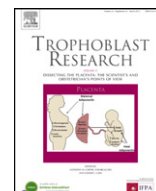


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## Placenta

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## Review: Exploration of placentation from human beings to ocean-living species

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## ABSTRACT

This review covers four topics.

1) Placental pathology in Himalayan mountain people. To determine morphological changes of the placenta at high altitude, pathological examination was made of 1000 Himalayan placentas obtained in Nepal and Tibet and the results compared with Japanese placentas delivered at sea level. Characteristic findings in the placental villi of the Himalayan group included high incidences of villous chorangiosis and chorangioma. These processes were clarified by ultrastructural observation.

2) Placentation in Sirenians. The giant Takikawa sea cow, which lived 5 million years ago, was discovered on Hokkaido, Japan. It was an ancestor of the dugong as well as the manatees. Sirenia, the sea cow group, shares a common ancestor with Proboscidea, the elephants, even though they now inhabit quite different environments. A comparison was made of their zonary endothelial type of placentation.

3) Placentation in sharks and rays. The remarkable placentation of hammerhead sharks and manta rays is described.

4) Placentation in the Antarctic minke whale. Placental tissue samples of this whale were obtained from the Japan Institute of Cetacean Research. In an ultrastructural study of the utero–placental junction, microfilamentous processes of the allantochorionic zone and crypt formation were visualized.

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## 1. Introduction: The placenta in Japanese culture

Since ancient times in Japan, the placenta that nourished an infant in utero has been handled with care and been sacred to the memory. For example, Hakozaki Shrine, Hakata, Kyushu was founded over one thousand years ago and is the site where the Empress Jingu gave birth to a son, Emperor Oujin. The placenta was put in a box (Hako) and worshiped [1].

## 2. Hiroshima 1945

On August 6, 1945, the B29 bomber Enola Gay dropped a 15 kiloton uranium bomb on Hiroshima. Some 70,000 people died

immediately and 150,000 more over the next few years. Three days later, on August 9, Fat Man, a 21 kiloton plutonium bomb, was dropped on Nagasaki, killing an estimated 50,000 people [2]. Four months later, in December 1945, when I was obliged to step off the train at the Hiroshima barracks station, the whole city as far as I could see was enveloped in darkness. Since then, 67 years have passed and Hiroshima has been transformed into a splendid city.

Reports on the outcome of pregnancy in women who were pregnant at the time of the atomic bomb explosions in Hiroshima and Nagasaki were very few because of difficulty in obtaining data at that time. From very few studies of the survivors of the atomic bombing of Hiroshima and Nagasaki, neonatal and infant mortality rates among pregnant women exposed within 2 km of the hypocenter were high (26.1%) compared with 3.6% at a distance of 4–5 km [3].

The outcome of 205 children exposed to the atomic bomb blast was miserable [4]. Microcephaly with mental retardation was the most frequent infant anomaly. Later, at the request of the late Prof. Naomasa Okamoto, Director of the Research Institute for Nuclear Medicine and Biology, Hiroshima University, who was the most

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eminent expert on pathology of congenital malformations in Japan [5], I examined 36 placentas associated with stillbirth or fetal malformations (Table 1). Of these specimens, the full term stillborn placenta (HG3194) had histologically small foci of chorangiomas near a large decidual hematoma (Fig. 1a). In this case the cause of stillbirth can be ascribed to the occurrence of retro-placental hematoma accompanied with villous chorangiomas.

Such a very small histological focus influenced the development of my future research.

3. Placental pathology in Himalayan mountain people

Whilst I was at the Pathology Department of Dartmouth Medical School in 1970, under its director Prof. Kurt Benirschke, a report from Peru caught my attention [6]. It showed that newborn infants at high altitude in the Andes weighed significantly less than those born at sea level, while the high altitude placenta weighed more than the sea level placenta [6]. Up until then comparative studies of the placenta at high altitude and at sea level had not been carried out.

Nepal is located in the Himalayan Mountains and a large proportion of its population falls into the lower socioeconomic bracket. It has high perinatal and maternal mortality rates. Therefore, in an attempt to clarify morphological changes of the placentas of the Himalayan people, I planned a design to investigate Nepalese placentas pathologically and the results were compared with those of a Japanese group. Pathological examination of 900 Nepalese placentas was performed over 20 years from 1977 at the Maternity Hospital, Kathmandu, Nepal (1600–3000 m above sea level). In addition 66 Tibetan placentas were examined at the People's Hospital, Lhasa (more than 3600 m above sea level) in 1986. The results were compared with those of 5500 Japanese placentas delivered at Saitama Medical School since 1990.

The mean birth weight of 811 neonates in the Nepalese group was 2743 ± 145 g (mean ± SD) and the mean placental weight in the Nepalese group was 389 ± 18 g. In contrast, neonatal birth weight and placental weight of 4175 cases in the Japanese group was 3072 ± 62 g and 431 ± 7.8 g, respectively. The infants and the placentas in the Nepalese group weighed significantly less than those in the Japanese group [7,8], but low economic status and low nutrition in high mountain people also should be considered as causative factors of reduced fetoplacental function [9].

The most characteristic histopathological lesions of the Himalayan placentas were high incidences of marked subchorionic fibrin deposition and chorionic cysts and increased incidences of chorangiosis and chorangioma; in contrast a low incidence of intervillous thrombosis was noted. Chorangiosis is histologically designated as more than 10 terminal capillaries within villous stroma, while chorangiomatic foci are here defined as

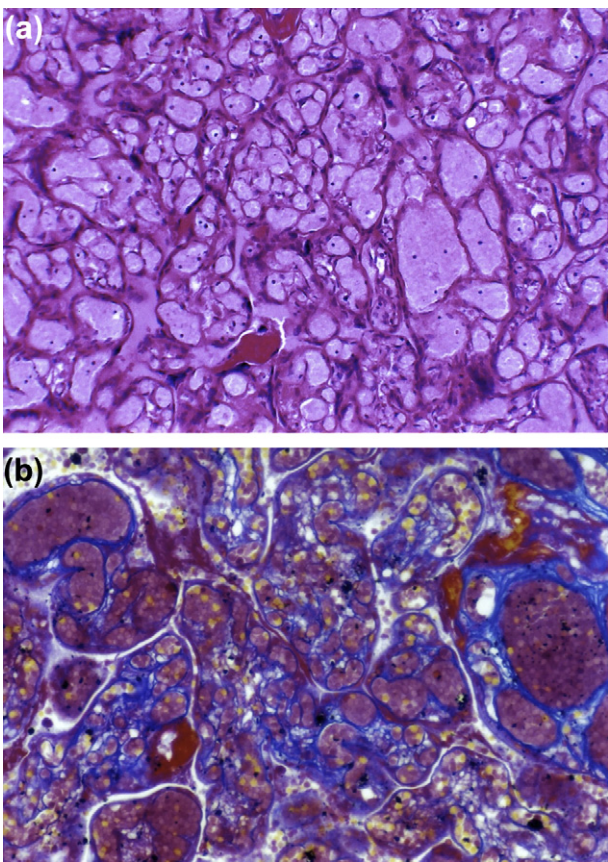


Fig. 1. (a) Histological chorangiomatic foci found from stillborn placenta at full term (HG3194) among 36 placentas associated with stillborn or fetal malformations at Hiroshima University. HE stain (x100). (b) Chorangiosis in a Nepalese placenta, Azan stain (x200).

a hypervascular pattern in the stem villi and the terminal villi. The incidence of chorangiosis and chorangioma in 533 Nepalese and Tibetan placentas was compared to 884 Japanese placentas. The incidence of chorangiosis and chorangioma in the Himalayan group (15.6%) was significantly higher than that of the Japanese group (7.5%) ( $P < 0.05$ ) (Table 2) [8–11]. Thus, an increased incidence of both chorangiosis and chorangioma was found in placentas at Himalayan high altitude. Later an increased incidence of chorangioma at high altitude in Kirghizstan and Tadzhikistan has been reported [12].

As the next step, we attempted to find out whether new capillary formation could be demonstrated in the villous stroma with chorangiosis and chorangioma by an ultrastructural study.

Case 1: A 25-year-old Nepalese woman, parity 1, was delivered of a female infant weighing 2900 g at 38 weeks of gestation. The umbilical cord was 58 cm long with 3 vessels. Placenta weighed

Table 1  
Histological examination of placental tissues from stillbirth or abortion at Research Institute for Radiation Biology and Medicine, Hiroshima University.

	No.
Stillborn placentas	15
Fetal malformations	10
Phocomelia	2
Anencephaly	1
Hydrocephalus	1
Spina bifida	1
Chromosomal anomalies	
E-trisomy	2
18-trisomy	1
21-trisomy	1
Meningocele	1
Horse kidney	1

Table 2  
A comparison of the incidence of chorangiosis and chorangioma between Japanese and Himalayan placental groups.

	Japanese group, N = 884	Nepalese group, N = 467	Tibetan group, N = 66	Himalayan group, total N = 533
	No. (%)	No. (%)	No. (%)	No. (%)
Chorangiosis	51 (5.8)	57 (12.2)	14 (21.2)	71 (13.3)
Chorangioma	15 (1.7)	8 (1.7)	4 (6.1)	12 (2.3)
Total	66 (7.5)	65 (13.9)	18 (27.2)	83 (15.6)

$P < 0.05$ .

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