a clear sex difference that merits further investigation. The triggers induced by a critical football match may not be due solely to mental or emotional stress. Notably, heavy alcohol use, overeating, and excessive smoking may also play a part.

The role of trigger factors in cardiovascular disease illustrates that prevention of cardiovascular events goes beyond management of risk factors for atherosclerosis. Increased awareness of the impact of stressors in vulnerable subjects seems crucial. In addition, aspirin or β blockers may prevent acute cardiovascular events being triggered in high risk subjects.[22 23]

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Streptokinase versus alteplase and other treatments for acute and delayed thrombolysis of blood stains in clothing

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Abstract

Objective To assess the usefulness of heparin, alteplase, and streptokinase in removing blood stains.
Design Randomised controlled trial.
Setting Hospital laundry.
Interventions Blood stains were allocated to treatment with alteplase, streptokinase, heparin, a commercial enzymatic stain remover, or no treatment at all after three or seven hours and then washed in hot or cold water two hours later.
Results Both hot water and early treatment were strongly associated with improved stain removal. All four treatments were associated with a worse outcome than no treatment at all, although for streptokinase this trend did not reach significance. The commercial stain remover gave the worst results of all treatments tested.
Conclusions Contrary to popular wisdom, hot water is much more effective than cold in removing blood stains. Methodologically rigorous research and evidence based principles are needed within the laundry industry, and the role of thrombolytic drugs should be assessed further.

Introduction

Thrombolytic drugs are used for a widening and often controversial array of indications, including myocardial infarction, ischaemic stroke, and massive pulmonary embolism.[1–3] However, little attention has been given to their role in treating blood stains in clothing, an event that causes appreciable morbidity to the affected medical officer.

Although laundry products fuel a $4.1bn (£2.7bn) a year industry in the United States alone,[4] no scientific evidence is publicly available concerning their effectiveness. Some articles, however, offer scientific sounding classifications of stain removers into absorbents, bleaches, detergents, solvents, soaps, and enzymes[5] or classifications of stains into absorbed, built-up, or compound.[6] Many of the methods suggested for removing blood stains are contradictory and use a broad and sometimes fanciful variety of cleansing agents, such as ammonia, salt, hydrogen peroxide,[5] borax,[7] aspirin, talcum powder, starch,[8] and unseasoned meat tenderiser.[9] One article says that any acidic compounds should be avoided because they will make the stain worse,[10] whereas others recommend vinegar[11] or lemon juice.[9] Disagreement also exists over water temperature, although most experts,[5 6 9 10 12] along with an informal sample of mothers and colleagues whom I consulted, favour cold water because hot water would "set the proteins" and result in an intractable stain.

One thing almost all published homecraft and housekeeping guides have in common, however, is a separate section addressing blood stains. This confirms the impression that blood stains are particularly difficult or need special handing. This study seeks to inject some quality evidence on treatment of blood stains and to assess whether "clot busting" drugs have as large a role on shirtsleeves as they do in coronary arteries.

Methods

Using 5 ml syringes, I applied 1 ml blood stains to the centre of 112 numbered regions evenly spaced across 14 identical white cotton hospital pillowcases. The blood was drawn from a healthy male volunteer with a normal full blood count and coagulation profile who was blind to the eventual treatment allocation of each blood stain.

A computer generated cluster randomisation algorithm was used to allocate each stain to one of five possible treatment conditions: alteplase, streptokinase, heparin, Neon "triple enzyme power" colour safe stain remover (Kiwi Brands, Clayton South, Victoria), and no treatment. Treatment involved applying 1 ml of the relevant substance in its standard formulation on to the centre of the blood stain (equating to 1 mg of alteplase, 50 000 units of streptokinase, and 1000 units of heparin).

In parallel with the treatment allocations, each of the 14 pillowcases was randomly allocated to either hot or cold cycles in a Simpson Genesis 525 heavy duty toploading washing machine (Simpson Manufacturing, Avalon, NSW) with the directed quantity of Hurricane super concentrate laundry detergent (Campbell Brothers, Bowen Hills, Queensland). The algorithm further allocated each pillowcase to either acute treatment (2-3 hours after blood stain deposition) or delayed treatment (6-7 hours after blood stain deposition). The cluster randomisation algorithm ensured that the five treatment conditions would be evenly distributed among the four combinations of temperature and timing conditions. The pillowcases were washed two hours after application of the treatment and then dried for 90 minutes on the half heat setting of a Simpson Maxidry 1200 dryer.

A panel of four professional laundry operators and stain removing staff assessed the resultant severity of each blood stain. The judges were blinded to the treatment allocation of the blood stains and pillowcases. Each judge gave every stain a rating of 0, 1, or 2 corresponding to the suggested descriptions of invisible, barely visible, or easily visible. The four judges' ratings were then combined to provide each stain with an outcome measure ranging from 0 to 8, where a lower score represents better stain removal. Agreement between the four judges was good (Cronbach's $\alpha = 0.87$).

Table 1 Mean (SD) stain severity by washing temperature, timing of treatment, and treatment condition*

	Treatment					All treatments
Treatment	None	Alteplase	Streptokinase	Heparin	Neon	
Hot wash:						
Acute	2.25 (1.47)	4.85 (2.29)	1.33 (1.51)	3.67 (2.23)	4.58 (1.46)	3.28 (2.16)
Delayed	4.33 (2.08)	4.90 (2.70)	5.25 (3.59)	5.08 (2.11)	6.00 (3.16)	5.11 (2.56)
Total	3.29 (2.04)	4.88 (2.36)	2.90 (3.11)	4.38 (2.20)	5.29 (2.46)	4.17 (2.52)
Cold wash:						
Acute	1.67 (0.75)	4.50 (1.12)	3.75 (3.01)	6.17 (2.38)	5.71 (2.11)	4.35 (2.45)
Delayed	6.48 (1.07)	6.90 (1.34)	7.00 (0.71)	7.31 (0.96)	7.13 (0.80)	6.96 (0.97)
Total	4.08 (2.67)	5.70 (1.72)	5.05 (2.83)	6.74 (1.83)	6.42 (1.34)	5.61 (2.29)
All temperatures:						
Acute	1.96 (1.16)	4.68 (1.71)	2.54 (2.60)	4.92 (2.56)	5.15 (1.51)	3.82 (2.36)
Delayed	5.41 (1.94)	5.90 (2.27)	6.13 (2.57)	6.20 (1.95)	6.56 (2.28)	6.04 (2.13)
Total	3.68 (2.35)	5.29 (2.05)	3.98 (3.10)	5.56 (2.32)	5.85 (2.02)	4.89 (2.50)

*Acute treatment=2-3 hours after stain depostion; delayed=6-7 hours after. Lower score represents a less visible stain.

Statistical considerations

The principal aim of this study was to compare stain severity after application of each of the treatments. Data were double entered and validated on an Excel spreadsheet and then imported into SPSS version 9.0 for further analysis. Multiple regression was used to assess the contribution of temperature, timing, and treatment on the severity of the stain. Although all pillowcases were identical, theoretical clustering effects were excluded by provisionally including pillowcase allocation in the regression. As there were no significant clustering effects, adjustment for pillowcase randomisation was not necessary. The sample size was restricted to 20-24 blood stains per group because of the limited availability of the pharmaceuticals. However, the sample size was deemed sufficient because of the limited variation expected from the standardised staining and washing conditions for each sample.

Results

Table 1 shows the mean stain removal score for the 20 permutations of treatment, timing, and water temperature. Multiple regression controlling for the other variables (table 2) showed that acute treatment was significantly more effective than delayed treatment (mean stain score 3.82 *v* 6.04; $P < 0.0001$) for all treatments studied. Hot water was significantly more

Table 2 Multiple regression results of timing, temperature, and treatment variables on stain severity

Variable	β coefficient	SE	P value
Hot water	–1.446	0.377	0.0002
Acute treatment	–2.165	0.379	<0.0001
Alteplase	1.604	0.604	0.0092
Streptokinase	0.508	0.606	0.4032
Heparin	1.873	0.576	0.0016
Neon	2.171	0.576	0.0003

What is already known on this topic

Thrombolytic drugs are effective at breaking down clots in the body

No scientific data are available on treatment of blood stains on clothing

What this study adds

Thrombolytic drugs and a commercial stain remover were worse at removing blood stains than no pretreatment

Treatment after 2-3 hours produced better results than later treatment

Washing in hot water was more effective than washing in cold water

effective than cold water for most treatments (4.17 *v* 5.61; P = 0.0002).

Alteplase was significantly less effective than no treatment at all (5.29 *v* 3.68; P = 0.009), and streptokinase was marginally less effective than no treatment, but this difference was not significant (3.98 *v* 3.68; P = 0.4). Heparin was significantly less effective than no treatment (5.65 *v* 3.68; P = 0.001) under all washing conditions as was Neon, the commercial enzymatic stain remover (5.85 *v* 3.68; P = 0.0003). No interaction or clustering effects were detected.

Discussion

This study shows that treatment of blood stains requires early action, as is the case when treating heart attacks and strokes. Blood stains that were treated within three hours and washed within five hours after deposition were much less prominent than those treated seven hours and washed nine hours after deposition. Interestingly, only two of the 20 stain removal guides reviewed emphasised the importance of acting quickly.[9 10] One suggested a likely mechanism: "Keep the stain wet."[10]

Contrary to the convictions of most experts, it is not a good idea to wash blood stains in cold water. In this study hot water was much more effective. However, as some guides recommended washing in warm water after immediate treatment with cold water,[8 13] hot water may be harmful only when the blood is fresh.

Unfortunately for the pharmaceutical industry, thrombolytic drugs were not effective stain removers. Application of alteplase, streptokinase, and heparin all made the blood stains worse, although the effect of streptokinase was not significant. This is perhaps a reassuring result as alteplase costs over $1000 a dose, probably far more than the article of affected clothing. Nevertheless, thrombolytic drugs may still have a role in selected cases. In this study the treatment was applied to the blood stain without any rinsing or rubbing until the pillowcase was put in the washing machine two hours later. As the primary mechanism of these drugs is to inhibit or reverse coagulation, whereas the mechanism of staining is likely to be cell lysis and haemoglobin deposition, the treatment may help the stain to spread and further infiltrate the fabric fibres. Further research is needed under different conditions to elucidate the role of thrombolytic drugs when fresh blood stains occur in the emergency department.

The most surprising finding of this study was the terrible performance of the commercial stain remover. It was the most detrimental of all treatments studied, even through the product was used according to the manufacturer's instructions and blood was mentioned as one of stains it is able to combat. This result is disappointing because many stain removal guides recommend commercial enzymatic stain removers as the most effective tool against "protein rich" stains such as blood.[5 6 14] The laundry industry clearly needs to embrace methodologically rigorous research and evidence based principles when developing products and giving advice on stain removal.

Although further research is required, the best advice for hapless casualty officers who find their favourite clothes stained by blood seems to be to eschew all stain removal products as well as the hospital formulary and, as far as possible, to keep the stain wet until washing in hot water as soon as practicable.

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Never too late …

For many people in Britain, the winter of 1972-3 is remembered for the miners' strike, the "three-day week," power cuts, and reading by candlelight. For Dr Miles Markus, however, more serious matters were brewing. Working at the time in London, he carefully prepared a letter and submitted it for publication to the *British Medical Journal*. The publication process ground slowly at the journal in those days (unlike the smooth, electronic office we have today?)—so it was not until June that Dr Markus's letter hit the press (1973;ii:666). To his dismay we had spelt his name wrongly, substituting a "c" for the "k." How could this have happened? Dr (now Professor) Markus has nursed his grudge for 27 years, and last month, by an indirect route, we came to hear of his displeasure. We would like to apologise to Professor Markus and wish him a merry Kristmas.