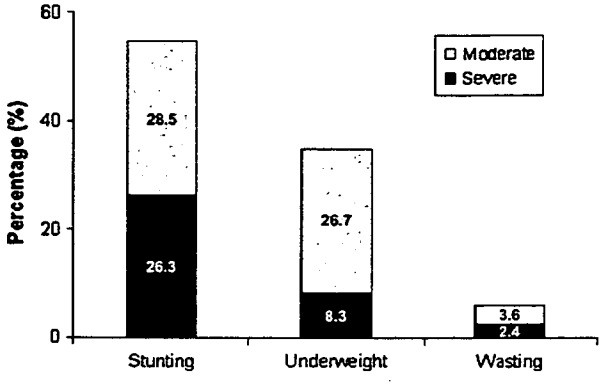

Fig. 1 The prevalence of stunting was 54.8%, while 26.3% and 28.5% had severe and moderate stunting, respectively. The prevalence of underweight and wasting were 35.0% and 6.0%, respectively. Severe underweight and severe wasting were 8.3 and 2.4%; moderate underweight and moderate wasting were 26.7% and 3.6%, respectively.

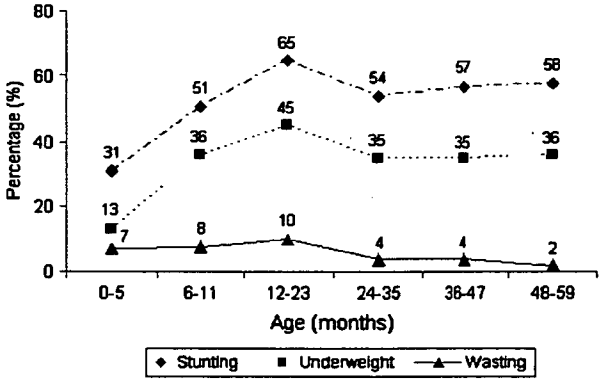

Fig. 2 Prevalence of malnutrition had an incremental trend, increasing from the age of 6–11 months and reaching its highest value in the 12–23 months age group, in which stunting was 65%, underweight was 45% and wasting was 10%.

Factors associated with protein–energy malnutrition

Low height-for age z-scores, HAZ < –2 SD (stunting)

The results of logistic regression analysis indicated that boys were more likely to be stunted than girls (odds ratio [OR], 1.51; 95% confidence interval [CI], 1.11–2.05; $P < 0.01$). Khmu ethnicity (OR, 3.10; 95% CI, 2.21–4.35; $P < 0.001$); low maternal education (OR, 1.87; 95% CI, 1.14–3.06; $P < 0.05$); low family income (OR, 1.49; 95% CI, 1.03–2.15; $P < 0.05$) and all the children's age groups were also found to be statistically significant (Table 2).

However, the study also found that restrictions on vegetables (OR, 4.84; 95% CI, 1.60–14.60; $P < 0.01$) and not consuming vegetables and fruits in the previous day (OR, 1.54; 95% CI, 1.12–2.11; $P < 0.01$), were also identified as risk factors for stunting (Table 3).

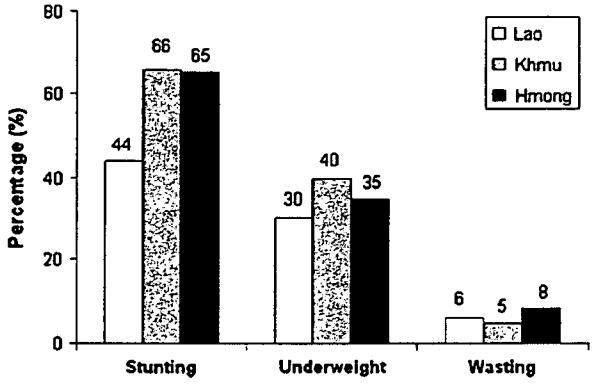

Fig. 3 Prevalence of protein–energy malnutrition by ethnic group. The Khmu ethnic group had the highest prevalence of stunting of 66% and of underweight of 40%. The Hmong ethnic group had a comparatively high prevalence of wasting of 8%, compared to the other groups.

Low weight-for-age z-scores (underweight)

Low maternal education (OR, 2.49; 95% CI, 1.43–4.33; $P < 0.01$); boys (OR, 1.61; 95% CI, 1.19–2.19; $P < 0.01$); child Khmu ethnicity (OR, 1.63; 95% CI, 1.17–2.28; $P < 0.01$); mother with poor nutrition education (OR, 1.40; 95% CI, 1.02–1.92; $P < 0.05$) and all the children's age groups were associated with underweight (Table 2). It was also found that restricted diet on meats (OR, 2.31; 95% CI, 1.37–3.90; $P < 0.01$) and vegetables (OR, 3.00; 95% CI, 1.28–7.02; $P < 0.05$) during illness; and not consuming vegetables or fruits in the previous day (OR, 1.42; 95% CI, 1.02–1.97; $P < 0.05$) were identified as risk factors for underweight (Table 3).

Low weight-for-height z-scores (wasting)

In terms of factors associated with wasting, only low maternal education (OR, 4.07; 95% CI, 1.12–14.79; $P < 0.05$) was found to be a risk factor for wasted children (Table 2).

Discussion

Prevalence of protein–energy malnutrition

Generally, the most common reference used to assess nutrition status is the US National Center for Health Statistic (NCHS) adapted by the World Health Organization (WHO). It was named the NCHS/WHO international reference population and is recommended for use in developing countries.[8–10] Laos is among those countries using the NCSH/WHO international reference for assessment of nutrition status of Laotian children. The present results confirm the high prevalence of stunting (54.6%), compared to 48% as mentioned in the first national

Table 2 Factors associated with PEM according to sociodemographic characteristics

	HAZ		WAZ		WHZ	
	OR	95%CI	OR	95%CI	OR	95%CI
Sex						
Girl	1		1		1	
Boy	1.51	1.11–2.05**	1.61	1.19–2.19**	0.8	0.44–1.46
Ethnic minority						
Lao	1		1		1	
Khmu	3.1	2.21–4.35***	1.63	1.17–2.28**	1.14	0.61–2.13
Hmong	1.81	0.90–3.64	1.1	0.53–2.26	0.73	0.21–2.06
Age (months)						
0–5	1		1		1	
6–12	2.53	1.31–4.90**	3.78	1.75–8.14**	0.79	0.25–2.46
13–23	4.47	2.63–7.58***	5.67	2.96–10.85***	0.64	0.26–1.56
24–35	2.97	1.71–5.17***	3.6	1.82–7.10***	1.76	0.57–5.42
36–47	3.81	2.17–6.70***	3.79	1.91–7.51***	1.64	0.53–5.05
48–59	4.03	2.28–7.46***	3.79	1.87–7.67***	4.18	0.85–20.61
Maternal education						
Up to high school	1		1		1	
Up to primary school	1.37	0.89–2.12	2.4	1.44–3.99**	2.36	0.48–11.50
Not attended school	1.87	1.14–3.06*	2.49	1.43–4.33**	4.07	1.12–14.79*
Income per person/month ($US)						
≥7.6	1		1		1	
<7.6	1.49	1.03–2.15*	0.93	0.63–1.36	0.83	0.40–1.72
Getting nutrition education						
Yes	1		1		1	
No	1.31	0.94–1.81	1.4	1.02–1.92*	0.98	0.50–1.06

*$P<0.05$; **$P<0.01$; ***$P<0.001$.
HAZ, height-for-age z-scores; OR, odds ratio; PEM, protein-energy malnutrition; WAZ, weight-for-age z-scores; WHZ, weight-for-height z-scores; 95%CI, 95% confidence intervals; 1 $US = 10 800 kip.

survey of nutritional status conducted in 1996 among 1365 children under 5 years of age, and slightly greater than the average in developing countries in the world and in South-East Asia.[11] The high prevalence of PEM that was found in several studies as well as in the present study implies that the growth of Laotian children might be less than those of NCHS/WHO standards. A study done in Saudi Arabia also noted that the growth of schoolboys was less than the NCHS/WHO standard.[12] Therefore, further studies on child growth and development are needed in Laos.

Table 3 Factors associated with PEM according to feeding patterns

	HAZ		WAZ		WHZ	
	OR	95%CI	OR	95%CI	OR	95%CI
Restriction on meats during sickness						
No	1.00		1.00		1.00	
Yes	1.27	0.91–1.76	2.31	1.37–3.90**	0.76	0.36–1.59
Restriction on vegetables during sickness						
No	1.00		1.00		1.00	
Yes	4.84	1.60–14.60**	3.00	1.28–7.02*	1.40	0.32–6.29
Consumption of vegetables or fruits on the previous day						
Yes	1.00		1.00		1.00	
No	1.54	1.12–2.11**	1.42	1.02–1.97*	1.84	0.95–3.59

*$P<0.05$; **$P<0.01$.
HAZ, height-for-age z-scores; OR, odds ratio; PEM, protein–energy malnutrition; WAZ, weight-for-age z-scores; WHZ, weight-for-height z-scores; 95%CI, 95% confidence intervals.

Prevalence of PEM and age group

Stunting (an expression of chronic malnutrition) was high in the 12–23 months age group in the present study (65%), but it was different from the national health survey in 2001 (48–59 months, 55%), which might be explained by the study site used in the present study and the broader age group in the national survey. Indeed, stunting in the 12–23 months age group might be linked to weaning food, lack of quantity of food and nutritional knowledge, which may lead to failure of catch-up growth in this age group. Thus they continue to be stunted until 48–59 months of age, as stated in the Saleemi *et al.* study in 2001, in which those children who were stunted at 6 months of age continued to be stunted through to 60 months.[13] When looking at the situation of wasting (an expression of acute malnutrition), the present findings again indicate a high prevalence in the 12–23 months age group (10%); as well as underweight (45%; an expression of combined chronic and acute malnutrition), which was explained by the high morbidity in this age group.

Prevalence of PEM and ethnic group

Laos is a multi-ethnic, country having 48 ethnic minorities living in different areas, and each having their own traditional cultures. Usually, people of Hmong and Khmu ethnicities live in mountainous and middle land, which is very remote, difficult to access and is far from public health facilities, while most of the other Laotian ethnic groups live in the lowlands. It was reported that the prevalence of stunting in rural areas for multi-ethnic children excluding the Lao ethnic group was 74.1% in the north and 62.6% in the southern part of Laos.[14] The present study found that prevalence of PEM was high in Khmu and Hmong ethnic groups, which can be explained by low maternal education and poor nutrition education.

Factors associated with protein–energy malnutrition

Socioeconomic factors

There are various factors associated with malnutrition worldwide, as highlighted in several studies. For example in Africa, geography, culture, basic housing condition, maternal education, maternal age, ethnicity, fertility, economic inequality, access to health services, and diet composition were independently associated with stunting.[15–18] In Asia, risk factors for child malnutrition included older age, male sex, ethnicity, rural area, mother's poor education, lower family income, higher birth order of the child, lower parental height, use of dung or firewood as fuel, mother's child rearing behavior and social support.[19–23] These results are similar to the present findings, which highlight low maternal education, and feeding pattern for mother and child during sickness, as being risk factors associated with malnutrition in children.

Feeding pattern for mother and child

In Laos it was noted that culture and tradition play a major role in selection of health services, such as place of delivery, onset and duration of breast-feeding and weaning food. These practices vary according to ethnicity and across geographic areas. Different practices can influence health outcomes, thereby contributing to the rates of mortality and morbidity in children. In very remote areas, children's diets were inadequate in quality as well as in quantity.[14] In addition, the great majority of Lao mothers breast-feed theirs infants but, because of poor food practices and food taboos, lactating mothers reduced the quality and diversity of their food intake, when it was most needed.[24] The present results imply that children who were offered less food and necessary nutrients such as vitamins and minerals (vegetable, fruits) during illness had more risks for becoming malnourished. In fact, sick children and lactating mothers need additional nutrients to quickly recover from infectious diseases, and to allow lactating mothers to appropriately breast-feed their children. We emphasize that there is a strong need to educate mothers and the community members and to clear misconceptions on various issues for better maternal and child health.

In conclusion, child malnutrition is still prevalent in Luangprabang province, Laos. Socioeconomic–demographic factors, low maternal education and poor nutrition knowledge for mother are related to stunting and underweight children. Thus, in general, the feeding pattern for sick children is affecting stunting and underweight. These findings suggest that a comprehensive approach is needed to address the issues of child malnutrition. An improvement in societal infrastructure with better maternal education and nutrition, and clarification of the rumors and misconceptions surrounding pregnancy, delivery and postnatal care, are required. It is recommended that a strong mass media campaign on health education be launched, which should involve not only the public but also the private sector (such as community-based organizations and non-profit organizations), thus ensuring access and strong community involvement at the grass roots level, in order to address and rectify this vital issue.

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Feature Article

Mother and child health in Asia and Africa

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Science and technology are quickly developing in the 21st century. However, war, poverty, and emerging–remerging diseases have also been increasing. It looks like peace is becoming more distant. This world situation affects not only adults but also mothers and children. In regard to child health, the total fertility rate has decreased recently in Japan, although it seems to have increased a little in 2006, but this rate is usually high in developing countries. Mortality of children under 5 years old and death caused by infection are also higher in developing countries.[1]

In these feature articles, six original articles by young and energetic researchers appear. In the articles, the general views related to each topic in mother and child health in Asia and Africa are included. Here I describe briefly the intention of each article in addition to the previous reports and general overview.

Phengxay *et al.* describe risk factors for protein–energy malnutrition of children under 5 years in Luangprabang province, Lao. They found that there was no official standard value of bodyweight and length in Lao. The bodyweight and body length had lower increases during the infant stage in comparison with international standard growth. Nutrition after birth may be important in Lao.

Hien and Ushijima described infant growth in minorities in Vietnam in this journal. They focused mainly on the development of low-birthweight infant to 1 year of age. The infants could not catch up to the normal values at 1 year. They previously reported that the frequency of prenatal visit by health workers is associated with a decrease in the number of low-birthweight infants.[2] This means that the intensive care by heath workers is important to decrease the number of low-birthweight infants. The rate of breast-feeding is higher in East Asian countries than in Japan.[3] Appropriate breast-feeding and quality of breast milk may be necessary in order for low-birthweight infants to catch up to the normal nutritious status.[4,5]

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Li *et al.* describe the improvement of nutritional state in low-birthweight infants and thiamin-deficient infants in minorities in Yunnan, China. Thiamin deficiency is an important disease in East Asian countries and destruction of vitamin B1 by cooking causes thiamin deficiency. Instruction in appropriate cooking stopped thiamin deficiency. Malnutrition in infants is also improved by guidance of health workers.[5] Maternal child-rearing behaviors and correlates are also important.[6] Combining the reports of Phengxay *et al.*, Hien and Ushijima, and Li *et al.*, guidance by health workers and action by households are necessary to improve child health. Access to the hospital or health center is also important.[7]

Another recent problem in the world is obesity. Nowadays obesity replaces malnutrition as the world's top health problem. Obesity causes diabetes mellitus, hypertension and others. Obesity is increasing in Asian children, especially in China.[8] One reason for obesity is excessive eating. Another reason is insufficient exercise. Li *et al.* studied the relationship between physical activity and body fatness in children in Beijing. Highly physical activity reduces body fat increase in children. Li *et al.* emphasized the importance of physical activity in children to decrease body fatness.

In addition to the studies of the child health in foreign countries, child health of foreign residents in Japan was studied. Hotta *et al.* studied the health condition of foreign mothers and children living in Japan according to local government. As a result, some local governments realized that more needs to be done. Government services were needed for mother and child health, but also for foreign university students.[9] This means that medical services for foreign residents should be conducted in their mother languages or by medical translators.

Infection is one of the most important causes of death in developing countries. Respiratory infection is the highest and HIV infection is the second. Kominami *et al.* describe the necessity of care visit before delivery, and spreading information on HIV/AIDS and paternal support to prevent mother–child transmission of HIV in Tanzania.

In conclusion, the main problems in child health in Asia and Africa are reported. To solve these problems, empowerment of local government, non-profit organization, and the related families are needed.

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Feature Article

Malnutrition improvement for infants under 18 months old of Dai minority in Luxi, China

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Abstract

Background: Child malnutrition and thiamine deficiency remain a matter of public concern in Dai children under 5 years old in Southwest areas of China. The aim of the present study was to understand the status and correlates of malnutrition and thiamine deficiency in Dai children under 18 months old in Yunnan, China, and to explore an effective intervention for improving their nutritional status and decreasing the prevalence of malnutrition and thiamine deficiency in Dai children.

Methods: Well-trained investigators completed a baseline evaluation survey, including questionnaire survey by maternal interviews, child physical measurements, lab examination of thiamine, and group discussions in a cross-sectional study. An intervention plan was constructed by a group consisting of the city governor, government officers, maternal and child health workers, community leaders, and villagers etc. A comprehensive community-based intervention was carried out for 352 children born after July 2001 and their mothers or caregivers in half of the baseline survey villages by the end of 2003. The intervention included participatory intervention, community nutrition education, child growth monitoring and distributing thiamine to new mothers just before or after delivery.

Results: The baseline evaluation survey in 2000 indicated that the prevalence of moderate and severe protein–energy malnutrition was 19.5% for underweight, 16.4% for stunting, and 6.7% for wasting, respectively. With increasing age, the prevalence increased, peaking at 12–15 months. The prevalence of underweight in girls was higher than in boys. A total of 10.5% of children suffered from thiamine deficiency, and 5.7% of the children were insufficient in thiamine supply. Low Kaup target (<25%) was significantly associated with lack of guidance by doctors, lack of nutrition knowledge, lack of knowledge of causes of malnutrition and local culture food taboos. The status of child nutrition has been improved significantly since the intervention measure implementation. The change of prevalence of underweight children aged 6–17 months prior to and after the intervention was significant: 20.5% before and 13.7% after the intervention in infants aged 6–11 months, and 39.0% before and 26.4% after the intervention in young children aged 12–17 months. Prevalence of girls was higher than that of boys. Some women began to eat vegetables and pork from the market, which were forbidden by the culture food taboos. There is no case report of child thiamine deficiency in project villages.

Conclusion: The prevalence of moderate and severe protein–energy malnutrition is high in Dai infants and young children. However, based on the local situation, participatory community-based comprehensive nutrition intervention effectively reduces the prevalence of child malnutrition and thiamine deficiency. It is highlighted that population nutritional intervention can produce better results with participation at a community level.

Key words China, Dai children, improvement, malnutrition.

The mortality rates of children under 5 years old and infants greatly decreased with the development of the economic level, increased health education, the construction of a maternal and child health network, and the implementation of programs reducing maternal mortality and child mortality nationwide in China in the 1990s.[1,2] However, in Western China, child mortality remains at a high level of 60.8/1000 live births in children under 5 years old and 49.2/1000 live

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births in infants as of 2000, and malnutrition is still one of the main causes of death in children.[2–4] Many studies have shown that malnutrition has an effect on physical growth, morbidity, mortality, cognitive development, reproduction, physical work capacity and risk for several adult-onset chronic diseases.[5–7] Malnutrition continues to be a major health burden throughout the developing world.[5–9] Yunnan province is southwest-most province with the highest number of minorities in China. The goal of the Children Development Outline of Yunnan Province in 1990–2000 ('By the year 2000 reduce the prevalence of moderate and severe malnutrition among children aged under 5 by 50% of that in 1990') was not realized. Child malnutrition is one of the common concerns in China. Some studies indicated that prevalence of malnutrition (assessed by underweight) in children peaks in the 12 months group.[10–16] Some other studies have shown that the prevalence of underweight in Dai minority children under 5 years old, especially under 2 years old, was the highest across the Yunnan nationalities.[17] Research has suggested that signs of thiamine deficiency occurred most often in the Dai ethnic group in Yunnan Province, with 5.1% of male Dai people and 6.6% of female Dai people suffering from thiamine deficiency. The incidence of signs of thiamine deficiency have not varied with time during the past several years.[18] There are always some reports of infants dead of thiamine deficiency each year. So the problem of reducing the prevalence of malnutrition and thiamine deficiency of Dai children under 5 years old has drawn much attention from child health-care workers in China.

Few intervention studies have been reported on rural infants and young children, therefore the aim of the present study was to understand the prevalence and correlates of malnutrition and thiamine deficiency in Dai children below 18 months in Yunnan, China, and to explore an effective intervention to improve the nutritional status and decrease the prevalence of malnutrition and thiamine deficiency in Dai children aged 0–18 months.

Methods

Study design and samples

The study was conducted in Luxi, a Dai and Jinpo autonomous city in Yunnan Province, which is located in the southwest of China, bordering on Myanmar. The city covers an area of 2987 km^2. Luxi is a subtropical area with a population of 321 000, half of which are minority individuals. The population consists of five major ethnic groups, the largest of which is the Dai minority, comprising 73.68% of the total population. The middle of the province is a center for economic development, and the GDP was $US467 in 2000. The study was implemented in two phases as follows.

(1) Baseline assessment survey: the survey was undertaken in two administrative villages in each of five sampled townships in July 2000. The total sample was 524 child–mother or child–caregiver pairs. Well-trained investigators completed a baseline evaluation survey, including questionnaire survey to mothers or child caregivers, and child weight and height measurements, determination of urine thiamine, group discussions and material review.

(2) Intervention: a comprehensive community-based intervention plan was constructed with the participation of the city governor, government officers, maternal and child health workers, community leaders and village representatives etc. The intervention had been implemented in the sampled villages since January 2002 and this included (i) setting up a city-level project leader group and research groups at a city and township level; (ii) undertaking a maternal and child nutrition education with video compact disc (VCD) and pamphlet developed by the research groups based on the Dai culture and language, implementing face-to-face discussion and demonstration of preparing weaning food, encouraging peer education, recording the frequency of infant food intake once every month; (iii) conducting growth monitoring of children between birth and 17 months (including weighing every 2 months); (iv) implementing integrated management of childhood diseases, supplying normal health-care services to children; and (v) distributing thiamine to women just before or after delivery. All new births from January 2002 until the end of 2003 were recruited as subjects for intervention.

Definitions of the terms

Child malnutrition is defined as weight for age (underweight), height for age (stunting), and weight for height (wasting) less than two standard deviations below the median of the National Central for Health Statistics/World Health Organization (NCHS/WHO) international growth reference.[19] After intervention, weight for age (underweight) was used as the indicator of child malnutrition. Thiamine deficiency was defined as deficiency at thiamine (μg)/creatinine (g) <120, and insufficient at thiamine (μg)/creatinine (g) between 85 and 120.

Statistical analysis

The baseline data came from the baseline assessment survey, and the data after intervention were collected from the records of child growth monitoring and weaning food supply by the end of 2003.

Statistical analyses were performed using SPSS version 10.0 (SPSS, Chicago, IL, USA). *t*-Tests were used to examine

differences in measurements before and after intervention. χ^2-tests were used to examine differences in count data before and after intervention. A series of logistic regression analyses were performed to estimate the association of child malnutrition with suspected relevant factors.

Results

Prevalence of malnutrition and correlates

The results of the baseline survey showed that the prevalence of moderate and severe protein–energy malnutrition was 19.5% for underweight, 16.4% for stunting, and 6.7% for wasting, respectively. With increasing age, the prevalence increased, peaking at 12–15 months (Fig. 1). The prevalence of underweight in girls was higher than in boys. A total of 10.5% of children suffered from thiamine deficiency, and 5.7% of the children were insufficient in thiamine supply. Low Kaup target (<25%) was significantly associated with lack of guidance by doctors (odds ratio [OR], 3.17; 95% confidence interval [CI], 1.22–8.22), lack of nutrition knowledge (OR, 2.97; 95%CI, 1.07–8.18), lack of knowledge of causes of malnutrition (OR, 1.82; 95%CI, 1.16–2.89) and local culture food taboos. Some Dai parents and grandparents believed that infants should be given rice the earlier the better, even 3 days after delivery, and children would suffer 'Bingu' if they were fed eggs and fish in the infant period. (Bingu is a traditional ancient superstition in Dai people. In children the signs are frequent diarrhea, dislike

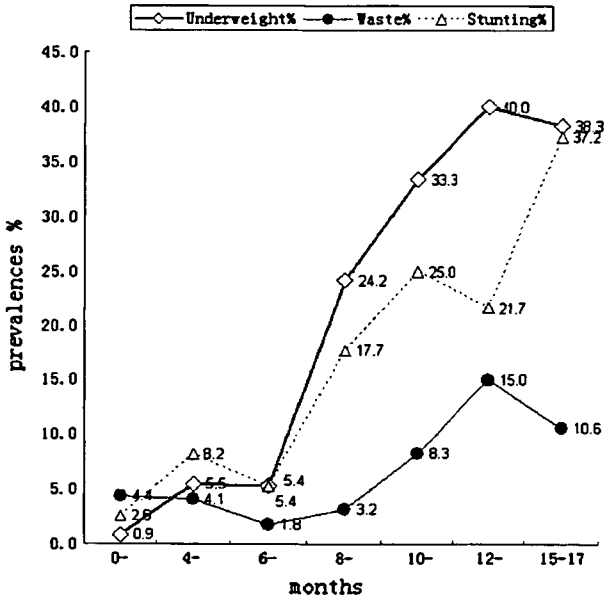

Fig. 1 Prevalence of malnutrition by age in Dai children in Luxi, China.

of eating food, growth retardation, easy loss of temper, and difficulty in sleeping. Bingu was generally considered as having two causes: (i) eating forbidden food, e.g. food with the smell of fish or seafood, such as fish, animal liver, eggs etc.; and (ii) being 'demon possessed'). They also obey the local culture food taboos that after delivery women can eat only polished white rice, sugar and salt. Eggs and chicken were allowed as a supplement. The food bought from the market was considered to be unclean, and it was forbidden to women in the first month after delivery. The Dai were used to eat undercooked vegetable and every food with sour sauce. Most parents indicated that they were interested in receiving help and guidance from doctors, and they were most likely to participate in training regarding children's feeding and care.

Infant mortality

The infant mortality due to malnutrition and thiamine deficiency was 611.96 per 100 000 live birth and infant mortality due to thiamine deficiency was 278.2 per 100 000 live births in Luxi, and 414.6 per 100 000 live births in the Dai area in 2000 (Table 1).

Change of average month of breast milk before and after intervention

The average time to initiate breast-feeding was 7.9 h earlier than that before intervention (26.9 h, $P < 0.01$). The ratio of first breast milk in <30 min increased by 6.6%. Table 2 indicates breast-feeding in different sex infants. No newborns are fed on rice chewed by adults now.

Change of weaning food supply before and after intervention

Most young mothers were likely to participate in the project activities and to practice preparing weaning food for their children according to the guidance. The average months to first supply of egg, pork, fish, bean, vegetable and fruits to

Table 1 Infant mortality before and after intervention

	Luxi		Dai areas	
	2000	2003	2000	2003
Infant mortality (/1000 live births)	23.6	21.0	20.3	18.7
Infant mortality due to thiamine deficiency (/100 000 live births)	278.2	0.0	414.6	0.0
Infant mortality due to other malnutrition (/100 000 live births)	333.8	123.8	250.3	87.0

Table 2 First breast milk before and after intervention

	Before			After		
	Male	Female	Total	Male	Female	Total
First breast milk (h)	27.8	29.8	28.5	17.7	20.3	19.0
First breast milk 30 min (%)	37.6	36.8	37.2	47.4	42.4	44.9
Weaning breast milk (months)	12.6	12.9	12.8	12.0	12.9	12.5

infants were earlier than that prior to intervention. Infants were fed rice later than those prior to intervention (Tables 3,4).

Mother's food and maternal care

The diet of most women after delivery became more varied after intervention. Some women began to eat vegetable and pork from the market, which was forbidden by the culture food taboos. Some families tried to change the rice cooking method by using rice-cooker or reducing the rice husking time. Every lying-in woman could take thiamine in project villages. In Dai areas 98.8% of pregnant women could visit doctors (including village doctors) at least one time, and 55.24% of them delivered in hospital and received thiamine deficiency prevention. Prevention of thiamine deficiency was also carried out city-wide. As a result, infant mortality due to malnutrition and thiamine deficiency was reduced significantly.

Change of average weight of children prior to and after intervention

The 352 children born after July 2001 and their mothers or child caregivers have been studied as subjects since January 2002, and have received monitoring to 18 months of age by the end of 2003. The results indicate that the weight of children aged 6–17 months increased significantly during the intervention (Table 5). The average weight of girls was significantly lower than that of boys at the same age ($P < 0.001$).

Prevalence children underweight reduced

Table 6 shows that the prevalence of underweight children aged 6–17 months was significantly lower than that prior to intervention. The prevalence of girls was higher than that of boys aged 6–17 months ($P < 0.05$).

Infant mortality due to malnutrition and thiamine deficiency decreased

The infant mortality due to malnutrition and thiamine deficiency was reduced significantly from 2000 to 2003 in Luxi (Table 1). In 2000, Dai infants accounted for 90% of the whole infants who died of thiamine deficiency. No infant died of thiamine deficiency and there has been no case report of thiamine deficiency in children in research villages after the intervention.

Discussion

Prevalence of child malnutrition and correlates

Child malnutrition is usually associated with population explosion, poverty, poor public health and lack of education.[16,20,21] In the present study the prevalence of underweight children aged 6–18 months in 2000 was higher than that in Yunnan Province and the whole of China in the same period.[1,12,22] The lack of guidance by doctors, lack of nutrition knowledge, lack of knowledge of causes of malnutrition, and local culture food taboos were the main risk factors for malnutrition. As a result, first breast-feeding was late, and complementary foods were introduced to the children inappropriately with regard to time, kinds and quantity, which is in accordance with the previous national weaning investigations.[21–23] Diarrhea and acute respiratory tract infection occurred in children more frequently, which enforced the incidence of malnutrition. Growth monitoring and promotion, protection and support of breast-feeding with appropriate caution against early weaning and with due emphasis on quality and quantity of complementary foods and frequency of administration, with a focus on children below 2 years, are essential.[24] Instruction on child feeding and encouraging the preparation of weaning food, and abandoning of the local culture food taboos that are harmful to children's and women's health are very necessary to improve the nutritional status of Dai mothers and children.

Infant mortality due to malnutrition and thiamine deficiency

The infant mortality due to malnutrition and thiamine deficiency was reduced significantly as the prevalence of malnutrition and thiamine deficiency reduced, from 2000 to 2003 in Luxi. The result is in accordance with the previous report that in children

Table 3 Age categories for introduction to each weaning food, before and after intervention (%)

Months	Rice		Egg		Pork		Fish		Liver		Milk		Bean products		Vegetable		Fruit	
	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After	Before	After
0–3	74.6	23.5	3.8	0.3	2.7	0.3	0.3	0.3	1.2	0.3	15.7	2.5	0.9	1.1	1.5		0.9	
4–5	16.0	39.4	7.7	11.0	21.0	8.8	6.8	3.1	3.6	1.4	10.7	8.5	9.5	5.9	14.2	10.8	10.7	9.1
6–7	4.4	29.5	24.6	38.0	27.2	45.0	11.8	18.4	9.2	8.5	8.0	21.8	25.1	32.9	35.5	45.6	31.7	38.0
8–9	2.4	5.4	17.2	33.1	28.4	33.7	10.7	27.5	8.9	21.6	4.1	17.8	24.6	35.4	18.6	30.9	25.1	32.9
10–11	0.6	1.4	5.0	11.6	7.1	9.9	5.3	27.2	4.7	22.4	3.6	17.0	6.5	16.4	9.8	10.5	10.4	15.0
12–14	0.6	0.6	26.9	5.1	11.8	2.0	36.7	17.6	26.9	23.9	5.3	13.9	18.0	7.1	11.5	2.3	17.5	4.8
15–17	0.3		2.4	0.8			4.1	4.5	1.2	14.8	0.9	7.4	0.6	1.1	0.9		1.5	0.3
None	1.2	0.3	10.4		0.9	0.3	21.3	1.4	42.9	7.1	51.2	11.0	13.9		7.7		1.5	

under 5 years age, mortality increases exponentially as protein–energy malnutrition (as assessed by low weight for age) becomes more severe,[25] and malnutrition may be indirectly responsible for approximately half of all deaths in young children.[2,26,27]

Effective intervention has contributed to the significant reduction of prevalence of malnutrition and thiamine deficiency

The study intervention produced results better than those in some reports done in other places in China and the world.[28,29] The participatory design of the intervention and effective implementation play an important role in reduction of prevalence of malnutrition and thiamine deficiency.

The intervention plan was designed by people in different social roles from multiple sections and multiple levels. In addition the plan was based on the community situation and designed in a practical way, making the intervention measures more feasible. Every measure could be implemented well according to the plan.

The city-level project leader group, with the governor as leader, coordinated the intervention. The government officers also participated in the field nutrition and evaluation and provided financial support to poor mothers in order to purchase food for their children.

Maternal and child health staff from city level, township level, and village doctors worked together to provide community-based nutrition education and guidance. Village doctors did home visits to all the pregnant women and postpartum women to carry out health care, nutrition education and to deliver thiamine.

Community leaders, women leaders and some key village women were encouraged to spread nutrition knowledge to villages in 3 day training sessions on child nutritional status. They encouraged pregnant women and young mothers to participate in the activities, and also participated themselves in order to set an example for fellow villagers.

The research enhanced the nutrition awareness of the Dai. Villagers now have more nutrition knowledge and are more likely to practise it. For example, in a villager interview and group discussion, after viewing a picture with a malnourished baby, villagers said that the head and belly of the baby looked bigger than normal, and the low part of his body looked too thin. The baby must be lacking in nutrients and suffer from some disease. The baby should eat nourishing food such as egg, animal liver and vegetables. The diet of most women after delivery became more varied after intervention. Mothers said that nourishing food may pass from breast milk to baby, and taking thiamine can make the body health and strong. So the mother should eat more kinds of food, even in the first month of delivery. An older woman said she could not read, but that she knew that children should eat more nourishing food due to

Table 4 Average age of introduction for each weaning food, before and after intervention

	Before		After		t	*P*
	Mean (months)	SD	Mean (months)	SD		
Rice	2.0	2.5	3.7	2.0	9.84	<0.01
Egg	9.0	3.7	6.5	2.1	10.86	<0.01
Pork	7.5	2.9	6.2	1.7	7.15	<0.01
Fish	10.6	3.5	8.3	2.6	9.76	<0.01
Animal liver	10.1	3.4	9.5	3.2	2.39	<0.05
Milk	5.9	4.2	7.5	3.4	5.49	<0.01
Bean products	8.4	2.9	6.9	2.2	7.64	<0.01
Vegetable	7.7	2.6	6.3	1.7	8.34	<0.01
Fruit	8.4	3.1	6.6	1.9	9.15	<0.01
Suger			6.4	3.0		
Soft drink			9.9	3.8		
Oil			6.5	2.1		

Table 5 Average weight before and after intervention

	Months	Before		After		t	*P*
		n	Mean (kg)	*n*	Mean (kg)		
Male	Birth			287	3.08		
	4–5	39	7.78	243	6.95	3.870	0.000
	6–7	28	7.32	155	7.54	1.668	0.244
	12–13	24	8.18	200	8.82	3.259	0.001
	15–16	26	9.01	172	9.43	2.240	0.026
Female	Birth			290	2.95		
	4–5	34	6.87	266	6.37	2.061	0.040
	6–7	28	6.86	178	6.92	0.326	0.745
	12–13	16	7.77	213	8.20	1.835	0.068
	15–16	19	8.13	181	8.71	2.378	0.018

Table 6 Prevalence of underweight children before and after intervention

Months	Before (%)			After (%)			t (total)	*P*
	Male	Female	Total	Male	Female	Total		
Birth				2.4	7.6	5.0		
0–5	1.0	4.4	2.7	2.9	0.8	1.8	0.202	>0.05
6–11	15.3	25.9	20.5	9.8	17.3	13.7	4.950	<0.05
12–17	36.7	41.3	39.0	21.8	32.7	26.4	8.281	<0.01

the VCD and pamphlet. She asked her daughter-in-law to make food for her grandson following the guidance of the pamphlet. Some grandmothers tried to cook egg, animal liver and fish for their grandchildren.

It is much easier for mothers to get help from doctors than before. There were fewer incidents of diarrhea and acute respiratory infections during the intervention, with the former being 2.38 and later 0.99, from birth to 1½ years of age.

Multi-sectional and multi-level participation in the intervention plan based on the community situation made the intervention measures more feasible. Every measure could be implemented well according to the plan.

Conclusion

The prevalence of moderate and severe protein–energy malnutrition is high in Dai infants and young children. However, based on the local situation, community-based comprehensive nutrition intervention, including a participatory intervention

plan design, community nutrition education, child growth monitoring, common diseases management and giving thiamine to new mothers just before or after delivery, effectively reduces the prevalence of child malnutrition and thiamine deficiency. It is highlighted that population nutritional intervention can produce better results with participation at a community level.

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HIV垂直感染と胎盤関門

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HIV感染妊婦における胎児，新生児に対する垂直感染の予防は人類保健上重要な課題の1つである．国際連合エイズ委員会の推定では，2004年1年間だけでも全世界で60万人の小児がエイズに感染し，その大部分は垂直感染によるとされている．無治療の場合，小児エイズの予後は不良であることから，早急な対策が必要である．先進国においては，HIV陽性妊婦は妊娠中の抗ウイルス薬の投与と選択的帝王切開により垂直感染率を1%以下にまで下げることが可能となっている．しかしながら，南アジアやアフリカにおける無治療妊婦でも垂直感染の程度は25～35%程度であり，不完全ながら胎盤関門が存在すると考えられている．また，脱落膜・胎盤における局所の免疫機構が子宮内感染の成立を左右するうえで重要な役割を果たしている．

はじめに

HIV感染によるAIDSは20世紀における新興感染症のなかで，最も感染者が多く，また致命率の高い疾患のひとつである．CCR5Δ32などきわめてまれな遺伝的背景を有する場合や，さらにまれな特異的免疫が成立する場合を除き，無治療で放置すれば，数年から十年程度で免疫機能の荒廃から日和見感染をきたして死に至る．わが国におけるHIV感染者は諸外国に比較して少数であるが，先進国のなかで唯一，依然として増加傾向にあり，今後生殖年齢に達するHIV感染女性の数も増加することが予想される．したがってHIV垂直感染機構の解析は生殖免疫学のみならず臨床的にも非常に重要である．

〔キーワード〕
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1．HIV垂直感染の管理

臨床的には，妊娠中の抗HIV薬の内服，陣痛発来前の選択的帝王切開術，断乳(人工栄養)によりHIVの垂直感染率は1%以下に抑えることが可能である[1]．厚生労働省研究班の作成した管理方針は，抗HIV薬の選択などは米国疾病予防管理センター(CDC)の基準に準拠しながら，わが国の実情を加味したものである(図1)．詳細はインターネットからダウンロード可能であるが[2]，わが国においては，妊婦検診におけるHIV抗体スクリーニングのほぼ全数検査(2005年の検査実施率94.7%)と，感染が疑われた場合の二次施設へ

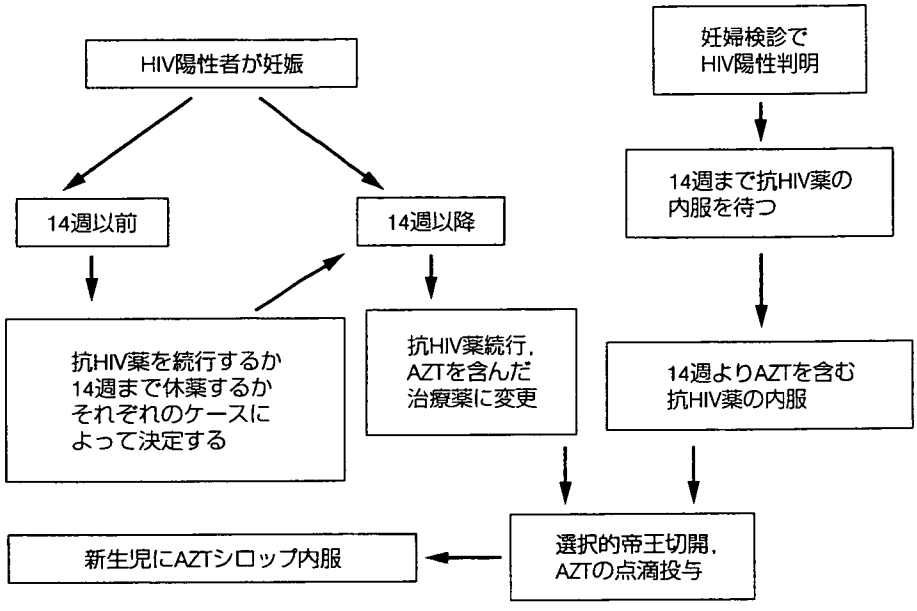

図 1. HIV 陽性妊婦の管理方針

の転送と妊娠・分娩管理により，世界で最高の予防率を達成しているといっても過言ではない．しかし，いかに厳重な産科管理をおこなっても子宮内感染を完全に防御することは困難である．臨床的には，患者の末梢血 CD 4 値の低下や HIV ウイルス量の増加に加えて，絨毛羊膜炎や切迫流早産，妊娠高血圧症候群，マラリア感染[3](日本ではまずみられないが)などがあると子宮内感染率が高まるという．

HIV の治療薬は大なり小なり，胎児に対する副作用を有する．アジドチミジン(AZT)は小児の就学期までの安全性が確認されている唯一の抗 HIV 薬であり，数年前までは妊婦に対しては AZT の単独療法が推奨されていた．しかし，現在では耐性ウイルス出現の危険性も高く，また多剤併用療法(HAART)と比較して母体のウイルス量を十分に下げることが困難であるため，母体に対する治療として推奨されるとはいいがたい．一方，HAART に使用する抗 HIV 薬は，妊娠中の投与による児の安全性が確認されていないものが多い．催奇形性のあるエファビレンツや乳酸アシドーシスをおこしやすいサニルブジン(d 4 T)＋ジダノシン(ddI)といった組み合わせは避けることが望ましい．また，HAART によって早産が増加する危険性や，胎児死亡，骨髄抑制などの重篤な副作用の報告もある．しかし，最近の統計では，HAART の児に対する影響は少なく，一時的な休薬は再開後の母体治療を困難なものとする可能性が指摘されているので，当該妊娠のみならず母体の長期予後を勘案し，十分なインフォームド・コンセントを得たうえで治療薬の選択をおこなう．

Camus らは，HIV 感染者の胎盤では multi-drug resistance 1(MDR-1)mRNA 発現が非感染者に比較して 3～4 倍となることを報告している．胎盤の MDR-1 のコードする P-glycoprotein は HIV 患者に投与されるヌクレオシド系逆転写酵素阻害薬やプロテアーゼ阻害薬の結合蛋白であり，これにより胎盤局所で大部分の抗レトロウイルス薬は不活化されると考えられる[4]．臨床的に，垂直感染の生じる機会の最も多いのは分娩時の母体血への曝露であり，母体血中のウイルス量を低下させることが最も重要であるという[5]．これは，経腟分娩を前提とした途上国の多くで投与される，分娩前数週間の short course program の臨床的意義を裏付けるものであろう．

図 2. HIV陽性妊婦(37週)の胎盤
酵素抗体法により，HIVp 24が染色される(右強拡大)．

2．胎盤関門の本態

胎盤には，胎児循環と母体循環を分別する物理的関門のみならず，Fcγレセプターを介した母体血中のIgG抗体の胎児側への選択的取り込みや，母体血中の薬物やホルモンの選択的な取り込み，あるいは局所における分解などをおこなう機能的関門が存在する．HIV感染者の胎盤を病理組織学的に検討すると，脱落膜免疫細胞や胎盤の絨毛細胞，Hofbauer細胞(胎児由来のマクロファージ)にHIV関連抗原が染色される(図2)．無治療，あるいは治療が不十分で血中ウイルス量が多い患者では，十分なコントロールを受けた患者に比較して，より強い染色性がみられる．CD 4を発現しない絨毛細胞にHIVが感染する機構として，白血球機能関連抗原(LFA-1)を介したリンパ球と絨毛細胞の直接接触[6]やトランスサイトーシスが関与するらしい．

われわれ[7]は，胎盤絨毛が発生の初期から種々のケモカインレセプターを発現し，ケモカインによってヒト絨毛性ゴナドトロピン(hCG)分泌や細胞の増殖といった基本的な機能の調節を受けていることを明らかにした．同様の所見はDolcini ら[8]や，Maldonado-Estrada ら[9]により追試証明された．CCR 5やCXCR 4はおのおのR 5ウイルス，X 4ウイルス感染のコレセプターとして必須のものであり，*in vitro* でも絨毛細胞はCD 4非依存性にHIVに感染しうること[10]から，CD 4非依存性の感染モデルとなると考えられる．しかし，Parry らは初代培養したtrophoblastをTNF-α処理するとHIVの侵入が著しく増強するが，これはCD 4のみならずCCR 5にもCXCR 4にも依存しないという知見を発表しており[11]，更なる検討が必要である．絨毛組織内のHofbauer細胞はCD 4，CCR 5，CXCR 4すべて陽性であり古典的経路による感染を説明しやすいが，HIVが母体血中から二重の栄養芽細胞層を通り越していきなりHofbauer細胞に到達するとは考えがたい．

HIV陽性妊婦の胎盤では，MoussaらがMIP-1α，MIP-1β，RANTES，IL-6の発現がコントロールに比較して著しく低下していることを報告している[12]が，すべての患者がAZTなど抗ウイルス薬の投与を受けており，治療の影響を否定できない．局所の炎症性サイトカインが栄養膜細胞への感染成立に必須であるとする報告もある[13]．これら炎症性サイトカインは絨毛羊膜炎で上昇す

ることから，サイトカイン自体の作用というよりも，HIV 垂直感染のリスク因子である絨毛羊膜炎の存在を示唆するものかもしれない．しかし，分娩前に抗生物質で絨毛羊膜炎を治療しても，脱落膜の炎症細胞浸潤の程度や，垂直感染率は変化がみられなかったとする報告もある[14]．

3．内在性レトロウイルスの意義

ヒトのゲノムには，進化の過程でレトロウイルスが生殖細胞系列の遺伝子内に組み込まれ宿主のゲノムの一部になったいわゆる内在性レトロウイルス(HERVs)が全ゲノムの 10～15%含まれる．これらの多くは不活性であるが，胎盤や生殖巣では生理的な発現がみられ，胎盤形成や減数分裂に係る未知の生理的意義が示唆される．ヒト胎盤では，syncytiotrophoblast(合胞体栄養細胞層)の形成を担う蛋白 syncytin は HERV-W に由来する[15]ため，合胞体形成に必須である．

近年，いくつかの実験系において内在性レトロウイルスが外部から侵入するウイルス感染に対して防御因子として作用するのではないかという仮説が提唱されているが[16]，ヒトにおける実証はほとんどなされていない．最近，Nagy ら[17]はヒト末梢血に発現する新たな内在性レトロウイルス産物 HRES-1/Rab 4 が HIV-1 Tat の遺伝子導入や HIV 感染によって up-regulation されること，これが HIVgag 24 の転写を抑制し，また CD 4 発現を調節することで HIV の感受性を抑制することを明らかにした．胎盤では HERV-W 以外にも複数の内在性レトロウイルスを発現しており，これが局所の感染制御に作用している可能性がある．

4．胎児・新生児の HIV 感受性と HIV 陽性母から生まれた非感染児の免疫応答

先に述べたように，HIV 陽性母においても子宮内で胎児に感染することは少ない．むしろ，HIV 陽性妊婦より生まれた新生児では本人が HIV に感染していないにもかかわらず，HIV に対する細胞性免疫応答が誘導されていることが多い[18)~20)]．かつては，胎児の免疫系は未熟で子宮内で曝露された抗原に対しては寛容になると信じられていたが，これは二卵性双胎やウシの free-martin など特殊な場合であり，子宮内でのウイルス感染に対しても CD 8 細胞を主体とする免疫応答が生じうることが明らかとなった[21]．

近年 PCR を使った研究により，母体と胎児の循環はかつて考えられていたほど完全には分離しておらず，少量の血球細胞が行き来していること(michrochimerism)が明らかになってきた．実際，HIV 陽性(無治療)の母親から 36 週で経腟分娩した男児が新生児期に子宮内感染を確認されたにもかかわらず，HIV に対する非常に強い CTL 活性が誘導され無治療で月齢 12ヵ月にはウイルスが消失した症例が報告されている[22]．おそらく，胎児は 280 日の妊娠経過中に何度も少量の HIV ウイルス粒子や HIV 感染細胞の侵入を受けているに違いないが，これを防御する機構が存在すると考えられる．われわれは当初，臍帯血リンパ球は HIV 感染に対して抵抗性があるのではないかと考え *in vitro* でウイルスをチャレンジしたが，成人と差がみられなかった．臍帯血清と臍帯単核球，成人血清と成人末梢血リンパ球を組み合わせを変えて検討したがいずれにおいてもウイルス複製に差を認めず，臍帯血自体の HIV 感受性が低いという仮説は成立しない．Sundaravaradan ら[23]は，臍帯血リンパ球，マクロファージを *in vitro* で HIV 処理すると成人末梢血に比較してはるかに感受性が高いことを示し，これは，HIV レセプターである CD 4 やコレセプターである CXCR 4，CCR 5 の発現レベルの差ではなく，HIV-1 LTR の転写亢進によるものであるとしている．臍帯血中の PLAP を指標として母体から胎児への microtransfusion の量を定量すると，一定量以上の母体血が胎児循環内に入れば垂直感染が成立するという[24]．おそらく，胎児は一定量までのウイルスや感染細胞の侵入には耐性であっても，

マラリア感染や絨毛羊膜炎，切迫早産，妊娠高血圧症候群などで胎盤関門が破綻し，許容量を超えたHIVが進入した場合には子宮内感染を避け得ないのであろう．HIV陽性母から出生した児の臍帯血において，感染が成立していない場合は，HIV-1 env抗原に対するヘルパーT細胞応答やβケモカイン産生を認めるが，感染をきたした児の場合にはこれが認められないことから，子宮内でHIVに対する有効な免疫応答を誘導できるか否かが垂直感染の成立に重要な要因と考えられる[25]．また，HIVに対する細胞性免疫応答を獲得した児は産道感染や，母乳を介した感染にも抵抗性であるという[26]．

Biggarら[27]は，HIV陽性の母から出生した胎児が男児の場合，女児にくらべて子宮内感染の比率が有意に少ないことから，Y染色体に連鎖した組織適合性抗原の認識が重要ではないかという仮説を提唱している．母児双方のHLAハプロタイプの組み合わせや，ウイルス抗原のバリアントにより胎児側の免疫応答の質と程度に相違を生じる可能性がある．

5．ウイルス側の要因

Wolinskyらは垂直感染をきたすウイルスは母体内に多数存在するHIVサブクローンのなかでもきわめてかぎられた変異株にすぎないという報告をしているが[28]，わが国においてもHIV垂直感染の成立した8例のうち6例はV3ループの29DがNに置換していた[29]．さらに66例のHIV垂直感染症例を検討したところ，母体内HIVの集団は様々なサブタイプ(A, B, B′, D, E)が混在するが，新生児においてはB，Dのみが存在していた．さらに個々の症例内でも，母親血中には多数のウイルスクローンが存在するのに対して，感染した児のHIV-1はほぼ単独もしくはきわめて少数のクローンであることから，母体に感染したHIVは変異を繰り返し，そのごく一部が胎児・新生児に感染すると考えられる[30]．この現象がウイルスの性状に相違によるものかそれとも単に感染効率がきわめて低い事実の反映であるのかは現在検討中であるが，日本では垂直感染症例がほとんどないこともあり十分な結論を得ることは困難である(外国の研究者と話す時に“fortunately as a clinician but unfortunately as a researcher”というのが早川の口癖である)．

おわりに
何が胎児を免疫するのか

脱落膜は子宮内膜間質が妊娠に伴う高エストロゲン・高プロゲステロン環境によって変化したものである．リンパ球，マクロファージ，樹状細胞など多くの免疫細胞が集簇するが，その主体をなすものはCD56陽性の未熟なNK細胞(dNK細胞)とNKT細胞である．これらの細胞の性状と内分泌支配については本特集の真島洋子の稿に詳しいが，われわれはこれらの細胞群のHIV垂直感染に及ぼす影響を現時点における研究の主要テーマの1つにしている．

NK細胞はHIV感染細胞を破壊するのみならず，複数のCCケモカインを産生して感染を抑制する[31]．一方，HIVに対して感受性であり，潜伏感染をきたすことによってHIVのreservoirとなる可能性が指摘されている[32]．同様にNKT細胞もHIVに高い感受性を有する[33]．筆者らは樹立NK細胞株におけるHIV複製が培養条件や液性因子によって調節を受けることを明らかにした(投稿中)．HIVに感染し，抗原を提示しながら複製できない母体側細胞が胎児側に侵入することで胎児にHIVに対する有効な免疫応答が生じているとすれば，“natural vaccine”となっている可能性があり，現時点ではいささか手詰まりとなっているHIVワクチン開発に新たな展開を期待できるのではないかと考えている．

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