Dr. Oguchi: Thank you very much, Dr. de Jong. It was a very interesting and instructive lecture. Dr. de Jong discussed the Rotterdam Study on AMD (age-related macular disease). I am surprised that the No. 1 factor in blindness among Caucasians is AMD, and that diseases differ from race to race. Now I would like to invite questions and comments from the audience.

Dr. Osamu Katsumi (Tokyo): Thank you, Professor de Jong. I have two questions. One regards the incidence. Does it differ according to locations, i.e. does it matter whether you live in Rotterdam or in Florida? Are there any differences in qualities of sunlight? Also, I was very surprised to see the results of hyperopia as a risk factor. What if myopia is more like 6 dpt?

Dr. de Jong: Your first question was if the incidence in Caucasians differs. We compared our data with those from the Beaver Dam Study in the USA and with the Blue Mountain Study in Australia. Incidences were slightly lower in the Rotterdam Study on AMD (age-related macular disease). I am surprised that the No. 1 factor in blindness among Caucasians is AMD, and that diseases differ from race to race. Now I would like to invite questions and comments from the audience.

Dr. Osamu Katsumi (Tokyo): Thank you, Professor de Jong. I have two questions. One regards the incidence. Does it differ according to locations, i.e. does it matter whether you live in Rotterdam or in Florida? Are there any differences in qualities of sunlight? Also, I was very surprised to see the results of hyperopia as a risk factor. What if myopia is more like 6 dpt?

Dr. de Jong: Your first question was if the incidence in Caucasians differs. We compared our data with those from the Beaver Dam Study in the USA and with the Blue Mountain Study in Australia. Incidences were slightly lower in the Rotterdam Study, but it was not a big difference. We also had a slightly lower prevalence in Rotterdam. This might be either due to small differences in examination techniques or to environmental factors. At this moment we are analyzing the data from the EUREYE Study. This study examines about 4,000 respondents from 8 different countries in Europe from Norway to Greece. Generally speaking, AMD prevalence data seem the same all over Europe. I cannot give definite figures yet, but we think that there is not really a big difference there despite differences in light exposure.

As to your questions about myopia... Myopia is of course a problem while defining AMD for two reasons. If we have a neovascular disciform reaction in the macular area of a –8 or –10 dpt myopic eye, we are not sure if that is due to myopic Fuchs degeneration or due to AMD. In general, we say we need to see drusen before we call it AMD. AMD is a diagnosis by exclusion. So when you have an aspecific scar in the macular area without clear drusen, we can neither rule out AMD nor for example juvenile macular degeneration or presumed ocular histoplasmosis. Myopic fundi, at least in Caucasians, are less pigmented than hyperopic eyes, especially when you have a large field of choroidal atrophy and white myopic degenerations. You cannot see the drusen very well anymore. This may make it more difficult to detect drusen. Each diopter shift towards hyperopia gave a 6% higher rate of AMD. So, we think it is not due to confounding factors or to missing a few correct diagnoses. Asians have more myopia than Caucasians with its known complications, but a good thing seems to be that this leads to less AMD.

Dr. Oguchi: Dr. Katsumi asked two questions. The first question was if there is any relationship between AMD incidence and location. Dr. de Jong related that he took part in prevalence studies in 8 locations in Europe, but there was no obvious difference in prevalence among locations. The second was about hypermetropia. Honestly speaking, it is a first time for me to hear that a higher level of hypermetropia causes more AMD. As there are more
farsighted people in Europe than in Japan, there may be more AMD cases in Europe than in Japan. More questions from the audience?

**Dr. Yutaka Imamura (Keio University):** Thank you very much for your wonderful lecture. In Japan, more males, 3 times more males than females, are likely to show AMD development while the data from Dr. de Jong show more females with prevalent AMD. Would you explain this, please? I guess that more Japanese males than females smoke.

**Dr. de Jong:** My first remark regards how you found out that Japanese males have more AMD than females. Are these clinic-based data or population-based data? If you are talking about clinic-based data, they can be confounding because, for example, perhaps the male goes to the doctor earlier than the female or the other way around. I am not sure if it is common in Japan, but I know that in parts of China or in India the male is considered more important than the female, so they send boys to the doctor earlier than girls. So this may lead to bias. Before we accept that males have triple the AMD rate, I would like to know exactly where you got the data from. I must say, however, that in the pooled data from the Beaver Dam, Blue Mountains and Rotterdam Studies there was no longer any difference in AMD prevalence between males and females.

**Dr. Imamura:** Thank you. How about smokers in Holland? Are males more likely to smoke than females?

**Dr. de Jong:** It seems there are more smokers in Japan than in Holland. So is there here a gene protecting against smoking effects?

Holland has another problem. Older males smoke less. Females smoke more and more. So, we see a rising incidence of lung cancer in women. Our main concern is that the highschool population smokes a lot. It is so difficult to teach these youngsters not to smoke. I have no exact data why people start smoking, but I know the bad side effects that in parts of China or in India the male is considered more important than the female, so they send boys to the doctor earlier than girls. So this may lead to bias. Before we accept that males have triple the AMD rate, I would like to know exactly where you got the data from. I must say, however, that in the pooled data from the Beaver Dam, Blue Mountains and Rotterdam Studies there was no longer any difference in AMD prevalence between males and females.

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**Dr. Yoshiko Matsuhashi (Nagoya City):** I would like to ask you one more question. Which causes the higher percentage of AMD, hyperopia, myopia or presbyopia?

**Dr. de Jong:** Hyperopia is a much higher risk factor than myopia. In all our age strata, myopia was protective against AMD. I am not aware of any report on the association between presbyopia and AMD after correcting for age.

**Dr. Oguchi:** Thank you very much, Dr. de Jong.
Dr. Kuwayama: So the answer to the first question is ‘yes’, right? My second question is that if we find drusen in a patient, should we always recommend good nutrition?

Dr. de Jong: With regard to the AREDS Study with nutritional supplements I am convinced after seeing our data on antioxidant intake in the diet that a well-balanced diet with vitamin C and E, β-carotene and zinc protects against AMD. I think that would be a good suggestion. People having a diet with above median antioxidant intake in the Rotterdam Study had less AMD. So if I have a patient with stage 2 AMD or higher, I recommend taking antioxidants, but not in such high doses as in the AREDS Study, 5 times more than the recommended daily dose. I would like everyone with large drusen to change dietary habits and eat more green vegetables. Also zinc seems especially important. I'm not sure if rice contains much zinc, but fish, poultry, meat, dairy products and brown bread do. So I would recommend taking them.

Dr. Yozo Miyake (Nagoya University): Let me ask an additional question. I noticed the report of a very large-scale supplementation study in the archives dating back a few years ago. In the Rotterdam Study 99% were of Caucasian origin. I am not quite sure if African Americans have the same prevalence of early AMD, but they have less late-stage AMD (stage 4). I do not know of any studies comparing dietary intake or other lifestyle factors. I know for example that in a study, African blacks and Aborigines in Australia had less AMD. But I cannot compare the lifestyles or even the evidence for the higher frequency of polypoidal disease in blacks than in Caucasians. Do they present more with AMD associated with PCV?

Dr. de Jong: We can only correctly diagnose polypoidal disease when you have angiograms and preferably indocyanine green ones. In the Rotterdam Study, we made no angiograms, and thus it is hard to identify PCV. We can only guess from color fundus photographs for evidence of PCV. As far as I hear from incidental clinic-based reports, PCV is much more common in Japan than in Europe. I would very much like to see fundus pictures made in Japanese epidemiological AMD studies to compare them with ours.

Dr. Negi: The population in the Rotterdam Study included a substantial number of black people. I think the prevalence among black people may be somewhat lower than the prevalence in our data. I think their lifestyle is similar to the western style. Do the initial diagnostic findings of AMD in black people resemble those seen in Caucasians, or do they present more with AMD associated with PCV?

Dr. de Jong: I am not quite sure if African Americans have more PCV than whites. I think that African Americans have the same prevalence of early AMD, but they have less late-stage AMD (stage 4). I do not know of any studies comparing dietary intake or other lifestyle factors. I know for example that in a study, African blacks and Aborigines in Australia had less AMD. But I cannot compare the lifestyles or even the evidence for the higher frequency of polypoidal disease in blacks than in Caucasians. By the way, in the Rotterdam Study 99% were of Caucasian origin.

Dr. Negi: Thank you very much. Regarding epidemiological studies, Japanese researchers have recently concluded a study on glaucoma and obtained very accurate data for the first time in Japan. The results were considerably different from those of western studies. As we understand from this experience, epidemiological studies are important as the bases for a scientific approach. Thank you very much again, Dr. de Jong.