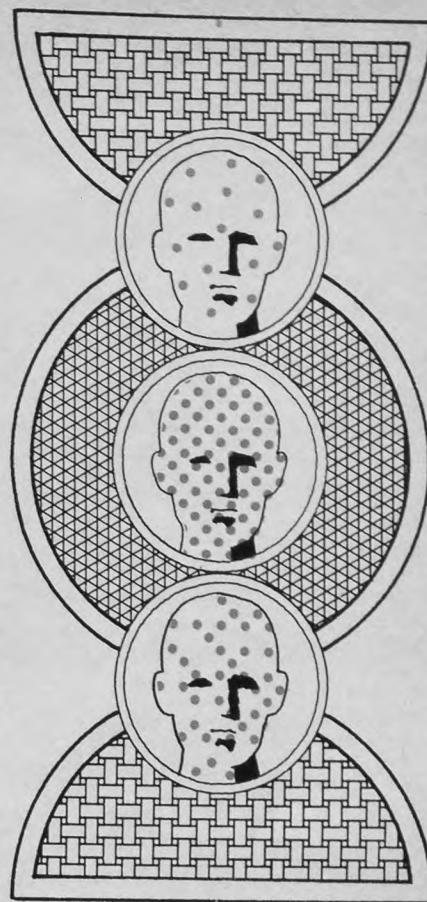


# Serum Immunoglobulin Levels in Healthy Adults of Various Ethnic Groups in a Rural Family Practice in Israel

Yair Yodfat, MD, Lea Keren, and Avinoam Zlotnick, MD  
Jerusalem, Israel



A study on the immunoglobulin levels of five ethnic groups in a rural population in Israel was carried out. The ethnic groups comprised Yemenite, Cochin, Kurd, North African, and Ashkenazi Jews. Yemenites have a low level of IgA, Ashkenazis have a high IgM level, Cochins and North Africans have high levels of IgG and IgA, and Kurds show low IgM levels. Females have higher IgM levels than males. No positive correlation between immunoglobulin levels and age could be demonstrated. A connection between these levels and exogenous and endogenous factors in the various ethnic groups is discussed.

## The Study Populations

The survey comprised 621 healthy individuals, all aged above 18 years, randomly selected from four villages and one kibbutz (collective settlement) in a rural area near Jerusalem. The inhabitants of the villages are of pure ethnic origin; they are Yemenites, Cochins from southwest India, Kurds from a mountainous region of northern Iraq, and Moroccans from North Africa. Ashkenazi Jews, either born in Israel or immigrants from South Africa, make up the population of the kibbutz. The four villages were all established by immigrants who came in the early 1950s, soon after the establishment of the State of Israel in 1948. According to household interviews, including grading of income and education, the villages are of a similar middle socioeconomic class.

Although the inhabitants of the four villages have different backgrounds, they have lived and labored under very similar conditions for many years. Customs and cultural heritage

have kept these villages distinct and internally homogeneous. The villagers are mostly poultry farmers and fruit growers. The mainstay of their diet is poultry, vegetables, bread, and rice. In the kibbutz, the population lives under equal material conditions in an economy largely based on agriculture. The villages and the kibbutz receive similar health care by the "Shimshon" Family Medical Center affiliated with the Department of Medicine A of the Hadassah University Hospital and Medical School, Jerusalem. A detailed description of the operation of this health center has been published elsewhere.<sup>2</sup> The entire population under the care of the center was screened by household interviews, extraction of past histories, and general medical examinations including urinalysis, erythrocyte sedimentation rate, blood count, and 16 biochemical determinants including glucose, urea, total protein, albumin, globulin, bilirubin, cholesterol, alkaline phosphatase, SGOT, sodium chlo-

Surveys carried out in different countries have shown a wide variation in the range of the immunoglobulin levels in normal adults.<sup>1</sup> Most of these studies were done on a limited number of individuals without taking into account the effect of age, sex, and race on these values. In our routine examinations of serum immunoglobulin levels we, too, were impressed by the wide range of these levels in healthy individuals. Since the population of Israel is not homogeneous and comprises many ethnic groups, we decided to study the serum immunoglobulin levels in five ethnic groups, each group consisting of not less than 100 individuals of both sexes.

From the Shimshon Family Medical Center, Kupat Holim Bet Shemesh and the Research Laboratory of Autoimmune Diseases, Department of Medicine A, Hadassah University Hospital and the Hebrew University-Hadassah Medical School, Jerusalem, Israel. Requests for reprints should be addressed to Dr. Yair Yodfat, the Shimshon Family Medical Center, Bet Shemesh, Israel.

Table 1. Comparison of sex and ethnic group differences in serum IgG concentration

Ethnic group	Male					Female				
	No. of subjects	Mean* (mg/100ml)	S.D. (mg/100ml)	Range (mg/100ml)	Mean* IU	No. of subjects	Mean* (mg/100ml)	S.D. (mg/100ml)	Range (mg/100ml)	Mean* IU
Ashkenazi	66	1,002	376	600-2,275	95	67	1,079	217	650-1,600	109
Kurd	54	1,239	318	675-1,600	129	70	1,066	322	500-2,100	103
Yemenite	70	1,103	474	700-1,875	107	64	1,105	380	625-2,000	107
Cochin	54	1,130	328	550-1,825	109	58	1,422	422	500-2,425	138
North African	60	1,230	450	650-2,500	118	58	1,231	438	760-2,175	118

\*Age adjusted

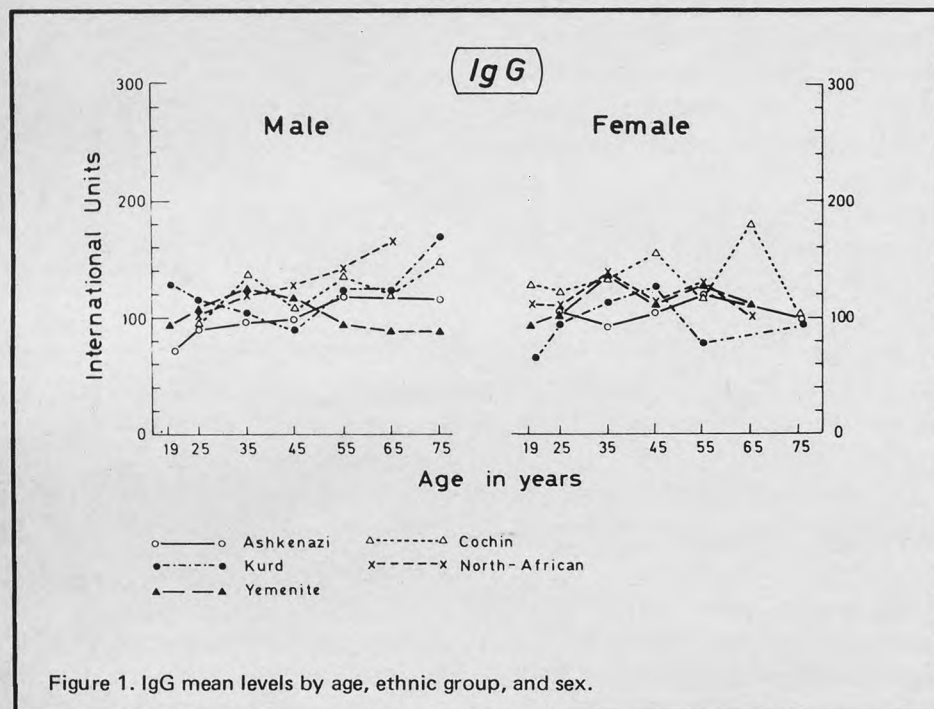


Figure 1. IgG mean levels by age, ethnic group, and sex.

ride, potassium,  $\text{HCO}_3^-$ , calcium, phosphorus, and uric acid.

**Methods**

Blood samples were obtained by venepuncture and stored at  $-20\text{ C}$  for up to four weeks until examined. (These tests were carried out during the summer of 1973.) Immunoglobulin levels were determined by single radial immunodiffusion technique<sup>3,4</sup> with a commercial reference standard (Behringwerke AG) and the World Health Organization standard 67/69.<sup>5</sup> Duplicate estimates indicated that the error of the technique was  $\pm 10$  percent. Immunoglobulin levels were expressed in mg/100 ml and in inter-

national units (IU). Statistical methods used were: multiple comparisons with Scheffe's method based on a three-way analysis of variance with factors (sex, age group, country of origin) and allowing for interactions between age and sex and between sex and country of origin. (Other interactions could not be allowed for because of missing cells.) The majority of the cells included 10 to 15 individuals. The significance level was 0.05 throughout. (Although the underlying distributions were asymmetric, the departure from normality was not so extreme as to invalidate the use of analysis of variance.) Immunoglobulin levels were age-adjusted to age distribution of the Jewish population in Israel.

**Results**

The mean serum IgG, IgA, and IgM levels for the entire population were  $1157 \pm 378$  mg/100 ml ( $111 \pm 36$  IU),  $224 \pm 96$  mg/100 ml ( $111 \pm 48$  IU) and  $134 \pm 52$  mg/100 ml ( $157 \pm 61$  IU), respectively.

**Immunoglobulin G.** Table 1 shows the mean IgG levels of both sexes in the five ethnic groups. No significant difference was found between IgG levels and sex. Both Cochins and North Africans have significantly higher mean levels of IgG than Kurds, Yemenites, and Ashkenazis. No age effect was found with IgG mean levels. Only mean levels in the age group of 70 to 80 years were found to be significantly higher than those found in the age group of 20 to 30 years (Figure 1).

**Immunoglobulin A.** The mean IgA levels are shown in Table 2. No significant difference could be demonstrated between IgA levels and sex. Yemenites were found to have the lowest IgA mean levels. Cochins have higher IgA levels than Kurds, Yemenites and Ashkenazis. IgA levels in the age group of 70 to 80 years were significantly higher than in all other age groups, while mean levels in the age group of 40 to 50 years were found to be higher than those found in the age group of 20 to 30 years (Figure 2).

**Immunoglobulin M.** The mean values for IgM are shown in Table 3. IgM mean levels were found to be significantly higher in females. Ashkenazis have the highest mean IgM levels. Kurds have lower IgM levels than Ashkenazis, Cochins, and Yemenites. Subjects in the 50 to 60 year age group have significantly lower

Table 2. Comparison of sex and ethnic group differences in serum IgA concentration

Ethnic group	Male					Female				
	No. of subjects	Mean* (mg/100ml)	S.D. (mg/100ml)	Range (mg/100ml)	Mean* IU	No. of subjects	Mean* (mg/100ml)	S.D. (mg/100ml)	Range (mg/100ml)	Mean* IU
Ashkenazi	66	252	67	140-460	125	67	220	64	140-560	109
Kurd	54	205	66	110-350	102	70	212	100	100-550	105
Yemenite	70	161	66	80-340	80	64	187	69	120-340	92
Cochin	54	250	112	120-560	124	58	278	157	110-650	138
North African	60	243	148	100-620	120	58	233	95	100-450	115

\*Age adjusted

IgM mean levels than those found in the age groups of 18 to 20, 30 to 40, 40 to 50 and 60 to 70 years (Figure 3).

**Discussion**

Serum immunoglobulin levels in healthy individuals are controlled by the rate of synthesis and catabolism of the proteins. Exogenous and endogenous factors may play a role in setting these levels. Exogenous factors, such as infections, immunizations, seasonal changes, which Kalf called "environmental factors"<sup>1</sup> were ruled out in our study population. Socio-economic factors, which may have some effect on immunoglobulin synthesis, are minimized in the four villages since all have more or less the same socioeconomic status. The kibbutz, on the other hand, has a higher socioeconomic status than the villages. The socioeconomic factors did not correlate, however, with immunoglobulin concentration studies carried out by Lichtman et al,<sup>6</sup> and Buckley and Dorsey.<sup>7</sup>

Age, sex, race, ethnic groups, and other genetic factors were included in the endogenous factors. We were not able to confirm the results reported by other authors,<sup>1,8</sup> that linear regression lines are obtainable between IgA-IgG levels and age. However, both IgA and IgG were significantly higher in the age group of 70 to 80 years. The influence of sex was seen only in IgM levels. In keeping with other studies, significantly higher IgM levels were found in females than in males.<sup>1,6,9,10</sup> The majority of the authors who described racial effects on immunoglobulin

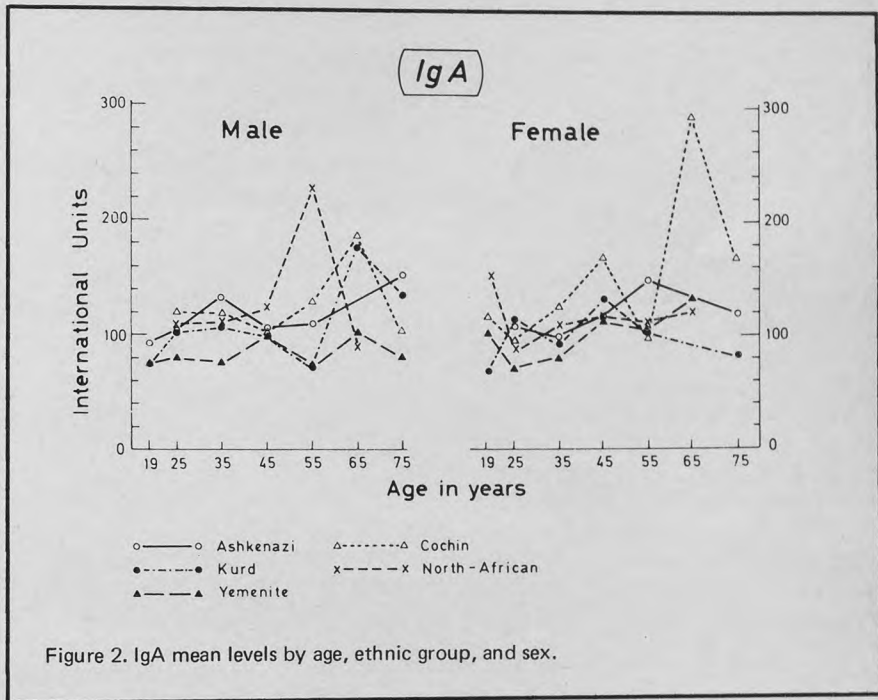


Figure 2. IgA mean levels by age, ethnic group, and sex.

levels compared Caucasians with Negroes.<sup>6,7,9,11</sup> These surveys showed significantly higher immunoglobulin levels, especially IgG and IgM, in Negroes. These differences were ascribed to genetic rather than to ethnic or socioeconomic background.<sup>7</sup>

The Jewish population in Israel is composed of many different Caucasian ethnic groups. Comparison of the mean immunoglobulin levels between five such ethnic groups pointed toward an ethnic pattern amongst each individual group. Thus, Yemenites show a low level of IgA, Ashkenazis lean toward high IgM levels, Cochins and

North Africans have high IgG and IgA levels, and Kurds have low IgM levels. It may be possible that at an early age certain environmental factors affect immunoglobulin concentrations. Such a possibility was suggested for different groups within the Bantu population, which differ widely in the occurrence of parasite infections.<sup>11</sup> This hypothesis is not applicable to the study population in the present work. Ashkenazis with high levels of IgM were never known to suffer from parasitic infections. Furthermore, environmental factors cannot explain the low IgA levels among Yemenites or the



Table 3. Comparison of sex and ethnic group differences in serum IgM concentration

Ethnic group	Male					Female				
	No. of subjects	Mean* (mg/100ml)	S.D. (mg/100ml)	Range (mg/100ml)	Mean* IU	No. of subjects	Mean* (mg/100ml)	S.D. (mg/100ml)	Range (mg/100ml)	Mean* IU
Ashkenazi	66	145	37	90-275	170	67	145	55	80-300	170
Kurd	54	94	33	70-180	110	70	120	36	75-150	140
Yemenite	70	127	50	85-270	149	64	139	67	62-290	157
Cochin	54	117	56	75-362	138	58	140	56	62-225	165
North African	60	109	40	70-225	128	58	128	50	90-280	150

\*Age adjusted

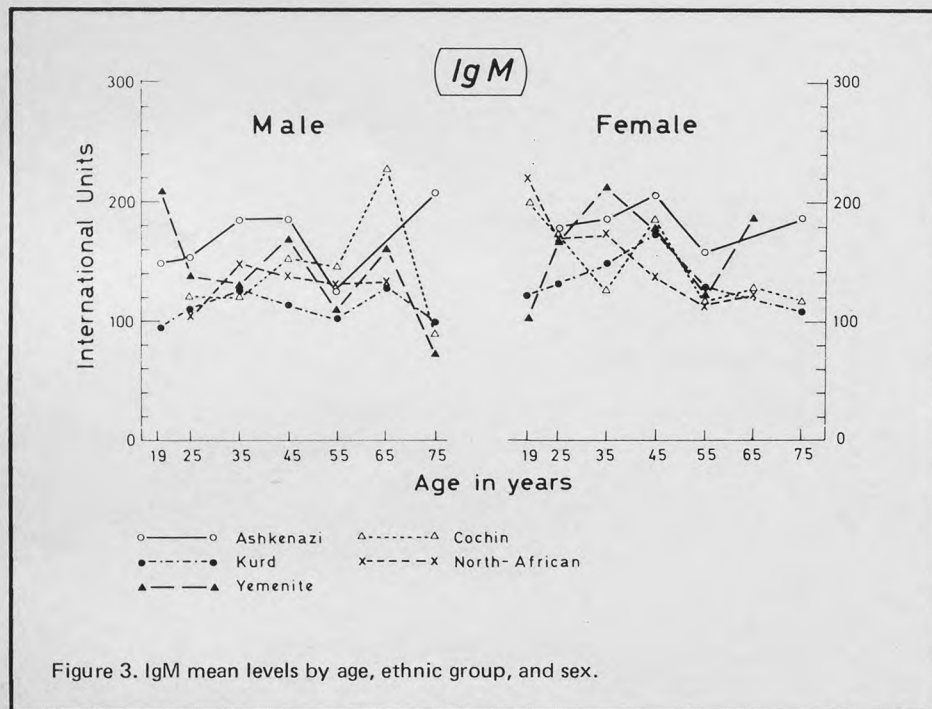


Figure 3. IgM mean levels by age, ethnic group, and sex.

low levels of IgM among Kurds.

A high prevalence of chronic obstructive pulmonary disease (COPD)<sup>12</sup> was found in the Cochin population. High IgA levels in patients with COPD have been demonstrated by others.<sup>13</sup> The question is raised as to a possible connection between the high IgA levels found in Cochins and their predisposition for this disease. A follow-up study of these healthy Cochin subjects is in progress, in an effort to discover whether there indeed exists a significant correlation between immunoglobulin levels and the development of COPD.

All individuals in our study population have been living in Israel for at least the last 15 years. No evidence of parasitic or patterns of infectious disease relating to the different ethnic backgrounds was found in their charts, physical examinations, or laboratory tests. It seems therefore likely that endogenous factors that are class-specific and might be genetically controlled, are responsible for the differences in immunoglobulin levels noted between the various ethnic groups.

The present study confirms that wide variations in immunoglobulin concentrations exist. Before deter-

mining the "normal" range of serum immunoglobulin levels, it is advisable to adjust these values for age, sex, and ethnic background.

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