

The Paediatric Cardiology Hall of Fame

Atsuyoshi Takao

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IT IS A GREAT HONOUR FOR ME TO WRITE ABOUT Atsuyoshi Takao (Fig. 1) on the occasion of his induction to the Paediatric Cardiology Hall of Fame. It is also very sad for me to announce that he passed away on August 8, 2006, at the age of 81. Everyone would agree that he was one of the most creative and active paediatric cardiologists in the world. Although he had officially retired, he was still seeing many patients at an outpatient clinic on the day before he was admitted to the hospital. He had back pain on August 1, 2006, and was admitted to the hospital the next day. An emergency coronary angiogram showed total occlusion of the left anterior descending artery. After percutaneous coronary intervention, he was busy reading medical papers in bed in the hospital when, on August 8, he died suddenly due to rupture of the left ventricular wall.

I first met Atsuyoshi Takao in 1974, when I graduated from Hiroshima medical school. I visited the Heart Institute of Japan and asked Dr Takao to allow me to come to the Institute after I finished my paediatric residency. At that time, he was already a famous paediatric cardiologist in Japan. In those days, he was a great professor, and in keeping with the Japanese tradition, I could not speak with him frankly. He was not a person who would talk freely for a long time. Just a short conversation every day was his style. I remember he used to say that "It is best to work with originality, it is second best to do some work anyway, and it is the worst to disturb colleagues from doing their work". Now, I always try to follow his advice.

In 1977, I left the Heart Institute to work as a research fellow at the University of California at Los

Angeles. While I was in the United States, Dr Takao sent me several letters. In one of them, he said that, rather unexpectedly, he had become the director of the Heart Institute of Japan. Traditionally, the Heart Institute of Japan had been led by either a cardiac surgeon or a cardiologist. He did an excellent job as the director of the institute. He showed well-balanced leadership among cardiac surgeons, cardiologists, and paediatric cardiologists. After I returned from the United States of America, I spent more time with him, and gradually began to know him better, finding that he was an honest, sincere, and warm person.

In March, 1990, Atsuyoshi Takao retired from the position of professor of paediatric cardiology (Fig. 2). During the lecture made on his retirement, he read a poem composed by a young boy named Kou Murakami. The child had a congenitally malformed heart, had undergone a palliative operation, and died with his mother at his side when he was only an elementary school student.

I will present the poem "My treasure", which I have translated into English.

"One day, after one day, goes away,
Each day, which goes away, is beautiful,
Each beautiful day is my treasure,
When each day goes away,
My treasure goes far away,
I feel that way."

Dr Takao could not read the poem to the end without tears in his eyes. At that moment, I felt that, for Dr Takao as for Kou Murakami, each day was his treasure, and he also lived that way.

Education

Atsuyoshi was born in 1925. The Takaos originate from an ancestor who started to serve as local ruler in Kyushu Island, one of 170 daimyo under the

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Figure 1.
Atsuyoshi Takao. He wrote as "Development, Unfolding".



Figure 2.
Atsuyoshi and Yukie Takao at the retirement party in 1990.

Shogun, in the Edo era, about 370 years ago. The Takaos had been doctors for the rulers during the Edo era. Atsuyoshi's grandfather moved to Tokyo at the end of the Edo era as a doctor. His father opened a private clinic in the centre of Tokyo, and had nine children, including Atsuyoshi. His father died early, and the family had to move back to Kyushu, because it was easier for the family to live there among relatives. Atsuyoshi went to high school and medical school in Nagasaki, in Kyushu. Of the 9 children, 6 became medical doctors. Kazuo Momma, a professor emeritus of paediatric cardiology in our



Figure 3.
Atsuyoshi Takao at New York University in 1962.

institute, was a classmate of Atsuyoshi's youngest brother, who is now an ophthalmologist, at Tokyo University.

Atsuyoshi Takao graduated from Nagasaki medical school in 1945. After graduation, during the Second World War, he served at the army medical school. He was in Yamagata prefecture, the northern part of the main island of Japan, when the atomic bomb was dropped in Nagasaki, and the War ended in August, 1945. He studied general paediatrics at Nagasaki and Yamaguchi medical schools for 5 years. In 1950, he started to work at the Atomic Bomb Casualty Commission in Nagasaki, serving as an assistant in the Division of Pediatrics. At that time, James Yamazaki, a clinical professor at the University of California at Los Angeles and an author of "Children of the Atomic Bomb" was working in Nagasaki. About 30 years later, I drove Atsuyoshi to meet Dr Yamazaki in Los Angeles, and we had an enjoyable time together. Atsuyoshi worked at the Atomic Bomb Casualty Commission in Nagasaki and Hiroshima for two years.

In 1952, Atsuyoshi went to New York University to train in general paediatrics (Fig. 3). He travelled to the west coast of America by ship, and from Los Angeles to Chicago by train named El Captain. He did not talk very much about the details of his life in the United States of America while I worked with him, and I can only guess that he worked hard. He was certainly well trained as a paediatrician, because he had profound knowledge of general paediatrics. He spent four years at New York University. After finishing his residency, he went to Texas Children's hospital, where Dan G McNamara



Figure 4.
Stella and Richard Van Praagh, Atsuyoshi Takao, and Young Chang Tockgo at the Takao meeting in 1988.

was the chief, and where he spent 3 years as a clinical fellow in pediatric cardiology. Later in life, Atsuyoshi met Richard Van Praagh. Both Richard and Dan had finished their clinical fellowships at Johns Hopkins University, and they knew each other from reunion parties. Since Richard and Dan were good friends, Richard felt instantly that Atsuyoshi was his friend, too (Fig. 4). Later, in 1971, Helen Taussig visited our institute to give a lecture to the students of Tokyo Women's Medical University (Fig. 5). The friendship of Atsuyoshi and Richard continued, and we were gratified that Richard was able to visit our institute in 2006 for the memorial service of Atsuyoshi Takao.

The Heart Institute of Japan

The Heart Institute of Japan was founded in 1955, and the first closure of atrial septal defect in Japan was performed at the Institute in 1956. Although many patients underwent cardiac surgery, the operative results were unfavourable and the indication for operation was unclear. This was not unlike the situation prevailing in many other countries at that time.

When Atsuyoshi came back to Japan, in 1958, Shigeru Sakakibara, the first chief cardiac surgeon, and founder of the Heart Institute of Japan, invited him to become Assistant Professor at the Department of Cardiac Surgery. Among surgeons, he soon showed his ability to make correct diagnoses from physical findings, electrocardiograms, and chest X-rays. He wondered, however, if he should continue to send patients to surgery, knowing that



Figure 5.
Atsuyoshi Takao, Helen Taussig, and Shigeru Sakakibara at Tokyo Women's Medical University in 1971.

the rate of mortality was very high, and that Dr Sakakibara insisted on performing intracardiac repair, rather than palliation, even with the high mortality rate. In this respect, Atsuyoshi was not loyal to the Institute, and sent some patients to other hospitals, with better results.

He became the professor, and chief, of paediatric cardiology in 1968. In the 1970s, Souji Konno and Yasuharu Imai started to operate on children with congenitally malformed hearts, and the operative results improved significantly. Kazuo Momma and Masahiko Ando joined the Department of Pediatric Cardiology, and the number of clinical fellows increased gradually. As the operative results improved, the reputation of the Heart Institute, along with that of Dr Takao, became widespread, and he attracted many patients from all over Japan (Fig. 6).

Marriage

On visiting the pediatric ward one day, Atsuyoshi met a pediatrician, named Yukie. In 1962, they got married. Yukie Takao then worked at a centre for public health until 1990, when both Yukie and Atsuyoshi retired. Subsequent to their retirement, they both enjoyed hiking and mountain walking together in the suburbs of Tokyo.

Hokkaido hot springs

Every summer, doctors who finished their fellowship and returned to their hometown in Hokkaido, a northern island of Japan, invited Atsuyoshi and Yukie to go mountain hiking. There are many hot springs in Hokkaido, and Atsuyoshi and Yukie enjoyed the hot springs in the mountains very much (Fig. 7). Once, the fellows organized a sushi party at the top of a mountain. They brought fish, and asked



Figure 6.
Atsuyoshi Takao at the pediatric ward in 1978.

a sushi master to climb the mountain with them. Dr Takao did not want the fellows to pay the expenses so he sent more than enough money in advance for the party.

Conotruncal anomaly face syndrome, or the Takao syndrome

In 1965, DiGeorge¹ commented on an infant with hypoparathyroidism and recurrent infections, along with 3 autopsied cases with absence of the thymus and parathyroid glands. Later, the association of cardiovascular abnormalities, such as interruption of the aorta, common arterial trunk, and tetralogy of Fallot, with DiGeorge syndrome was established by the work of Freedom and colleagues² and Van Mierop and Kutsche.³ From early 1980s, deletion of chromosome 22q11 started to be recognized as a cause of the syndrome,⁴ and microdeletion of this region was confirmed in 1991 and 1992.^{5,6}

Conotruncal anomaly face syndrome had first been reported in 1976.⁷ In the early 1970s, Atsuyoshi Takao had begun to recognize a characteristic facial appearance, with a flat nasal bridge, a small mouth, a nasal voice, a high arched palate, abnormalities of the ear lobes, and mental retardation among patients with abnormalities of the ventricular outflow tracts, mostly tetralogy of Fallot. He named this combination “conotruncal



Figure 7.
Atsuyoshi, enjoying Shiatsu massage by an ex-fellow Isamu Hamada.

anomaly face syndrome”. He was able to make the diagnosis simply by observing the face and listening to the voice of a patient, and sometimes the patient’s mother. When I first came to Tokyo Women’s Medical University as a fellow in 1976, the concept of the conotruncal anomaly face syndrome had already been established in the Heart Institute of Japan. Atsuyoshi asked Akiko Kinouchi to write a paper about the syndrome, and in 1976 she wrote a paper in Japanese.⁷ This paper was the first to describe conotruncal anomaly face syndrome. In those days, I did not imagine that a chromosomal abnormality could be identified in this syndrome. It was only several years later that Atsuyoshi told Rumiko Matsuoka, who was working with Richard Van Praagh, to study molecular biology in Boston. Later, he said that all the purposes of establishing our laboratory for molecular biology were to investigate the aetiology of conotruncal anomaly face syndrome.

Be that as it may, in the mid 1970s, Dr Takao wanted to evaluate the characteristics of the face and fingerprints of this syndrome. Akiko Kinouchi measured the length of various parts of the face in patients with this syndrome, and she published further papers in 1980.^{8,9} In those days, cardiac surgeons already had noted that some patients with the syndrome did not have a thymus. Recognizing that the syndrome shared some common phenotypes with DiGeorge syndrome, around 1980 Dr Takao and his fellow Takashi Shimizu studied immunodeficiency in patients with the syndrome.¹⁰ The

results showed that the population of T cells was subnormal in four-fifths of patients with the syndrome, but a decreased T cell count was noted in only 7%. In two-thirds of patients, however, they also found a poor response to the phytohemagglutinin skin test, an indicator of a T-cell mediated immune response. Atsuyoshi Takao also noted a high frequency of anomalies of the aortic arch, such as cervical aortic and abnormal origin of the subclavian artery, in these patients, and these results were published in 1985.¹¹ Later, after confirmation of chromosome 22q11 deletion, Kazuo Momma reviewed cardiovascular abnormalities in the syndrome, by then known appropriately as Takao syndrome.¹²

Velo-cardio-facial syndrome, or Shprintzen syndrome

In 1978, Shprintzen and colleagues¹³ published a paper about patients with a cleft palate, cardiac anomalies, typical facies, and learning disabilities, which they called the velo-cardio-facial syndrome. After reading their paper, Atsuyoshi sent a letter to Shprintzen suggesting that conotruncal anomaly face syndrome and velo-cardio-facial syndrome might be the same entity. In reply, Dr Shprintzen asked if he could see patients with conotruncal anomaly face syndrome, but somehow, there was no chance for him to see the patients. There was also no chance for them to meet each other. In 1992, however, velo-cardio-facial syndrome was found to be associated with microdeletion of chromosome 22q11,¹⁴ while in 1993, similar deletion was confirmed in conotruncal anomaly face syndrome.^{15,16} Throughout his life, nonetheless, Atsuyoshi never claimed that he was the first to have described this syndrome.

Kawasaki disease

The mucocutaneous lymph node syndrome, or Kawasaki disease, was first reported by Kawasaki in 1967. Atsuyoshi Takao once saw a patient with severe mitral regurgitation. When he looked at a chest X-ray carefully, he noted a calcification at an unusual site in the cardiac silhouette. He thought that the calcification might be in the wall of a coronary artery, and that the mitral regurgitation might have been due to the coronary arterial calcification associated with Kawasaki disease.¹⁷ He was the first to emphasize the importance of aortography or coronary angiography in Kawasaki disease.¹⁸ Now, Kawasaki disease is well established as a cause of mitral regurgitation in children.¹⁹

Basic science in the 1970s and 1980s

Dr Takao was very interested in the research of cardiac morphogenesis. In the 1970s, he wanted to produce cardiac anomalies to clarify the mechanisms of congenital cardiac disease. In the early 1970s, together with Shizen Ishikawa, he noted that the frequencies of ventricular septal defect and anomalies of the aortic arch were high in chick embryos after centrifugation.²⁰ In the late 1970s, he instructed his fellows to study the effect of radiation and electric shock on cardiac development.^{21,22} In the early 1980s, he told his fellows to study the effect of various drugs, such as a retinoic acid, bisdiamine, and nimustin.^{23,24} They found that maternal administration of a retinoic acid caused heterotaxy syndrome and transposed great arteries in the mouse.^{25–27} They also found thymic abnormalities and interruption of the aortic arch between the left common carotid and left subclavian arteries. Despite these experiments, Dr Takao began to feel a limitation of methodology in experimental teratology to clarify the mechanism of the malformed heart.

The Takao meeting

To resolve these inadequacies, Dr Takao determined to hold an international conference to stimulate and integrate research on the morphogenesis of the heart. The Sankei Takao symposium was first held in 1978, with the financial support of The Sankei Newspaper, and donations from ex-fellows of the Department of Pediatric Cardiology at the Heart Institute of Japan. Dr Takao did not want to use his name as the title of the symposium, and the conference was called “Symposium on the Etiology and Morphogenesis of Congenital Heart Disease” (Fig. 8). Dr Takao also did not like to receive donations from pharmaceutical companies, as he thought such donations could possibly involve a conflict of interest. A book was published after each symposium, appearing in 1980, 1984, 1990, 1995, and 2000.^{28–32} The co-editors were Richard Van Praagh, James Nora, Roger Markwald, Edward Clark, and Makoto Nakazawa.

Molecular biology

Dr Takao realized the importance of molecular biology in the late 1970s. After Atsuyoshi retired in 1990, he began to study molecular biology himself, striving hard to learn the various techniques. Although he did not perform experiments himself, he became a good molecular biologist. In 1990, he set up the International Molecular Cellular



Figure 8.

The Takao meeting in 1993. Front, from left, Kenneth Chien, Julie Korenberg, Ed Clark, Atsuyoshi Takao, Roger Markwald, Charlotte Ferencz, John Burn. Behind Ed Clark, Kazuo Momma, and Brad Keller.

Immunological Research Center. He worked as a director of the Institute until 2006. In 2003, investigators of the Institute, including Atsuyoshi Takao and Rumiko Matsuoka, published a paper suggesting that mutation of the *TBX1* gene was responsible for conotruncal anomaly face syndrome.³³

Thanatology

Dr Takao also studied hard with regard to thanatology. In the textbook of pediatric cardiology “Clinical Developmental Cardiology”, he wrote a chapter on thanatology, placing the poem shown above at the top of the chapter.³⁴ In the text, he emphasized the importance of thanatology in pediatric cardiology and said, “The art of dying is the art of living”, “We can live just because we die” and “Pediatric cardiology should become longitudinal cardiology if we look at patients with congenital heart disease from the point of view of thanatology”. I sometimes wonder what the death of patients with congenitally malformed hearts meant to him? Upon the death of patients, Atsuyoshi showed a deep sympathy to the parents, and they thanked him. He showed me the importance of sharing the notion of thanatology with the families of the patients.

Conclusion

Atsuyoshi Takao was a father of paediatric cardiology in Japan. He showed me the way to live, and was my life-long mentor. Many cardiac fellows admired him, loved him, and felt like he was a father to them. He will continue to live on in our memory.

References

1. Cooper MD, Peterson RDA, Good RA. A new concept of the cellular basis of immunity. (A comment by DiGeorge AM.) *J Pediatr* 1965; 67: 907–908.
2. Freedom RM, Rosen FS, Nadas AS. Congenital cardiovascular disease and anomalies of the third and fourth pharyngeal pouch. *Circulation* 1972; 46: 165–172.
3. Van Mierop LHS, Kutsche LM. Cardiovascular anomalies in DiGeorge syndrome and importance of neural crest as a possible pathogenetic factor. *Am J Cardiol* 1986; 58: 133–136.
4. de la Chapelle A, Herva R, Koivisto M, Aula P. A deletion in chromosome 22 can cause DiGeorge syndrome. *Human Genet* 1981; 57: 253–256.
5. Wilson DI, Cross IE, Goodship JA, et al. DiGeorge syndrome with isolated aortic coarctation and isolated ventricular septal defect in three sibs with a 22q11 deletion of maternal origin. *Br Heart J* 1991; 66: 308–312.
6. Driscoll DA, Budarf ML, Emanuel BS. A genetic etiology for DiGeorge syndrome: consistent deletions and microdeletions of 22q11. *Am J Med Genet* 1992; 44: 261–268.
7. Kinouchi A, Mori K, Ando M, Takao A. Facial appearance of patients of conotruncal anomalies. *Pediatrics of Japan (in Japanese)* 1976; 17: 1–2.
8. Kinouchi A. A study on facial features associated with conotruncal anomalies of the heart. *J Tokyo Wom Med Coll* 1980; 50: 396–409.
9. Takao A, Ando M, Cho K, Kinouchi A, Murakami Y. Etiologic categorization of common congenital heart disease. In: Takao A, Van Praagh R (eds). *Etiology and morphogenesis of congenital heart disease*. Futura Pub. Co., Mount Kisco, NY, 1980, pp 253–269.
10. Shimizu T, Takao A, Ando M, Hirayama A. Conotruncal anomaly face syndrome: its heterogeneity and association with thymus involution. In: Nora JJ, Takao A (eds). *Congenital heart disease – causes and processes*. Futura Pub. Co., Mount Kisco, NY, 1984, pp 29–41.
11. Terai M, Takao A, Ando M, et al. Cardiovascular anomalies associated with conotruncal anomaly face syndrome. *J Japan Pediatric Society* 1985; 89: 1651–1658.
12. Momma K, Kondo C, Matsuoka R, Takao A. Cardiac anomalies associated with a chromosome 22q11 deletion in patients with conotruncal anomaly face syndrome. *Am J Cardiol* 1996; 78: 591–594.
13. Shprintzen RJ, Goldberg RB, Lewin ML, et al. A new syndrome involving cleft palate, cardiovascular anomalies, typical facies, and learning disabilities: velo-cardio-facial syndrome. *Cleft Palate J* 1978; 5: 56–62.
14. Scambler PJ, Kelly D, Lindsay E, et al. Velo-cardio-facial syndrome associated with chromosome 22 deletions encompassing the DiGeorge locus. *Lancet* 1992; 339: 1138–1139.
15. Burn J, Takao A, Wilson D, et al. Conotruncal anomaly face syndrome is associated with a deletion within chromosome 22q11. *J Med Genet* 1993; 30: 822–824.
16. Burn J, Wilson DI, Cross I, et al. The clinical significance of 22q11 deletion. In: Clark EB, Markwald RR, Takao A (eds). *Developmental Mechanisms of Heart Disease*. Futura, Armonk, NY, 1995, pp 559–567.
17. Hamada I, Takao A, Mimori S, et al. Cardiovascular involvement in mucocutaneous lymph node syndrome; mitral regurgitation and coronary aneurysm. *Clinical Pediatric Medicine (in Japanese)* 1973; 21: 163–182.
18. Takao A, Kusakawa S, Hamada I, Ando M, Asai T. Cardiovascular lesions of mucocutaneous lymph node syndrome. *Circulation* 1974; 49: III–39.
19. Takao A, Niwa K, Kondoh C, et al. Mitral regurgitation in Kawasaki disease. In: Shulman ST (ed). *Kawasaki Disease*. Alan R. Liss, Inc., New York, 1987, pp 311–323.

20. Ishikawa S, Takao A, Ando M, Mori K. The teratogenic effect of centrifugal force on the cardiovascular system of chick embryo. *Cong Anom* 1975; 15: 11–27.
21. Ishikawa S, Nagao M, Okawa H, et al. The spectrum of double outlet right ventricle induced by electrical shocks to the conotruncus of the embryonic chick. Implications of tissue dynamics. *Jpn Heart J* 1982; 23: 771–782.
22. Kawamura T, Takao A, Ando M. Spectrum of the coarctation type of ventricular septal defect in the chick induced by neutron radiation. In: Takao A, Van Praagh R (eds). *Etiology and morphogenesis of congenital heart disease*. Futura Pub. Co., Mount Kisco, NY, 1980, pp 235–251.
23. Zen I, Ando M, Takao A. The effect of nimustin Hcl on cardiac morphogenesis in chick embryo. *J Japan Pediatric Society* 1984; 88: 1756–1762.
24. Zen I, Ando T, Takao A. Cardiac malformation caused by bisdiaminein chick embryo. *J Japan Pediatric Society* 1987; 91: 637–641.
25. Irie K, Ando M, Yakao A. All-trans retinoic acid induced cardiovascular malformations. *Ann NY Acad Sci* 1990; 588: 387–388.
26. Yasui H, Nakazawa M, Morishima M, Miyagawa-Tomita S, Momma K. Morphological observations on the pathogenetic process of transposition of the great arteries induced by retinoic acid in mice. *Circulation* 1995; 91: 2478–2486.
27. Yasui H, Nakazawa M, Morishima M, Ando M, Takao A, Aikawa E. Cardiac outflow tract septation process in the mouse model of transposition of the great arteries. *Teratology* 1997; 55: 353–363.
28. Van Praagh R, Takao A. *Etiology and Morphogenesis of Congenital Heart Disease*. Futura, Mount Kisco, New York, 1980.
29. Nora JJ, Atsuyoshi T. *Congenital heart disease – causes and processes*. Futura Pub. Co., Mount Kisco, NY, 1984.
30. Clark EB, Takao A. *Developmental cardiology: morphogenesis and function*. Futura Pub. Co., Mount Kisco, NY, 1990.
31. Clark EB, Markwald RR, Takao A. *Developmental mechanisms of heart disease*. Futura Pub, Armonk, NY, 1995.
32. Clark EB, Nakazawa M, Takao A. *Etiology and morphogenesis of congenital heart disease twenty years of progress in genetics and developmental biology*. Futura Pub. Co., Armonk, NY, 2000.
33. Yagi H, Furutani Y, Hamada H, et al. Role of TBX1 in human del22q11.2 syndrome. *Lancet* 2003; 362: 1366–1373.
34. Takao A, Momma K, Nakazawa M, Nakanishi T. *Clinical Developmental Cardiology*, 3rd ed. Chugai Igakusha, Tokyo, 2001.
35. Takao A. Electrocardiogram in pure pulmonary. *Bull Heart Inst Japan* 1960; 4: 1–12.
36. Takao A, Kusakawa S. Right precordial electrocardiographic pattern and right ventricular pressure in congenital malformation of the heart. *Bull Heart Inst Japan* 1962; 5: 53–62.
37. Sakakibara S, Hashimoto A, Miyamoto AM, Takao A. Origin of both great vessels from the right ventricle. *Bull Heart Inst Japan* 1964; 6: 27–52.
38. Takao A, Takarada M, Koyanagi H, Sakakibara S. Tricuspid atresia with right bundle branch block. *Bull Heart Inst Japan* 1965; 7: 10–22.
39. Sakakibara S, Yokoyama M, Takao A, Nogi M, Gomi H. Coronary arteriovenous fistula nine operated cases. *Am Heart J* 1966; 72: 307–314.
40. Sakakibara S, Takao A, Arai T, Hashimoto A, Nogi M. Both great vessels arising from the left ventricle (double outlet left ventricle) (origin of both great vessels from the left ventricle). *Bull Heart Inst Japan* 1967; 9: 66–86.
41. Sakakibara S, Nogi M, Ebina K, et al. Anomalous origin of the left coronary artery from the pulmonary artery (Bland-White Garland Syndrom) two case reports including one operated case. *Bull Heart Inst Japan* 1968; 10: 72–90.
42. Yokoyama M, Takao A, Sakakibara S. Natural history and surgical indications of ventricular septal defect. *Am Heart J* 1970; 80: 597–605.
43. Momma K, Mimori S, Takao A. Natural history of ventricular septal defects with pulmonary hypertension in infancy and childhood: a serial catheterization study. *Bull Heart Inst Japan* 1971; 13: 57–71.
44. Niibori S, Ando M, Takao A, Sakakibara S. Viscero-atrial heterotaxic syndrome. *Bull Heart Inst Japan* 1971; 13: 72–88.
45. Arai T, Ando M, Takao A, Sakakibara S. Intracardiac repair for single or common ventricle: creation of a straight artificial septum. *Bull Heart Inst Japan* 1972; 14: 81–93.
46. Ishikawa S, Ando M, Takao A. Persistent fifth arterial arch produced by the teratogenic effect of centrifugal force on the cardiovascular system of chick embryo. *Bull Heart Inst Japan* 1974; 16: 79–84.
47. Kitamura N, Takao A, Ando M, Imai Y, Konno S. Taussig-Bing heart with mitral valve straddling: case reports and postmortem study. *Circulation* 1974; 49: 761–767.
48. Tatsuno K, Ando M, Takao A, Hatsune K, Konno S. Diagnostic Importance of aortography in conal ventricular-septal defect. *Am Heart J* 1975; 89: 171–177.
49. Komatsu Y, Nagai Y, Shibuya M, Takao A, Hirokawa K. Echocardiographic Analysis of intracardiac anatomy in endocardial cushion defect. *Am Heart J* 1976; 91: 210–218.
50. Ando M, Takao A. Racial differences in the morphology of common cardiac anomalies. *Bull Heart Inst Japan* 1978; 20: 47–66.
51. Mori K, Ando M, Takao A, Ishikawa S, Imai Y. Distal type of aortopulmonary window Reports 4 cases. *Brit Heart J* 1978; 40: 681–689.
52. Takao A, Ando M, Mori K, Kawamura T. Gene-environmental interaction in the etiology of congenital heart disease. *Jpn Circ J* 1978; 42: 1121–1123.
53. Satomi G, Shimizu K, Komatsu Y, Takao A. Echocardiographic identification of aorta and main pulmonary artery in complete transposition. *Brit Heart J* 1979; 41: 356–359.
54. Wada J, Endo M, Takao A, Kawamura T. Mucocutaneous lymph node syndrome: successful aortocoronary bypass momograft a four-year-old-boy. *Chest* 1980; 77: 443–446.
55. Momma K, Takao A, Ando M, Nakazawa M, Takamizawa K. Natural and post-operative history of pulmonary vascular obstruction associated with ventricular septal defect. *Jpn Circ J* 1981; 45: 230–237.
56. Momma K, Takao A, Shimizu S, Satomi G. Transarterial pulmonary venous wedge arteriography in pulmonary atresia, ventricular septal defect and intact atrial septum. *Cathet Cardiovasc Diagn* 1982; 8: 419–427.
57. Takao A. Complete left bundle branch block in children. *Jpn Heart J* 1982; 23 (Suppl): 154–156.
58. Nakazawa M, Takao A, Chon Y, Shimizu T, Kanaya M, Momma K. Significance of systemic vascular resistance in determining on large ventricular septal defects. *Circulation* 1983; 68: 420–424.
59. Satomi G, Nakamura K, Takao A, Imai Y. Two-dimensional echocardiographic detection of pulmonary venous channel stenosis after Senning's operation. *Circulation* 1983; 68: 520–527.
60. Momma K, Toyama K, Takao A, et al. Natural history of subarterial infundibular ventricular septal defect. *Am Heart J* 1984; 108: 1312–1312.
61. Momma K, Takao A, Sone K, Tashiro M. Prostaglandin E1 treatment of ductus-dependent infants with congenital heart disease. *Int Angiology* 1984; 3 (Suppl).

Selected Published Works

62. Nakata S, Imai Y, Takanashi Y, et al. A new method for the quantitative standardization of cross-sectional areas of the pulmonary arteries in congenital heart diseases with decreased pulmonary flow. *J Thorac Cardiovasc Surg* 1984; 88: 610–619.
63. Nakazawa M, Nakanishi T, Okuda H, et al. Dynamics of right heart flow in patients after Fontan procedure. *Circulation* 1984; 69: 306–312.
64. Satomi G, Nakamura K, Narai S, Takao A. Systemic visualization of coronary arteries by two-dimensional echocardiography in children and infants: evaluation in Kawasaki's disease and coronary arteriovenous fistulas. *Am Heart J* 1984; 107: 497–505.
65. Nakanishi T, Takao A, Nakazawa M. Mucocutaneous lymph node syndrome: clinical hemodynamic and angiographic features of coronary obstructive disease. *Am J Cardiol* 1985; 55: 662–668.
66. Nakanishi T, Okuda H, Nakazawa M, Takao A. Effect of acidosis on contractile function in the newborn rabbit heart. *Pediatr Res* 1985; 19: 482–488.
67. Ando M, Takao A. Pathological anatomy of ventricular septal defect associated with aortic valve prolapse and regurgitation. *Heart Vessels* 1986; 2: 117–126.
68. Kurosawa H, Imai Y, Takanashi Y, et al. Indundibular septum and coronary anatomy in Jatene operation. *J Thorac Cardiovasc Surg* 1986; 91: 572–583.
69. Kurosawa H, Imai Y, Nakazawa M, Takao A. Standardized patch infundibuloplasty for tetralogy of fallot. *J Thorac Cardiovasc Surg* 1986; 92: 396–401.
70. Nakazawa M, Miyagawa S, Takao A, Clark EB, Hu N. Hemodynamic effects of environmental hyperthermia in stage 18, 21, and 24 chick embryos. *Pediatr Res* 1986; 20: 1213–1215.
71. Satomi G, Nakazawa M, Takao A, et al. Doppler echocardiography blood flow pattern of the interatrial communication in patients with complete transposition of the great arteries pulsed doppler echocardiographic study. *Circulation* 1986; 73: 95–99.
72. Lue H-C, Takao A, Ando M. Subpulmonic ventricular septal defect proceedings of the Third Asian Congress of Pediatric Cardiology. Springer-Verlag, Tokyo, New York, 1986.
73. Momma K, Takao A, Ito I, Nishikawa T. In situ morphology of the heart and great vessels in fetal and newborn rats. *Pediatr Res* 1987; 22: 573–580.
74. Momma K, Takao A. In vivo constriction of the ductus arteriosus by nonsteroidal antiinflammatory drugs in near-term and preterm fetal rats. *Pediatr Res* 1987; 22: 567–572.
75. Nakanishi T, Okuda H, Kamata K, Sekiguchi M, Takao A. Development of myocardial contractile system in the fetal rabbit. *Pediatr Res* 1987; 22: 201–207.
76. Nakazawa M, Nojima K, Okuda H, et al. Flow dynamics in the main pulmonary artery after the Fontan procedure in patients with tricuspid atresia or single ventricle. *Circulation* 1987; 75: 1117–1123.
77. Takao A, Niwa K, Kondo C, et al. Mitral regurgitation in Kawasaki disease. *Prog Clin Biol Res* 1987; 250: 311–323.
78. Terai M, Nakazawa M, Takao A, Imai Y. Thrombocytopenia in patients with aortopulmonary transposition and an intact ventricular septum. *Brit Heart J* 1987; 57: 371–374.
79. Kurosawa H, Imai Y, Nakazawa M, Takao A. Conotruncal repair of tetralogy of Fallot. *Ann Thorac Surg* 1988; 45: 661–666.
80. Matsuoka R, Chambers A, Kimura M, et al. Molecular cloning and chromosomal localization of a gene coding for human cardiac myosin heavy-chain. *Am J Med Genet* 1988; 29: 369–376.
81. Miyagawa-Tomita S, Ando M, Takao A. Cardiovascular anomalies produced by Nimustine Hydrochloride in the rat fetus. *Teratology* 1988; 38: 553–558.
82. Nakanishi T, Takao A, Kondo C, Nakazawa M, Hiroe M, Matsumoto Y. ECG findings after myocardial infarction in children after Kawasaki disease. *Am Heart J* 1988; 116: 1028–1033.
83. Nakazawa M, Oyama K, Imai Y, et al. Criteria for twostaged arterial with operation for simple transposition of great arteries. *Circulation* 1988; 78: 124–131.
84. Nakazawa M, Miyagawa S, Ohno T, Miura S, Takao A. Developmental hemodynamic changes in rat embryos at 11 to 15 days of gestation. *Pediatr Res* 1988; 23: 200–205.
85. Kondoh C, Hiroe M, Nakanishi T, Takao A. Detection of coronary artery stenosis in children with Kawasaki disease. Usefulness of pharmacologic stress 201Tl myocardial tomography. *Circulation* 1989; 80: 615–624.
86. Matsuoka R, Yoshida M, Kanda N, Kimura M, Ozawa H, Takao A. Human cardiac myosin heavy chain gene mapped within chromosome region. *Am J Med Genet* 1989; 32: 279–284.
87. Momma K, Takao A. Increased constriction of the ductus arteriosus with combined administration of indomethacin and betamethasone in fetal rats. *Pediatr Res* 1989; 25: 69–75.
88. Nakazawa M, Ohno T, Miyagawa S, Takao A. Hemodynamic effects of acetylcholine in the chick embryo and differences from those in the rat embryo. *Teratology* 1989; 39: 555–561.
89. Kurosawa H, Imai Y, Fukuchi S, et al. Septation and Fontan repair of univentricular atrioventricular connection. *J Thorac Cardiovasc Surg* 1990; 99: 314–319.
90. Momma K, Takao A, Shibata T. Characteristics and natural history of abnormal atrial rhythms in left isomerism. *Am J Cardiol* 1990; 65: 231–236.
91. Momma K, Takao A. Transplacental cardiovascular effects of four popular analgesics in rats. *Am J Obstet Gynecol* 1990; 162: 1304–1310.
92. Momma K, Ando M, Takao A. Fetal cardiac morphology of tetralogy of Fallot with absent pulmonary valve. *Circulation* 1990; 82: 1343–1351.
93. Nakanishi T, Seguchi M, Tsuchiya T, Yasukouchi S, Takao A. Effect of acidosis on intracellular pH and calcium concentration in the newborn and adult rabbit myocardium. *Circ Res* 1990; 67: 111–123.
94. Nakazawa M, Aotsuka H, Imai Y, et al. Ventricular volume characteristics in double-inlet left ventricle before and after septation. *Circulation* 1990; 81: 1537–1543.
95. Seguchi M, Nakazawa M, Doi S, et al. Myocardial perfusion after aortic implantation for anomalous origin of the left coronary artery from the pulmonary artery. *Eur Heart J* 1990; 11: 213–218.
96. Momma K, Ando M, Takao A, Miyagawa-Tomita S. Fetal cardiovascular morphology of truncus arteriosus with or without truncal valve insufficiency in the rat. *Circulation* 1991; 83: 2094–2100.
97. Morishima M, Ando M, Takao A. Visceroatrial heterotaxy syndrome in the NOD mouse with special reference to atrial situs. *Teratology* 1991; 44: 91–100.
98. Nakazawa M, Katayama H, Imai Y, et al. A quantitative analysis of hemodynamic effects of the right ventricle included in the circulation of the Fontan procedure. *Circulation* 1991; 83: 822–826.
99. Imamura S, Kimura M, Hiratsuka E, Takao A, Matsuoka R. Effect of caffeine on expression of cardiac myosin heavy chain gene in adult hypothyroid and fetal rats. *Circ Res* 1992; 71: 1031–1038.
100. Miyagawa-Tomita S, Kitamoto T, Momma K, Takao A, Momoi T. Cellular retinoic acid binding protein type II was preferentially localized in medium and posterior parts of the progress zone of the chick limb bud. *Biochem Biophys Res Commun* 1992; 185: 217–223.

101. Mori K, Ando M, Satomi G, Nakazawa M, Momma K, Takao A. Imperforate tricuspid valve with dysplasia of the right ventricular myocardium/pulmonary valve and coronary artery: A clinicopathological study of nine cases. *Pediatr Cardiol* 1992; 13: 24–29.
102. Matsuoka R, Takao A, Kimura M, et al. Confirmation that the conotruncal anomaly face syndrome is associated with a deletion within 22q11.2. *Am J Med Genet* 1994; 53: 285–289.
103. Momma K, Kondo C, Ando M, Matsuoka R, Takao A. Tetralogy of fallot associated with chromosome 22q11 deletion. *Am J Cardiol* 1995; 76: 618–621.
104. Hirota H, Matsuoka R, Kimura M, et al. Molecular cytogenetic diagnosis of Williams syndrome. *Am J Med Genet* 1996; 64: 473–477.
105. Morishima M, Yasui H, Ando M, Nakazawa M, Takao A. Influence of genetic and maternal diabetes in the pathogenesis of viscerotrial heterotaxy in mice. *Teratology* 1996; 54: 183–190.
106. Matsuoka R, Kimura M, Scambler PJ, et al. Molecular and clinical study of 183 patients with conotruncal anomaly face syndrome. *Hum Genet* 1998; 103: 70–80.
107. Morishima M, Yasui H, Nakazawa M, et al. Situs variation and cardiovascular anomalies in the transgenic mouse insertional mutation inv. *Teratology* 1998; 57: 302–309.
108. Yamagishi H, Ishii C, Maeda J, et al. Phenotypic discordance in monozygotic twins with 22q11.2 deletion. *Am J Med Genet* 1998; 78: 319–321.
109. Furutani M, Trudeau MC, Hagiwara N, et al. Novel mechanism associated with an inherited cardiac arrhythmia: defective protein trafficking by the mutant HERG (G601S) potassium channel. *Circulation* 1999; 99: 2290–2294.
110. Matsuoka R, Furutani Y, Hayashi J, et al. A mitochondrial DNA mutation cosegregates with the pathophysiological U wave. *Biochem Biophys Res Commun* 1999; 257: 228–233.
111. Momma K, Matsuoka M, Takao A. Aortic arch anomalies associated with chromosome 22q11 deletion (CATCH 22). *Pediatr Cardiol* 1999; 20: 97–102.
112. Machida S, Noda S, Furutani Y, Takao A, Momma K, Matsuoka R. Complete sequence and characterization of chick ventricular myosin heavy chain in the developing atria. *Biochim Biophys Acta* 2000; 1490: 333–341.
113. Momma K, Takao A, Matsuoka R, et al. Tetralogy of Fallot associated with chromosome 22q11.2 deletion in adolescents and young adults. *Genet Med* 2001; 3: 56–60.
114. Kato T, Kosaka K, Kimura M, et al. Thrombocytopenia in patients with 22q11.2 deletion syndrome and its association with glycoprotein Ib-beta. *Genet Med* 2003; 5: 113–119.
115. Yagi H, Furutani Y, Hamada H, et al. Role of TBX1 in human del22q112 syndrome. *Lancet* 2003; 362: 1366–1373.
116. Hirayama-Yamada K, Kamisago M, Akimoto K, et al. Phenotypes with GATA4 or NKX2.5 mutations in familial atrial septal defect. *Am J Med Genet* 2005; 135A: 47–52.