Clinical implications

- Cancer is often seen in patients with deep venous thrombosis
- This study shows that cancer is five times more commonly diagnosed within six months after deep venous thrombosis than a control group matched for age and sex
- Most of the cancers were easily detected by routinemethods (history, physical examination, and laboratory tests)
- Extensive screening of the 1383 patients with deep venous thrombosis would have resulted in beneficial earlier diagnosis in only two patients
- Extensive screening of patients with deep venous thrombosis does not seem cost effective

association between idiopathic venous thrombosis and subsequent development of cancer, with most cancers becoming clinically apparent within the first year after the diagnosis of the venous thrombosis. In contrast Griffin *et al* found no increased risk of subsequent cancer in patients with objectively documented deep venous thrombosis or pulmonary embolism compared with a control group of patients who did not have thromboembolism.[13]

RECOMMENDATIONS FOR SCREENING

The contradictory results have made it difficult to define suitable recommendations on when to look for an underlying cancer. The selection of patients differs widely in the studies and it is unclear whether detecting an underlying cancer will lower the case fatality rate.[14] Levine *et al* recommended looking for a tumour only if there are signs or symptoms suggesting an underlying cancer or if there is migratory thrombophlebitis or recurrent idiopathic thrombosis.[15] Based on previously published papers, Myrup recommended that patients should be investigated only if they have symptoms suggesting cancer, and that patients under 50 years should be regularly checked for cancer symptoms.[16]

We studied all patients with deep venous thrombosis in one city. Sixty six patients developed cancer within six months after the deep venous thrombosis. Thirty eight of the cancers were easily detected by a combination of a medical history, physical examination, and routine blood tests. Of the remaining 28 (42%) patients with occult cancer, 18 (64%) were older than 75 years. In this study 14% of the deep venous thromboses occurred after surgery or trauma.

Further analysis of the cancers in the patients with delayed diagnosis shows that extensive screening of the 1300 with thrombosis would have identified 11 patients who had cancer without metastasis. Only two, however, would have benefited from earlier diagnosis because of other factors such as age, general health, and tumour type. We therefore suggest that screening all patients with deep venous thrombosis for cancer would not be cost effective and that routine diagnostic tests (including clinical examination and laboratory blood tests) are able to detect cancers if used properly.

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Compliance with recommendations for giving vitamin K to newborn infants

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Newborn infants have low plasma concentrations of vitamin K and are at risk of haemorrhagic disease if not given supplemental vitamin K.[1] In 1992 an association between intramuscular vitamin K and childhood cancer was reported.[2] The British Paediatric Association subsequently recommended that oral vitamin K supplements should be given to newborn infants, with repeat doses for breast fed infants.[3] However, the chief medical officer has stated that there is no licensed preparation of vitamin K for oral use available in the United Kingdom.[4]

The policy regarding vitamin K administration at our hospital was recently changed to follow the British Paediatric Association's recommendations. All infants are given a first oral dose of 0·5 mg of vitamin K within the first 24 hours after birth. A second dose of 0·5 mg vitamin K is dispensed to the mother at discharge from hospital and the community midwife gives it to infants being breast fed at 1 week. The general practitioner is advised by letter to give a further single dose of 0·5 mg oral vitamin K at six weeks to infants who are still breast fed, including those infants receiving supplemental bottle feeds.

This policy was introduced in April 1993, but general practitioners and community midwifes were concerned about giving vitamin K, particularly because the product was not licensed for oral use. We therefore determined compliance with the policy.

Subjects, methods, and results

We attempted to contact by telephone all mothers who delivered live infants at our hospital during June 1993. Mothers whose infants were admitted to the neonatal unit were excluded. We asked mothers about the method of infant feeding, information provided about vitamin K, and administration of vitamin K.

There were 336 deliveries in June 1993 and 348 babies were born. Two of the infants were stillborn and 25 required admission to the neonatal unit; 15 mothers did not have a telephone, four had moved, and a further 95 were not contactable. A total of 207 mothers answered the telephone question-

Number of women who were breast feeding and the number and proportion of breast fed infants who received vitamin K

	No of women breast feeding (n=207)	No (%) of infants who received vitamin K
At discharge	162	161 (99)
At 7 days	162	143 (88)
At 6 weeks	145	57 (39)

naire. The table shows the results. Two of the 207 mothers refused to allow their children to receive any vitamin K.

The second dose of vitamin K was administered by the community midwife in 132 out of 143 cases, by the general practitioner in four, at our hospital in six, and by the mother in one. Fifty seven children received the six week dose of vitamin K; it was given by the general practitioner in 38 cases, at our hospital in seven cases, by the community midwife or health visitor in six cases, and by mothers in six cases. Ninety nine women felt they had been given enough information on vitamin K, and 176 had been asked to give oral consent before vitamin K was given to their child.

Comment

Compliance with current recommendations on vitamin K supplementation of newborn infants was poor. More than 10% of breast fed infants did not receive the second dose of vitamin K and less than 40% received a third dose. These infants were therefore at risk of developing late haemorrhagic disease of the newborn. Many mothers reported that the general practitioner or community midwife was reluctant to prescribe and give vitamin K because the preparation was not licensed for oral use. This caused considerable anxiety, and many mothers had contacted the hospital to seek advice.

The association between intramuscular vitamin K and childhood cancer has been questioned.[5] Nevertheless, even if the association is disproved, prophylaxis with intramuscular vitamin K may not become routine in the United Kingdom because of the adverse publicity that has arisen. Late haemorrhagic disease has been reported in breast fed infants who received only a single oral dose of vitamin K and therefore repeated doses are necessary. A licensed oral preparation of vitamin K that can be given by parents would improve compliance with current recommendations and is urgently required.

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Vitamin K regimens and incidence of childhood cancer in Denmark

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A case-control study by Golding *et al* found that children who had received vitamin K intramuscularly at birth had a significantly greater risk of leukaemia than children who had received it orally or not at all.[1] Draper and Stiller, however, questioned whether the relation was causal,[2] and the finding was not verified in two recent case-control studies in Sweden and the United States.[3,4] We compared the cumulative risk of cancer in Danish infants given vitamin K intramuscularly with that of infants who never received any form of manufactured vitamin K and infants whose mothers were given vitamin K during pregnancy.

Subjects, methods, and results

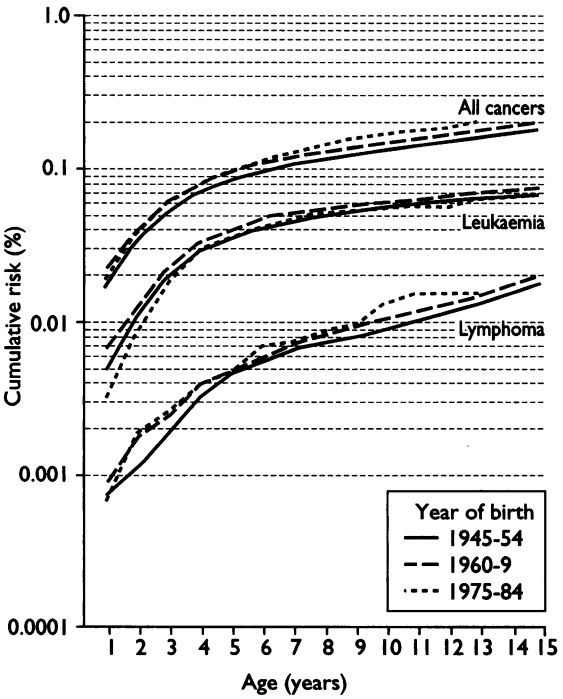
A national cancer registration system has been operating in Denmark since 1942.[5] Regimens for administration of vitamin K to neonates have varied greatly over the 50 years of notification. No vitamin K was given to either newborns or mothers before 1955, we could define a non-exposed cohort as all children born in Denmark during 1945-54 (n=835 430).

Oral vitamin K was introduced for pregnant women in the late 1950s, and the practice was recommended by the Danish Board of Health in August 1960. All children born during 1960-9 were therefore included in the cohort with mothers who received vitamin K during pregnancy (n=797 472). A review of a random sample of 300 medical charts from one area of Zealand for 1960-3 (done by KB shortly after the birth of each child) showed that 3·3% of the children had received vitamin K intramuscularly.

Intramuscular injection of vitamin K to newborns became accepted practice in the early 1970s. From 1975, when less than 1% of Danish children were born at home, it can be assumed that nearly all children received vitamin K intramuscularly. We therefore defined the cohort that received vitamin K intramuscularly as children born in 1975-84 (n=586 378).

We identified all cases of childhood cancer in the three birth cohorts from the files of the cancer registry. The figure shows the cumulative risk for all types of cancer combined and for leukaemia and malignant lymphomas separately. The data are for children aged 1-15 years for the 1945-54 (no administration) and 1960-9 (maternal administration) birth cohorts and children aged 1-13 years for the 1975-84 cohort (intramuscular administration).

The relative risk, defined as the ratio between cumulative risks at age 13 (intramuscular vitamin K *v* no vitamin K) was 1·00 (95% confidence interval 0·93 to 1·09) for leukaemia, 1·15 (0·97 to 1·36) for



Cumulative risk of childhood cancer among children born 1945-54 (no vitamin K), 1960-69 (maternal vitamin K), and 1975-84 (intramuscular vitamin K)