The Report on Inoculated Tuberculosis Accidentally Caused by Typhoid Vaccin Injection. The Clinical Observation

Part II

Masashi TAMURA, M.D.*

From the Hyogo National Sanatorium (Chief: G. OGAWA, M.D.), Hyogo Prefecture, and the Division of Paediatrics (Chief: Prof. I. SAGAWA, M.D.), Tuberculosis Research Institute, Kyoto University, Japan.

(Received for publication June 11, 1955)

VI. Blood Sedimentation Rate

Table 6 indicates one-hour values of blood sedimentation tests on pupils with local lesions in Jan. 1947, 1948 and 1949, and on the other negative tuberculin reactors. According to the table, the values were higher in Jan. 1947 than in Jan. 1949 in case of the affected pupils. But this does not mean that the sedimentation rate on the pupils with local lesions was remarkably higher than that of the negative tuberculin reactors. Because in Jan. 1947 the affected pupils had incised wounds in their infection locals or infected wound after the extirpation of axillary lymph ncdes.

Sedi- men-		Persons with local lesions									Negative tuberculin		
tation	n	Jan., 1947			Jan., 1948			Jan., 1949			reactors		
Rate m.m.	boy	girl	total	boy	girl	total	boy	girl	total	boy	girl	total	
0 10	25	27	52 (55.3)	28	21	49 (53.4)	39	39	78 (86.6)	28	16	44 (48.8)	
11 20	10	14	24 (25.5)	4	11	15 (18.1)	3	3	6 (6.6)	7	22	29 (32.2)	
21 30	5	1	6 (6.3)	3	4	7 (8.4)	0	2	2 (2.2)	4	7	11 (12.2)	
31 40	2	2	4 (4.2)	2	3	5 (6.0)	1	2	3 (3.3)	0	3	3 (3.3)	
41	5	3	8 (8.4)	4	3	7 (8.4)	0	1	1 (1.1)	1	2	3 (3.3)	
no test	2	6	8	8	11	19	6	6	12	9	7	16	

Table 6. Blood Sedimentation Rate

() %

VII. X-Ray Photography of chest

Since Oct. 1946, X-ray photography of chest was held regularly every 3-4 months

*田村政司

on 101 pupils out of 102 pupils who all had local lesion. Pathological findings were observed in 20 pupils.

First of all, miliary tuberculosis case (Case 45) was found in Sept. 15, 1946, by Prof. Z. Ishikawa, of Surgical Division of the Hyogo Prefectural Medical College. Small light dots were seen in the 4 cases (No. 22, 32, 35, 31). But these shadows vanished about one month after at the earliest or six months at the latest. (Case No. 18, 27, 60). There were three cases that had ill-defined hazy shadows. These shadows were all in the middle or lower pulmonary field, but they were all transitory. There were two cases (Case No. 67, 11) that indicated round shadows in X-ray films.

The two cases had calcificated shadows (Case No. 58, 70). A well-defined shadow of the left hilar lymph node was seen in Case 2. Case 2 and Case 67 (appeared a round shadow in the right middle pulmonary field) were brother and sister, and their father was an open pulmonary tuberculosis. Shadow of pleurisy was observed in the 11 cases (Case No. 1, 2, 4, 11, 15, 18, 20, 32, 51, 54, 62).

Distinct exudation was seen in case 62 in Oct., 1946 and in Case 20 in Aug., 1947 (tubercle bacilli culture was positive from sputum in Jan., 1947). The all other cases revealed the picture of pleurisy without any subjective symptom. Except 2 cases, (Case 18 and Case 20) which combined tuberculosis of the bone and the joint, two third of pleurisy cases started six months after the injection.

X-ray photography of chests was done on 57 persons out of 59 who were negative reactors or did not receive tuberculin reaction test in 1944, and had no local lesion in 1946, but who became positive reactors afterwards in 1946. Of 57 cases, one was a patient of miliary tuberculosis (whose mother was an open pulmonary tuberculosis), 9 indicated calcification shadows, 3 fresh little infiltration shadows, and 5 pleurisy shadows. Nine pupils of them were residing here from their infancy and another 9 were new residents from town.

Out of 70 positive tuberculin reactors who had neither local lesion nor connection with the typhoid vaccin injection, X-ray photography of chest was made on 68 cases. There found 7 pupils with calcification shadows, 2 with fresh little infiltration shadows and one with pleurisy shadow.

X-ray photographs of chest were taken on 106 negative tuberculin reactors. Only one was found to have an ill-defined hazy shadow in the right lower area of lung, but 2 months later it disappeared. Cultivation of tubercle bacilli was negative. Others had no lesion at all.

VIII. Cultivation of tubercle bacilli from sputum.

Sputum or mucus of pharynx and larynx from 99 persons with local lesion was taken for cultivation of tubercle bacilli from Jan. to Feb. 1947, from Dec. 1947 to Jan. 1948, in Oct. 1948 and in Apr. 1949. Five cases were found to be positive.

The cultivations were held on Jan. 24, 1947 on case 20, on Jan. 30, 1947 and on

Dec. 18, 1947 on case 18, on Oct. 22, 1948 on case 67, on Apr. 2, 1949 on case 11 and Apr. 26, 1949 on case 53, and a colony of tubercle bacilli was proved from each case. For the case 18 and case 20, the cultivation tests were made several times after the above mentioned-dates, but were all negative. Pathological shadows were seen in X-ray pictures of chest little after the cultivation of tubercle bacilli turned positive.

Case 67. In spite of a pathological shadow found in Oct. 1946, sputum culture was twice proved negative.

Case 11. Pathological shadow of chest was found by X-ray when cultivation of tubercle bacilli turned positive.

Case 53. No abnormal shadow was observed by X-ray photography of chest till Jun. 1949.

In the above-mentioned 4 cases out of 20 cases which indicated pathological shadows in X-ray pictures of chest, tubercle bacilli were positive by culture, but the examination of sputum could not be held for the case 45 which showed remarkable changes. Cultivation was made on case 62 for the first time early in April, 1949 but was negative while other 14 cases were proved negative all the time.

IX. Cases considered to be reinfection.

The three cases out of 102 cases with local lesions were positive tuberculin reactors in 1944. (Cases 58, 64 and 78).

The above-mentioned 6 case were all positive tuberculin reactors in 1944, and from the X-ray exam of the pathological investigation of their lymph nodes. They were most likely to be the reinfection cases. Every one of them did not indicate any acute skinulcer which might correspond to Koch's phenomenon, but the swelling of their regional lymph nodes was noticed in them all.

X. Tuberculosis of the bone and the joint.

Most cases simply regional lymph nodar swelling along with local lesions, though, 20 of them had pathological changes in X-ray pictures of chest, 3 of them, however, showed lesions in bones and joints. These were case 18, 20 and 97.

After all, it is not clear whether or not the appearance of tuberculosis of bone and joint, in these three cases, had any connections with the extirpation of regional axillary lymph node, because in case 18 it was found before the extirpation, and in case 20 after the extirpation of nodes, while no extirpation was held in case 97.

Summary

The cutaneous inoculation tuberculosis was observed on 102 children. As the cause was not clear, they revealed primary tuberculous complex of skin, consisting of the skin lesion on the injection site and the changes of its regional axillary lymph nodes, in consequence of typhoid vaccine injection.

The injection was held by three operators, of which a female doctor was an open

Masashi TAMURA

pulmonary tuberculosis while the others were quite healthy. The affected pupils received the injection from anyone of these three operators. In addition, it seems that there was an equal chance of infection at the end injection as well as at the first. The quantity of the inoculated tuberculous bacilli was naturally unknown.

One hundred and two pupils indicated local lesion after the injection, and this number corresponded to 16.1% of the total pupil-number who received the injection there were, among these 102 pupils, some pupils who indicated the change of lymph nodes without skin lesion, or revealed the local change of skin about a year after the injection, or in whom the transitory subcutaneous inducation vanished spontaneously as the time passed by. There may have been some that did not reveal local lesion in spite of the simultaneous inoculation of tubercle bacilli at the time of typhoid vaccine injection, but it was very difficult to prove the case exactly.

Ninety six pupils had the local changes on the left side, while 6 on the right side. In one-third of the patients, the primary foci of skin were noticed a month after the supposed incculation, but there was one case whose induration was first found about a year after. The incised wound indicated a slight tendency to heal, so it needed one month at the earliest and several months at the latest to recover. Moreover, in some cases the induration or the abscess of the same place appeared again in spite of the former ciatricial healing. The primary foci seemed to be absorbed and disappear in two cases. Subcutaneous metastasis was found in 40 pupils, of which 6 cases showed the metastasis in the centrifugal path way lymph stream. In one case the metastasis appeared inside of the upper arm two years and two months after the typhoid vaccine injection in spite of that the local change had healed and that the axillary lymph nodes had been extirpated. One case showed spontaneous rupture of subcutaneous metastatic induration close to the primary focus 2 years and 4 months after the injection.

Swelling of axillary lymph nodes seemed to appear soon after the appearance of primary foci, but there was one case in which the nodular swelling preceded apparently to the primary changes. Most nodes consisted of one to several pieces, each being about the small-finger-tip size, but one case showed a infant-fist-sized swelling of nodes, forming a glandular mass of many pieces. Extirpation of nodes was held on 83 pupils, while on the other hand some cases indicated re-enlargement of nodes to the small-finger-tip or pea-size in spite of that the local lesion completed cicatricial healing and extirpation was once held upon the same place. Re-extirpated cases were 18 in number. Even two years after the typhoid vaccine injection, there was one case in which lymph nodes became suddenly palpable, while they had shrunk spontaneously before hand. In addition, 6 cases received incision or extirpation of their supra-clavicular nodes as they enlarged. In one of these cases, the swelling of supra-clavicular nodes appeared and was incised before that on axillary nodes.

Our 102 pupils were all positive tuberculin reactors, revealing apparent erythema and induration, and even double erythema or blister formation. Within 2 and half a year after the typhoid vaccine injection, no case that became anergic was found.

As to the result of blood sedimentation rate held in Jan. 1947, we could not pull a conclusion that there were many high-rate owners among the positive reactors in comparison with negative reactors.

By X-ray examination of chest morbid changes of lung were found in 20 cases, but the manifest subjective symptoms were only felt by one case of miliary tuberculosis of lung and two exudative pleurisy cases. Miliary tuberculosis was affirmed 4 months after the injection. Light dotted shadows were seen in apex and middle pulmonary field in 4 cases, mostly 5 or 6 months after. Ill-defined hazy shadows were seen with a year after the injection in three cases, mostly in the middle and lower area, but were transitory as the above-mentioned light dotted shadows. Round shadows were seen in two cases, calcification shadows in two and well-defined shadow of hilar lymph node. Shadow of pleurisy was observed in eleven cases. Excluding the cases combined with bone and joint tuberculosis, the changes appeared within 6 months after the typhoid vaccine injection in two-thirds of those eleven cases. In general, morbid shadows appeared mostly within 6 months after the typhoid vaccine injection and the appearance of them became less frequent with the run of time.

By cultivation of sputum, a colony of tubercle bacilli was observed in 5 cases, but soon disappeared as the culture was repeated again and again. Soon after the positive result of culture, morbid changes appeared in X-ray film of chest in two cases, but no change was found in one case.

The majority of the pupils who had local lesions were or primary infection, but there were 6 pupils who seemed to be or reinfection. But in any of both cases, acute skin ulcer corresponding to Koch's phenomenon was not seen at all, but swelling of regional lymph nodes was palpated. Muscular tuberculosis of the left upper arm was proved in one of the cases which hinted the reinfection.

Tuberculosis of bone and joint was found in three cases; a case of left first metatarsal tuberculosis, caries of the 9th and 10th dorsal spines and a case of cranial bone tuberculosis.

Among 102 pupils examined, one removed to the other school in Nov., 1946 without being known since afterwards and one died or high fever (without meningeal symptome) one the 3rd day from the extirpation held on a small-finger-tip sized axillary node, but the rest of the pupils were all healthy at present, so that no one died of apparent tuberculosis.

(P.S. The case with caries of the 9th and 10th dorsal spines complicated tuberculous meningitis afterwards and lied on Sep. 29, 1949.)

Acknowledgement

On concluding this report, I would like to exprese my hearty gratitude to the following people who helped me in various way in accomplishing this report: These people are Dr. G. Ogawa, Chief of the sanatorium, Prof. Dr. I. Sagawa of Kyoto University, Dr. T. Iwasaki of Tuberculosis Preventing Association, Prof. Dr. Y. Aoyagi, Prof. Dr. S. Ueda, Prof. Dr. E. Kondo, Asst. Prof. Dr. S. Amano, Kyoto Univ., under whose quidance and advice the report was completed, Dr. M. Tomita, Chief of Section of Medical Affairs in Kochi National Sanatorium, Dr. H. Imai, ex-chief of the medical section of Hyogo National Sanatorium, Dr. R. Sato new taking Dr. H. Imai's place and the personnels of the section who co-operated with me, the authority of the Dojo Primary School who gave me the opportunity of this medical observations, the Tuberculosis Preventing Association, Division of Survey of Prof. Dr. Z. Ishikawa of the Hyogo Prefectural Medical College, the Shunkaen National Sanatorium and two doctors at Dojo village, Dr. Y. Isayama, Dr. H. Kondo, who gave me very important data, and etc.

References

- 1) DENEKE; Dtsch. med. Wschr., 1890, S. 262.
- 2) Elsenberg; Berl. Kl. Wschr., 1886, S. 581.
- 3) HAMANO; At the 22nd meeting of Japanese Association for Tuberculosis, 1947.
- 4) HIKI; Kekkaku, V. 4, S. 282, 1926.
- 5) ISHIKAWA and NARUMI; At the 61st Sergical meeting in Kwansai area, 1947.
- 6) LEHMANN; Dtsch. med. Wschr., 1886, S. 144, 165, 182.
- 7) LINDEMANN; Dtsch. med. Wschr., 1883, S. 442.
- 8) MITANI; Arch. Jap. Chir., B. 13, S. 616, 1936.
- 9) NARABAYASHI; At the 18th meeting in the Association for Tuberculosis, 1948.
- 10) SHIRAISHI and KATAYAMA; At the 17th meeting in the Association for Tuberculosis, 1947.
- 11) SELTER; Dtsch. med. Wschr., Nr. 29, S. 1181, 1925.