

Current Status of Semen Quality in Japan

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We have just heard Dr. Jørgensen reported on the study conducted in Europe. We have participated in this study from Japan since 1997. I would like to report on a study involving two groups: fertile men and healthy male college students as young men.

There is very little information on the sperm of Japanese men. A survey of young males of the Sapporo Medical University group was the only reported study with a large sample size that was conducted to observe changes in sperm quality over time. In this study, sperm concentration data from 1975 to 1980 was compared with recent data obtained in 1998. The method of recruiting subjects for the study has varied somewhat over the 20-year period, but because the average age was 24.2 years and because the study was conducted at the same laboratory, we felt that it may be valid for comparison. Twenty years ago, the sperm concentration was about 70 million per milliliter. In 1998, it was 79.6 million, so no decrease in sperm concentration of young men in the Sapporo area has been observed.

For our study of fertile men, we send all data to the Department of Growth and Reproduction, Copenhagen University Hospital (Rigshospitalet) for analysis that Dr. Jørgensen mentioned a little while ago.

Quality control was of course carried out for our semen study in order to standardize the technology. During the time the study was conducted, we received 5 specimens for the quality control from Copenhagen that were measured by our technicians, and then sent back to Copenhagen. Thus external quality control is being carried out. When comparing results of studies conducted in various countries or regions, it is important to remember that data must be integrated.

As for the inclusion criteria of the study, the subjects must be 20 to 44 years of age, and the man and his mother must be born in Japan. As for the examination of the man, semen analysis and sampling of blood must take place between the 16th week of gestation and delivery of his wife. The current pregnancy must have been achieved by normal sexual relations without any kind of treatment for infertility. As has already been mentioned by Dr. Jørgensen concerning the data from Europe, this graph including data for Kawasaki and Yokohama is the raw data and has not yet done the necessary corrections, so I would like to mention it in advance. The average age of the subjects for all countries was 30 to 32. Characteristic of the study was the fact that the abstinence period for Japan was longer than for the other countries.

Next, to see whether there is any regional difference in sperm concentration in Japan, the study was conducted in Sapporo, Osaka, Kanazawa and Fukuoka (4 cities) using the same protocol. If you compare with the data of Kawasaki/Yokohama (209 hrs.), the abstinence period is somewhat shorter for Osaka (157 hrs.) and a little bit longer for Kanazawa (227 hrs.). Of the 5 cities, sperm concentration is lowest for Osaka (96.8 million) and highest for Fukuoka (125 million). So I think perhaps there may be no regional difference in Japan.

Two weeks ago, data were reported for 4 cities in the USA by Dr. Swan, who has played a central role in the US group of epidemiological studies on the semen quality. The US study was also conducted by protocol that conforms to international cooperative research, so we can compare this data with ours. The average age for California was 29.8, 36.1 for New York. New York was a little higher than for the other areas. As you see here, they could only get 39 cases in New York during the same study period. I heard they really had to struggle to get them.

Sperm concentration for Missouri was 58.7 million/ml, which is lower than the 77 million/ml for Copenhagen mentioned a little while ago. Dr. Jørgensen mentioned Fish's data a little while ago. New York was the highest in the data of Dr. Swan, and I believe was followed by Minnesota California in that order. It was reconfirmed that there is a regional difference within USA.

Dr. Swan questioned the reason why sperm concentration is low in Missouri in his paper. There is a lot of farmland in this area. I think. It is surmised that the fact there is a lot of farmland may be connected to the lowness of the sperm concentration. On the other hand, I hear there is not much farmland in Copenhagen where sperm concentration is also low, so we must consider many factors as to what the cause is.

Next is the study of young men in terms of reproductive function. Subjects of 4 countries of northern Europe mentioned a little while ago decided if they wanted to participate the study at the end of their military service examination. I would like to speak about criteria at the beginning. Thinking it would be better to select uniform subjects between 18 and 22 years of age, we made it a prerequisite that the subjects had to be university students. The rest of the survey items were identical to those for fertile men, for example, of course, the specimen and his mother had to be born in Japan.

We compared our study of young men with similar studies conducted in Europe. As I said earlier, the subjects differed from each other, so we should think that there was probably bias. The average age in the Kawasaki area was 20 years of age, whereas it was 2 years younger (17 to 19) in Europe. The abstinence period was more or less the same for young men in all countries. Although I have said this over and over, the data given in the slide is raw – there have been no revisions among the data of 4 countries of northern Europe. You might have noticed, but there were 57 million/ml for Denmark. With the values for all conditions, as Dr. Jørgensen mentioned little while ago, there were 41 million/ml for Denmark and Norway, and the figures are clearly different from Estonia and Finland (57 and 54 million/ml).

When you compare the data of the various countries as you see here, quoting the figures from the paper as they are, and plug them into a graph like this, the data could be grossly misinterpreted as you see here in the slide. At around 70 million, the Japanese data more or less resembles the 2 countries of Europe, and is about 43% lower than for fertile men.

This graph represents the Japanese data. It shows sperm concentration distribution of young men and men with a pregnant partner. The peak with young men is about 40 to 60 million/ml; this appears to be like such a shape. In the case of fertile men, it is more wide-ranging. Here we see the abstinence period differs largely, but we cannot explain such a difference merely by the difference in abstinence period.

Some reports have mentioned seasonal variation in sperm concentration, while some have mentioned there is no seasonal variation. We conducted a study of 334 young men with the same sample size for all seasons throughout one year. This slide shows seasonal variation in sperm concentration.

As you see here, the data shows that sperm concentration was highest in spring. As for evaluation of the spermatogenesis on the other hand, a marker called inhibin B secreted by the Sertoli cell, is known as an index for spermatogenesis. Sperm count and the inhibin B level have a correlation, albeit slight. From what we have seen, the data for inhibin B doesn't change very much for spring, summer, autumn and winter. Inhibin B secretion however varies during the day just like other hormones. So appropriate collections are probably needed for this data as well.

What I am talking about now is that we divided 334 cases of the young men into spring, summer, autumn and winter. Intra-individual variation was analyzed for 72 cases which was recruited from the 334 cases by examining 4 times a year in every four season. As the mean

concentrations are shown on left side of this slide, you can see spring is significantly higher than any of the other seasons. Here is the data for which season the highest value of sperm concentration were obtained for the individual young men. Sperm concentration is high in spring for approximately 45%, showing a significant difference with other seasons. A little while ago Dr. Jørgensen presented data that shows sperm concentration to be high in winter and low in summer. That data disagrees somewhat with the Japanese data. Is the data showing that sperm concentration is high in the spring reproducible? Studies of young men are now being conducted in 5 cities in Japan including ours, and whether results can be reproduced and whether they can be observed in all regions are coming out in the studies.

To summarize, as far as we know from the raw data, we found sperm concentration of fertile men of Kawasaki/Yokohama to be approximately the same levels as that of men from Finland, Minnesota, and New York, and somewhat higher than that of men from Copenhagen, Missouri and California. We also found sperm concentration of young men of Kawasaki to be approximately the same as that of men from Finland and Estonia and we found it to be quite low for Norway and Denmark. We also found young men to be 30 to 40% lower than fertile men.

Further study will be required to determine if the cause for this is genetic or environmental difference or both. I would like to mention that this study was conducted with the help of many collaborators.

Q&A

Toppari: Thank you, Prof. Iwamoto. Now we have time for a couple of questions, please.

Toyama: I'm Toyama from the National Institute for Environmental Studies. I have two questions.

One is, you said that the Japanese data and European data had not been corrected and requires revision. If not so, you couldn't make a simple comparison. Could you tell us a little more about the parameters for revision?

My second question is, if I remember correctly, for the data on seasonal variation we saw in one of the slides near the end of your presentation, sperm density was 65 to 85 million. I think this is high compared to other data.

Iwamoto: Do you mean for fertile men?

Toyama: Yes. Is that right?

Iwamoto: Yes, I think so.

Toyama: OK. Could you answer my first question?

Iwamoto: The first question depends on the factors of collection. First there is external quality control. If data obtained by Japanese technicians are generally high, then we can collect simply by making this low. If there is a time trend, it is quite difficult to interpret, so analysis takes a long time.

Besides this external quality control, we have recorded age, abstention period and time after ejaculation for semen analysis. All of those things are conducted according to the same standard.

Toyama: How different are the factors such as difference in technicians or from country to country? Could you present approximate figures?

Iwamoto: I don't yet know accurate...

Could you answer, Niels, to this question?

Jørgensen: Yes, maybe I can. The data you showed also were compared with the European data of the young men. It was the raw data from these Nordic-Baltic countries, and data I presented were the corrected ones. What we had to correct for is, as you said, the confounders and that is for the concentration it shows up to be the abstinence period.

Then we have to correct for the laboratory difference, because even though we always do it exactly the same way in our laboratories, it turns out that we do not agree, so we have to correct for that.

In all of these European studies we have undertaken, that is both for the fertile men and for the young men, it appears that abstinence is actually the most crucial one to take into account. With a very low abstinence period this sperm concentration is declining; it is very low.

The WHO recommends that men should have at least a 2-day that means 48 hours, abstinence period. In these cross sectional studies, when we analyzed for the abstinence period, it appears that the concentration will be increasing steadily up to 96 hours. We had to correct for that, and we report, and in our analysis we have corrected in the regression analysis as if the men had an abstinence period of 96 hours.

For motility it is also very crucial to take into account how long it took from the ejaculation until the assessment was done, because the time this semen sample was standing on the table, it degraded the motility. So that should be taken into account. But we have found the same influence in all the centers we have examined. I have not been involved with the Japanese, but in these Nordic-Baltic countries.

Iwamoto: OK, a short question, please.

Q: Yes, it is a short question, I guess. It has to do with the abstinence period. Actually that question came to my mind only during the second

presentation, but it holds true for the first presentation as well.

What I was wondering was the following: it seems to be very clear that there is a strong correlation between the abstinence period and the semen quality in general, which is confirmed in many animal tests, especially in rabbits where that is confirmed as well. In addition to the abstention time also the ejaculation frequency seems to be very important.

I do not know whether the questionnaire, in this respect, has questions related to that matter. I ask that because I know from totally different surveys, surveys from sexologists and from psychologists that especially men tend not to answer the questions honestly. With that in mind, I think of especially the younger generation there was one figure of the previous speaker about young men of 19 years old that had such a low quality, it is also known that men in that age have usually a masturbation habit that can very strongly affect the outcome of the data.

I know that questionnaires can be developed to sort of fool the person that has to answer the question to make sure that the answers that you get are true answers. Maybe this speaker or the previous speaker could elaborate a little bit on that.

Jørgensen: First of all, I think we have heard this

question before about the frequency of how often they ejaculate, but I have not seen any solid data presented that this frequency should really be important, but we are currently taking a study in Copenhagen where we try to focus on that.

We are just a little into that, but it appears that it does not play any real role as long as the men have a proper abstinence period. How frequently he ejaculated before that, it does not matter very much.

Also, we should remember that these young men from these 4 countries, they are more or less the same. If you say they have more frequent ejaculation than older men, it may be the same in all countries, but we have not asked for that, how often do you usually. But we asked for it last time.

Q: I think there could also be a very big cultural difference in that as well. The only data, and now I go back to my early years when it did some scientific work myself 20-25 years ago, I had done studies in rabbits for instance where not only the abstinence time, but the frequency before the abstinence time very strongly contributed to the quality of the semen.

Iwamoto: Thank you very much. I am sorry but time is over, so we will move on to the next speaker.