	–4 years	–2 months	–1 month	Week 0	Week 7	Week 8	Week 12
Index baby							
IgM	..	..	..	..	11·1/1·2	..	..
IgM EIA	..	..	..	..	>3/0·9	>3/0·9	..
Index mother							
IgG (SRH)	..	14	..	..	..	..	..
IgM	..	<0·9/0·9	..	..	..	..	..
IgG shift	..	Equiv.	..	High	..	..	..
IgG AI	..	High	..	High	..	..	..
Contact baby							
IgG (SRH)	..	..	..	..	..	..	11
IgM EIA	..	..	..	..	..	..	>3/0·9
IgG shift	..	..	..	..	..	..	High
IgG AI	..	..	..	..	..	..	High
Contact mother							
IgG (SRH)	10	..	11	..	..	..	..
IgM	..	..	<0·9/0·9	..	..	..	..

Week 0 = birth of both index and contact babies. All measurements except those for IgM from index baby and IgG from index mother done at Public Health Laboratory Service, Preston, UK. EIA=enzyme immunoassay. SRH=single radial haemolysis zone diameter (mm). AI=avidity index. Equiv=equivocal. Figures for IgM and IgM EIA show optical density/cut-off value.

Table 1: **Results of laboratory testing**

Rubella vaccine is not yet recommended in the Expanded Programme on Immunisation. No accurate data exist for seroprevalence of rubella virus antibody or incidence of congenital rubella syndrome in Bangladesh, but estimates for other parts of south Asia suggest that up to 60% of women of childbearing age could be susceptible to infection. An estimated incidence of between 44 and 275 cases of congenital rubella syndrome per 100 000 livebirths is quoted.[3]

In our hospital, where almost half the attendees of the antenatal clinic are from Bangladesh, we calculated that 6% of this group are likely to be seronegative (table 2). This rate is higher than previously reported for a similar group of patients.[4] Recent immigrants to developed countries are likely to be at substantially higher risk of infection acquired either locally or abroad, especially since those who arrive as adults will have missed out on local vaccination schedules. Special attention should be paid to screening and immunisation of new arrivals against this and other vaccine-preventable diseases.

For this baby, there was no reason to suspect congenital rubella syndrome antenatally, and specific features of this disorder did not become apparent until some time after birth. The lack of an earlier serum sample from the mother highlights the importance of continuing antenatal care: since the mother first arrived at our hospital late in her pregnancy, she was no longer IgM positive when screened, which prevented an early diagnosis. Ascertainment of accurate antenatal details in recent arrivals is often difficult; therefore, such women should be questioned specifically about any illnesses in pregnancy, and rubella should be considered if there are signs or symptoms compatible with a congenital infection, even in the absence of compatible serology. Our patient highlights the need to consider the introduction of "catch-up" immunisation programmes for recent arrivals.

Finally, the secondary spread highlights the high infectivity of this disorder. Infected babies secrete large amounts of virus in their body fluids for up to a year, which poses a substantial risk of cross-infection. Nosocomial spread from affected infants to hospital staff has been well documented,[5] but to our knowledge has not been reported previously to other infants.

	Number of attendees	Number seronegative
Bangladeshi	1965	117 (6%)
Other Asian*	155	14 (9%)
White	875	18 (2%)
African/Caribbean/mixed	428	14 (3%)
Other/unknown	67	2 (3%)
All groups	3490	165 (5%)

*Indian, Pakistani, Chinese, Thai, Vietnamese.

Table 2: **Prevalence of seronegativity to rubella virus by ethnic group, as measured at antenatal screening at the Royal London Hospital (Jan 1, 2000–Dec 31, 2000)**

Contributors

E Sheridan wrote the paper and calculated the seroprevalence figures; C Aitken supervised the laboratory investigations and revised the paper; D Jeffries reviewed the final draft; M Hird and P Thayalasekaran cared for the patient and collected specimens in the hospital and community.

Conflict of interest statement

None declared.

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Hormone replacement therapy and prevention of pressure ulcers and venous leg ulcers

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Pressure ulcers and venous leg ulcers are common chronic wounds. Oestrogens in the form of hormone replacement therapy (HRT) might have an effect on wound healing, but this possibility has not been studied in detail. Using a case-cohort study including elderly patients in the UK General Practice Research Database, we showed that patients who received HRT were less likely to develop a venous leg ulcer (age-adjusted relative risk 0·65 [95% CI 0·61–0·69]) or a pressure ulcer (0·68 [0·62–0·76]) than those who did not use HRT. Therefore, we believe that HRT could be beneficial for the prevention of these wounds.

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Chronic non-healing wounds are a substantial medical problem. Two such chronic wounds are the venous leg ulcer and the pressure ulcer. Oestrogens are known to have an effect on skin and other soft tissues,[1] but the effect of hormone replacement therapy (HRT) on the prevention and repair of chronic wounds has not been well studied. The ideal study would be a randomised clinical trial in which oestrogens are used as an adjuvant to standard therapy. However, such a study would be very expensive, difficult to design, and, owing

Confounder	Relative risk (95% CI)*	
	Venous leg ulcers	Pressure ulcers
Thrombophilia	0·65 (0·61–0·71)	0·69 (0·62–0·76)
Osteoporosis	0·65 (0·60–0·70)	0·68 (0·61–0·77)
Cellulitis	0·64 (0·58–0·69)	..
Diabetes	0·64 (0·60–0·69)	0·68 (0·62–0·77)
Myocardial infarction	0·64 (0·60–0·69)	0·67 (0·60–0·75)
Congestive heart failure	0·63 (0·58–0·68)	0·68 (0·60–0·76)
Cerebrovascular accident	0·62 (0·60–0·69)	0·68 (0·61–0·76)
Parkinson's disease	..	0·67 (0·60–0·75)
Paralysis	..	0·68 (0·61–0·76)

*Adjusted for patient's age, HRT use, and the variable listed.

Effect of potential confounders on risk of venous leg ulcers or pressure ulcers associated with HRT use

to ethical concerns, difficult to execute properly. As an alternative, we designed two separate case-cohort studies to determine whether use of HRT by women older than 65 years was associated with onset of fewer venous leg ulcers or pressure ulcers than non-use. Case-cohort studies compare information on a subset of all individuals in a population (ie, the cohort) with information on all patients with the disorder of interest in that population (ie, cases).

The population for this study was taken from the UK General Practice Research Database (GPRD) and included individuals enrolled between 1988 and 1996. Patients were eligible if they received care from a general practitioner who was a member of the GPRD, if they had at least two consultations with their doctor while they were aged between 65 and 95 years, and if they did not have a diagnosis of a venous leg ulcer or pressure ulcer for the first 6 months after the start of their database record. The cohort was generated by the UK Epidemiology and Pharmacology Information Core (EPIC) and comprised a 10% random sample of elderly women (older than 65 years); cases were all women enrolled in the GPRD in the same age range with venous leg ulcers or pressure ulcers. A patient was regarded as having a diagnosis of venous leg ulcer or pressure ulcer on the basis of an explicit and previously assessed algorithm.[2] We used Prentice's proportional hazards models for a case-cohort study[3] and the Peanuts program in Epicure 2.10 (Hirosoft, Seattle, WA, USA) to analyse data.

There were 44 195 eligible women in our random 10% sample of elderly women. Venous leg ulcers occurred in 1744 women and pressure ulcers in 802 women. HRT was received by 4944 women (11·2%), 108 of whom developed a venous leg ulcer, and 49 of whom developed a pressure ulcer. Since thrombophilia is supposedly a contraindication to HRT use and is a risk factor for developing a venous leg ulcer, we noted that 908 patients had a documented previous history of thrombophilia in the medical record and, unexpectedly, 117 (12·9%) of these individuals received HRT. There was no difference between the proportion of patients who received HRT with or without a history of thrombophilia.

The relative risk of association of the use of HRT and the development of a venous leg ulcer was 0·53 (95% CI 0·49–0·56). As expected, the patient's age significantly confounded the estimate of the association of HRT and the development of a venous leg ulcer. The age-adjusted relative-risk estimate for HRT use was 0·65 (0·61–0·69). The relative risk of association of the use of HRT and the development of a pressure ulcer was 0·46 (0·42–0·52). The patient's age also significantly confounded the estimate of the association of HRT and the development of a pressure ulcer. The HRT effect estimate adjusted for age was 0·68 (0·62–0·76). Other potential confounders (disorders potentially associated with the wound of interest or the patient's general health) had little effect on the association between HRT use and the development of a venous leg ulcer or pressure ulcer (table). The effect of HRT was not modified by age. Owing to database constraints, we were not able to explore whether a dose effect was present or if a particular formulation of HRT had the greatest effect.

Venous leg ulcers occur because of underlying abnormalities in the venous system of the lower extremities. Patients with these wounds commonly have a history of chronic localised tissue necrosis (lipodermatosclerosis) that predates their ulcer. Patients with pressure ulcers have a similar problem in that their wounds are commonly predated by non-blanchable erythema, which is thought to be a clinical representation of localised tissue ischaemia. In both cases, the patient's inability to repair these repeated and localised insults leads to the wound.

Current treatments for these illnesses are not adequate. Other investigators have previously shown that HRT can improve wound healing in aged individuals.[4] In our study, we showed that women older than 65 years who received HRT were significantly less likely to have a venous leg ulcer than those who did not receive HRT. Similarly, women who received HRT were significantly less likely to develop a pressure ulcer than those who did not. This was an observational study and for that reason our results, the adjustment for potential confounders, and our understanding of all biases, such as selection bias, was limited by the information recorded in the database.

This study did not directly observe whether HRT could help heal a venous leg ulcer or pressure ulcer undergoing therapy. Instead, we assessed whether patients on HRT were more or less likely to develop a venous leg ulcer or a pressure ulcer. Since the formation of these ulcers occurs after the culmination of several cutaneous insults (ie, cutaneous events that need to heal), we feel that the prevention of the occurrence of a venous leg ulcer or a pressure ulcer is probably a good marker for healing. In fact, the standard treatment for both of these wounds—compression for a venous leg ulcer and pressure relief for a pressure ulcer—is the same as that for prevention of the respective wound.[5]

In summary, we have shown that HRT users older than 65 years are about 30–40% less likely to develop a venous leg ulcer or a pressure ulcer than non-users. We view this finding as early evidence that HRT could have a beneficial effect in preventing chronic wounds. Finally, we were surprised to note that having a history of thrombophilia did not seem to dissuade physicians from prescribing HRT. The long-term consequences of this practice need to be reassessed.

Contributors

D Margolis was involved in planning the study, obtaining funding, analysing data, interpreting the results, and writing the paper; W Bilker was involved in planning the study, analysing data, interpreting the results, and writing the paper; and J Knauss was involved in analysing data, interpreting the results, and writing the paper.

Conflict of interest statement

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Role of Purkinje conducting system in triggering of idiopathic ventricular fibrillation

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Ventricular fibrillation is the main mechanism of sudden cardiac death, but the source of its spontaneous initiation has not been mapped. 16 patients were investigated by electrography and radiofrequency ablation after resuscitation from recurrent idiopathic ventricular fibrillation. Triggers of ventricular fibrillation originated from various locations within the Purkinje system in 12 patients and from the ordinary myocardial muscle in four. The accuracy of mapping was confirmed by acute elimination of triggers by radiofrequency delivery, and there was no recurrence of ventricular fibrillation in 14 patients. Long-term follow-up is necessary to establish that ablation is curative and avoids use of a defibrillator.

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Ventricular fibrillation is the main mechanism of sudden cardiac death. Although results of mapping have shown that fibrillation is perpetuated by re-entrant or spiral waves, there are few data about sources of initiation of arrhythmia in man. We aimed to investigate the source of spontaneous ventricular fibrillation.

16 patients underwent mapping of recurrent idiopathic ventricular fibrillation in six centres: 13 had received a defibrillator and the other three presented with repetitive runs of ventricular premature beats after initial cardiac arrest. The coupling interval of premature beats to previous sinus beat varied in 14 patients, with the shortest couplings initiating ventricular fibrillation (table, figure). The mean number of premature beats was 9618 per day (SD 10 136).

All patients had a seemingly normal heart on the basis of established criteria:[1,2] normal physical examination; electrocardiogram; exercise testing; coronary angiography; and right and left ventricular ejection fraction; plus normal endomyocardial biopsy findings in six patients. Ergonovine provocation was negative in five patients and coronary spasm was excluded in the others by documentation of isoelectric ST segment preceding ventricular fibrillation. Normal QRST complexes were noted during oral class IA (n=14) or intravenous class IC (12) drug administration, thus excluding a long QT or Brugada syndrome.[1]

After we obtained written informed consent, two to four multielectrode catheters were placed percutaneously through the femoral vessels. Surface electrocardiogram leads and bipolar intracardiac electrograms filtered at 30–500 Hz were recorded simultaneously.

The origin of arrhythmogenic triggers was localised by the earliest intracardiac electrogram relative to the onset of the ectopic QRS complex. An initial sharp potential (<10 ms duration) before a larger and slower ventricular electrogram during sinus rhythm represented a Purkinje component. This potential, preceding ventricular activation during premature beats, suggested ventricular activation originated from the Purkinje system, whereas its absence at the site of earliest activation signified origin from ventricular muscle.[3]

Radiofrequency ablation was done at the site that had the earliest electrogram during premature beats; a target temperature of 55–60°C was applied for 60–120 s, and the endpoint was abolition of premature beats. After ablation, patients were monitored for 3–5 days with Holter recordings. Patients who had premature beats successfully eliminated were followed-up without antiarrhythmic drugs for recurrent syncope or defibrillator shocks. Furthermore, the data-logging capabilities of the defibrillator were investigated for analysis of any arrhythmic event. Continuous variables were expressed as group mean (SD) and were compared with the Mann-Whitney *U* test.

Premature beats that were positive in V_1 (n=8) mapped to the left ventricle; all patients but one had clinically important variations, mainly in limb leads, with a short QRS duration of 116 ms (SD 14). Premature beats that were negative in V_1 (n=9, one patient had positive and negative forms) originated from the right ventricle and had a important longer QRS duration than beats that started from the left ventricle (145 ms [9]; p=0·008). The axis was inferior and superior in four and five patients, respectively, with only subtle morphological variations in five.

Premature beats originated from the right ventricular outflow tract muscle in four patients. In the remaining 12,

	Sex, age (years)	Family history of sudden death	Number of episodes of VF before ablation	Number of unsuccessful drug treatments	Origin of premature beats	Ectopic QRS duration (ms)	Coupling interval initiating VF (ms)	Cycle length of repetitive runs (ms)
Patient								
1	F, 33	No	1	5	RVOT	150	380	195
2	F, 30	No	1	3	RVOT	140	380	200
3	F, 29	No	6	4	RVOT	160	320	240
4	M, 16	No	2	2	RVOT	130	340	200
5	M, 35	Yes	5	2	RV Purkinje	150	280	220
6	M, 74	No	24	4	RV Purkinje	140	300	260
7	F, 58	No	9	2	RV Purkinje	150	260	180
8	M, 47	No	8	2	RV Purkinje	140	260	240
9	F, 58	No	1	2	LV Purkinje	90	320	165
10	M, 33	No	26	6	LV Purkinje	110	240	200
11	F, 25	No	1	4	LV Purkinje	110	320	360
12	M, 26	Yes	19	8	LV Purkinje	120	260	190
13	M, 33	No	2	6	LV Purkinje	130	280	220
14	F, 38	No	2	4	LV Purkinje	115	300	220
15	F, 40	Yes	5	2	LV Purkinje	120	280	180
16	M, 30	Yes	52	5	LV and RV Purkinje	135	280	200
Total, mean [SD]	38 [15]	..	10 [14]	3·7 [2]	..	130 [19]	300 [41]	219 [24]

VF=ventricular fibrillation; RVOT=right ventricular outflow tract; RV=right ventricle; LV=left ventricle.

Characteristics of patients and arrhythmias