

12. Other questions

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Q12-1: What did you learn from the examination of 76 thalidomide-impaired patients?

- **We found that some patients had block vertebrae while others had various structural abnormalities of the middle and inner ear. We are now able to diagnose high blood pressure in patients with upper limb defects, having fixed on a method of measuring blood pressure in these patients.**

In addition to the standard tests used in the one-day medical checkups, we aimed to investigate whether these patients had any previously unknown abnormalities of the internal organs, and to determine an accurate way of measuring blood pressure in those with missing or underdeveloped upper limbs. The three key results are presented below. Some of the specialist medical terminology and medical details may be difficult for the non-specialist to understand.

1) Block vertebrae were seen in 9.3% of patients, all of whom had upper limb defects

We examined the cervical vertebrae of 76 patients and found block vertebrae in 7 of them (9.3%). All seven had upper limb defects and none had hearing impairments. The vertebrae of the cervical spine (neck bones) are normally independent of each other, but in block vertebrae, some of these vertebrae have fused together (Fig. 1). This can occur as a result of injury or tuberculosis, but is thought to be a birth defect in thalidomide-impaired patients. The presence of block vertebrae is thought to restrict the range of neck motion, weaken muscle strength in both upper limbs and cause headache and neck pain. From the age of 30 onwards, it can also cause neurological symptoms due to cervical cord compression. We wondered if block vertebrae were responsible for the long-term deterioration in body movement that some thalidomide-impaired patients complain of. We, therefore, concluded that the cervical spine should be examined in checkups for thalidomide-impaired patients, even though this is not done for other patients.

Ten (13.1%) of the 76 patients had congenital absence of the gallbladder, and 4 of these had block vertebrae.

Fig. 1

2) We found a range of structural abnormalities of the middle and inner ear

When we examined hearing-impaired thalidomide patients for structural abnormalities of the middle and inner ear by head CT, we found various abnormalities, including hypoplasia of the auditory ossicles, hypoplasia of the semicircular canals and cystic changes in the vestibules. It is possible that inner ear abnormalities may be the cause of the dizziness of which some thalidomide-impaired patients complain.

3) We decided to measure blood pressure at the ankle in patients with upper limb defects

There was no established method for measuring blood pressure in patients with undeveloped upper limbs, which meant that these patients could not know their own blood pressure. Blood pressure is one of the basic pieces of information for understanding a patient's condition, and when performing endoscopy and surgery it is essential for the doctor to know the patient's blood pressure. Therefore, we measured blood pressure in both arms and both ankles, with the goals of:

1. Determining a method of measuring blood pressure that would be able to clearly identify patients with high blood pressure
2. Determining a method that could be used by patients diagnosed with high blood pressure to monitor their own blood pressure at home.

We concluded that the best method was to measure the pressure at the posterior tibial artery at the top of the ankle joint using an automatic blood pressure monitor.

Q12-2: How high does blood pressure measured at the ankle at home have to be for it to be considered hypertension?

- **Hypertension is very likely if systolic blood pressure reaches 145 mmHg**

Blood pressure measured at the hospital tends to be higher than when measured at home. The Japanese Society of Hypertension states that in middle aged people with no diabetes or cerebrovascular disorders, blood pressure measured at home is considered to be high if it is 135/85 mmHg or above, and normal if below 125/80 mmHg. Lower limb blood pressure appears slightly higher than upper limb blood pressure, and is highly likely to be hypertension if lower limb blood pressure is 145 mmHg or above, based on systolic pressure being $(135/0.88) - 8 = 145$ mmHg. Patients with this level of blood pressure should discuss the possibility of hypertension with their family doctor, showing them Chapter 6, 'Approaches to blood pressure measurement'. The criteria for assessing diastolic blood pressure have not yet been established.

Q12-3: Where is the posterior tibial artery located?

- **The posterior tibial artery is located behind the medial malleolus of the ankle (Fig. 2)**

Care should be taken, because if the cuff is wrapped so that the ring on the cuff is at the lateral malleolus, as shown in Figure 4, the measurement might not display or will be inaccurate.

Fig. 2



Figure 3 Correct wrapping of cuff



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Figure 4 Incorrect wrapping of cuff



Q12-4: How do you deal with the fact that blood pressure measured at the lower limbs can differ between left and right?

- **Hardening of the arteries seen in peripheral arterial disease causes poor blood circulation in the legs and can cause further medical problems. Patients concerned about this should consult their family doctor.**

People with diabetes and cardiovascular diseases are at risk of peripheral arterial disease, in which hardening of the arteries reduces blood circulation in the legs, potentially causing further medical problems. Blood pressure should ideally be measured in all four limbs, but this is not possible in people with undeveloped upper limbs. You should, therefore, discuss with your family doctor if you think there may be a difference in blood pressure in your left and right lower limbs.

After getting your family doctor to show section 6-5 of this Q&A to a doctor in the cardiology or cardiovascular surgery department, it may be possible to get your blood pressure measured using a device called a Doppler blood flow meter to measure systolic pressure at the dorsal artery of the foot (at the instep) and the posterior tibial artery, with a standard arm cuff wrapped around your ankle. Usually, the lower limb blood pressure is taken to be whichever is the higher value in these two arteries. This method shows whether there are actually any differences in blood pressure between left and right lower limbs. However, Doppler blood flow meters are only used in general clinics and specialist departments. If a Doppler meter is unavailable, it may be possible to measure systolic pressure using a stethoscope to listen to the pressure in the posterior tibial artery or dorsal artery of the foot, with an arm cuff wrapped around the ankle. However, sounds are sometime audible and sometime inaudible with a stethoscope when peripheral arterial disease is present. It is, therefore, not possible to rule out peripheral arterial disease simply by measuring blood pressure in the lower limbs with a stethoscope.

Because arterial hardening occurs throughout the body, hardening can be assessed using an ultrasound device to measure the amount of thickening of the carotid artery in the neck. This device can also be used to assess other blood vessels.

Q12-5: Have similar large-scale medical examinations and surveys been done in the United Kingdom and Germany?

- **Living conditions have been surveyed, but it appears that large-scale medical examinations have not been done. The results of surveys in the UK and Germany were provided to the Ishizue Foundation after being translated into Japanese, partly funded by**

a Grant-in-Aid for Research on Regulatory Science of Pharmaceuticals and Medical Devices from the Ministry of Health, Labour and Welfare, Japan.

- 1) Background and survey results from United Kingdom

<http://www.thalidomidetrust.org/SecureDocs/HealthGrantYear3FinalReport.pdf>

- 2) Background and survey results from Germany

http://www.contergan.de/671/files/20130125124745Contergan_Endbericht_final_20130108.pdf

Q12-6: Have other countries also compiled a detailed Q&A on health problems in thalidomide-impaired people?

- **Possibly, but we have not been able to find any.**

We investigated this on the assumption that thalidomide victims in other countries would have had similar problems, but we found no detailed Q&A collections relating to health problems in thalidomide-impaired people. However, the UK's Thalidomide Trust has a relevant website that also covers lipid metabolism abnormalities and blood pressure measurement. We have aimed to put together a detailed Q&A with reference to this website, and we hope that by translating this Q&A into English and German it will be useful to patients in other countries as well.

<http://www.thalidomidetrust.org/healthinfo>

Q12-7: When I go for medical appointments, the doctors say that they do not know about thalidomide-induced disabilities and ask me if there are any useful reference materials or articles. What should I say?

Please tell them about this Q&A.

Q12-8: Do thalidomide-impaired people have any particular health problems to be aware of?

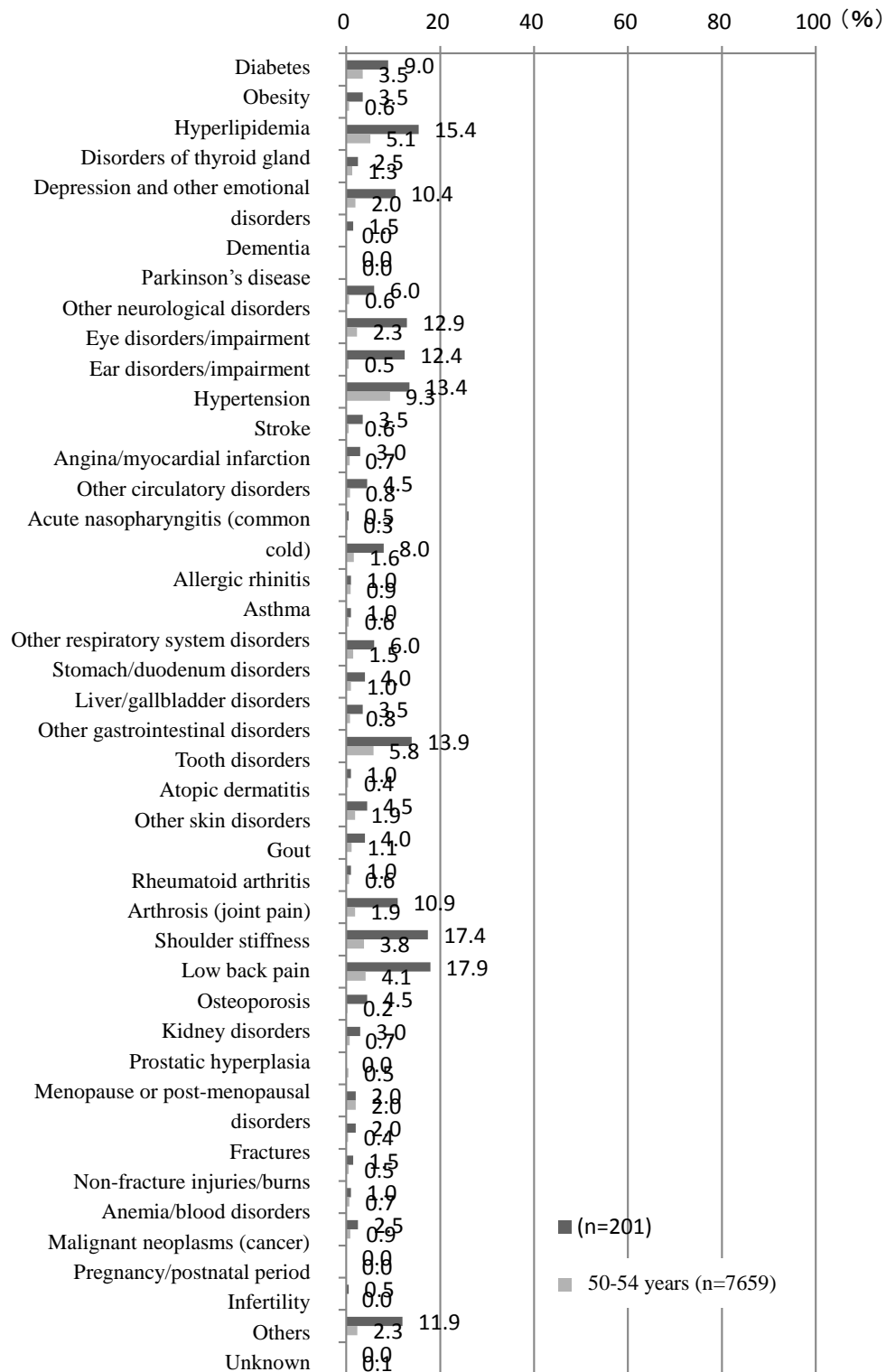
- **We strongly recommend that family doctors conduct regular checkups to determine whether patients have hyperlipidemia (dyslipidemia), hyperuricemia (high uric acid in blood) and diabetes.**
- **Our questionnaire survey found that the rates of diabetes, hyperlipidemia (dyslipidemia) and obesity in thalidomide-impaired people are 2 to 3 times greater than normal for their age group (Figure 5).**
- **Of the 76 patients who were examined, 41 (54%) had fatty liver and 17 (22%) had hyperuricemia.**

Although there are many aspects of disability-related pain and suffering that cannot be eliminated, future illness can be prevented. The questionnaire survey results showed that many patients have diabetes, hyperlipidemia (dyslipidemia) and obesity. Fig. 5 shows the results of a FY2012 questionnaire survey on the question of the kind of health problems for which the patient regularly visited a doctor.

The most common conditions overall were low back pain (27.7%) and shoulder stiffness (26.9%). The rate of hyperlipidemia (dyslipidemia) was also very high, at 23.8%. Rates of diabetes and hyperlipidemia (dyslipidemia) were 2 to 3 times higher than normal for their age group. Of the 76 people who participated in examinations over 3 years, 41 (54%) were diagnosed with fatty liver and 22% had hyperuricemia (serum uric acid >7.0 mg/dl).

There may also be a considerable number of people with hidden high blood pressure, since methods for measuring blood pressure in those with upper limb defects have not yet been established. Hyperlipidemia (dyslipidemia) and diabetes are diseases that are diagnosed from blood samples. We strongly recommend that family doctors conduct regular checkups to determine whether patients have hyperlipidemia (dyslipidemia) and/or diabetes.

Fig. 5: Health problems necessitating outpatient treatment: Comparison of normal patients in their 50s and thalidomide-impaired patients (multiple responses)



Q12-9: Is the ideal body weight for people with undeveloped upper limbs equivalent to that in the general population? How do I know whether or not I am obese?

- **People with undeveloped upper limbs should not be thought of in terms of ideal body weight. It is important to measure the waist circumference as well as body weight.**

Stricter criteria should probably be applied to those without upper limbs than for the general population. This means that a body mass index (BMI) of 25 or above is a reliable indicator of obesity. However, there is no obvious answer to the question of ideal body weight in those with missing or underdeveloped upper limbs, since the extent of underdevelopment varies. Therefore, rather than asking whether a person with undeveloped upper limbs is ‘obese’, it is probably better to ask whether they have ‘metabolic syndrome’, as this can be diagnosed even if body weight is uncertain. A waist circumference of 85 cm or more for men and 90 cm or more for women is in itself a warning sign. In the recent checkups, 17 (24%) of the 66 people whose waists were measured exceeded these thresholds.

BMI is calculated as body weight (Kg) divided by height (m) squared, and in Japan obesity is defined as a BMI of 25 or above. It is recommended that patients with this level of BMI go on a diet regardless of whether or not they have upper limb defects.

It is a little known fact that the Japanese medical community distinguishes between ‘obesity’, ‘pathological obesity’ and ‘metabolic syndrome’. A person with a BMI over 25 is considered ‘obese’, but they qualify as pathologically obese if then diagnosed with central obesity (also known as abdominal obesity or visceral obesity) based on an abdominal CT scan. People with a BMI of 25 or above are also considered pathologically obese if they have one or more of the following: diabetes, dyslipidemia, high blood pressure, fatty liver or low back pain.

The FY2012 questionnaire survey found that many respondents were troubled by low back pain, so a BMI of 25 would be sufficient to qualify those people as ‘pathologically obese’. In simple terms, ‘pathological obesity’ is ‘obesity’ accompanied by an illness requiring treatment.

<http://www.mhlw.go.jp/topics/bukyoku/kenkou/seikatu/himan/inspection.html>

In contrast, ‘metabolic syndrome’ is a set of criteria established to help predict and prevent arterial hardening. A waist circumference of 85 cm or above for men and 90 cm or above for women corresponds to 100 cm³ or over of visceral (abdominal) fat, and if this is accompanied by any two of

high blood sugar, abnormal lipid (fat) metabolism and high blood pressure, then a diagnosis of 'metabolic syndrome' is made. This is unrelated to BMI. People with undeveloped upper limbs who have the waist circumference given above are strongly urged to get examined for abnormally high blood sugar and lipid levels, even if they have a BMI below 25.

Rather than asking whether they are obese, thalidomide-impaired patients, particularly those with undeveloped upper limbs, should therefore think in terms of whether they have metabolic syndrome, which can be diagnosed even if body weight is uncertain. This means that measuring your waist circumference is very important. You can measure your waist with the help of this site.

<http://www.mhlw.go.jp/bunya/kenkou/metabo02/kiso/check/>

Q12-10: Are people with undeveloped or underdeveloped upper limbs susceptible to gaining weight?

- **This is probably true, because such people have low muscle mass and, therefore, consume relatively little energy.**

It appears that many people with upper limb defects do not exercise regularly. Also, people with undeveloped upper limbs have less muscle mass than the general population, and hence, are thought to burn up less energy.

In general, energy intake (kcal) = ideal body weight × amount of physical activity

- Ideal body weight (kg) = height (m) × height (m) × 22
- Amount of physical activity:

Light activity (e.g. desk work) 25–30 kcal × ideal body weight

Moderate activity (e.g. standing work) 30–35 kcal × ideal body weight

If the above formula is applied to someone 155 cm tall who does desk work, then the person's energy intake should be = $1.55 \times 1.55 \times 22 \times 30 = 1585$ kcal, for which 1600 kcal is obviously sufficient. People with undeveloped upper limbs have less muscle mass and are, therefore, thought to burn up less energy than the general population. So somebody with undeveloped upper limbs who is

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155 cm tall is likely to become obese if they consume 1600 kcal or more a day. Such people might well feel that they put on weight easily despite not eating very much.

Q12-11: I worry about having my blood taken because it is always difficult. Are there any leaflets or information I can show the nurses when they take my blood?

Please show 'Source document 1: Techniques for taking blood from thalidomide-impaired patients' to the person in charge of taking your blood beforehand.