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Frequency of rubella antibodies among adult population in Greece

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INTRODUCTION

Rubella was considered of little clinical and epidemiological significance until 1941 when Gregg (1941) discovered the relationship between maternal rubella and congenital defects. The isolation of rubella virus and the application of laboratory techniques in the identification of the disease made possible the study of various aspects of the epidemic of 1964 (Rubella Symposium, 1965). These recent epidemiological studies have contributed to the recognition of rubella as a major Public Health problem and have resulted in a more realistic estimate of the risks of maternal rubella. Great interest in producing an effective vaccine against rubella followed the above discoveries and various groups are now actively working on it (Parkman, Meyer, Kirschtein & Hopps, 1966; Plotkin, Farquhar, Katz & Ingalls, 1967). In view of this fact the determination of the immune status of Greek adults on a national scale was undertaken, as an attempt to estimate the risk of contracting rubella during pregnancy. This would greatly simplify the initiation of any future prophylactic programme against rubella. The results of this study are reported in the present paper.

MATERIAL AND METHODS

It was shown in previous studies (Papaevangelou, 1967) that no significant difference in the prevalence of rubella antibodies existed among the various age groups of young adults at the reproductive period of their life. The immunity status of the age group 20–25 was determined in this study. A preliminary comparison of the sex incidence of immunity to rubella of this age group was undertaken. The sample consisted of 144 males and 120 females born and living in Greater Athens area and 50 males and 52 females from the rural Department of Corinthia. An attempt was made to match them for age, social class, and geographical location.

The prevalence of immunity to rubella was then studied in a representative sample of males 20–25 years old. This consisted of 1200 recruits born and living in every district of Greece. Each district was represented proportionally to its population.

Serum specimens were drawn under aseptic conditions and were kept frozen until tested. The immunity was determined by the detection of the neutralizing

rubella antibodies. The 'Judith' strain of the rubella virus and the technique described by Leehrøy (1966) with stationary instead of rolled tube cultures of the rabbit cornea cell line (S.I.R.C.)* were used. The highest dilution of serum that protected 50% or more of the cultures from rubella virus cytopathic effect was taken as the neutralizing titre. The presence of neutralizing antibodies in a titre of 1/4 or higher was considered as indicating immunity to rubella.

RESULTS

Table 1 shows the results of the study on the sex incidence of immunity to rubella. No difference between the sexes was found in the Greater Athens area or in the Department of Corinthia.

Table 1. *Comparative study of the sex incidence of immunity to rubella in Greater Athens area and the Department of Corinthia*

	Greater Athens area		Department of Corinthia	
Sex	No. examined	No. with antibody titre < 1/4	No. examined	No. with antibody titre < 1/4
M	144	10 (6·9)	50	8 (16)
F	120	9 (7·5)	52	9 (17·3)
Total	264	19 (7·2)	104	17 (16·3)

Figures in parentheses indicate percentages.

Table 2. *Frequency of rubella antibodies among males 20–25 years old*

Place of birth	No. examined	No. with antibody titre < 1/4
Greater Athens	266	21 (7·9)
Rest of Central Greece and Euboea	139	32 (23·0)
Peloponnesos	158	16 (10·1)
Ionian Islands	30	8 (26·7)
Epirus	50	10 (20·0)
Thessaly	99	39 (39·4)
Thessaloniki	74	3 (4·1)
Rest of Macedonia	196	23 (11·7)
Thrace	51	16 (31·4)
Aegean Islands	68	18 (26·5)
Crete	69	15 (21·7)
Total	1200	201 (16·8)

Numbers in parentheses indicate percentages.

The immunity status of the representative sample of young adult males, aged 20–25, is shown in Table 2. In 201 (16·8%) neutralizing antibodies were absent. The percentage of susceptible men among the various districts ranged from 4·1% for Thessaloniki to 39·4% for the district of Thessaly.

The existence of any difference in the proportion of susceptibles between rural

* The 'Judith' strain as well as the rabbit cornea cell line (S.I.R.C.) were kindly provided by Dr J. Leehrøy, Enterovirus Dept., Statens Serum Institut, Copenhagen, Denmark.

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and urban areas was studied among 674 recruits, who had never moved from their place of birth. It was shown (Table 3) that the proportion of susceptibles was higher for the rural population (25·8 %) than for the urban population (14·0 %).

Table 3. *Comparative study of the prevalence of rubella antibodies between urban and rural populations*

	Urban		Rural	
Place of birth and permanent home	No. examined	No. with antibody titre < 1/4	No. examined	No. with antibody titre < 1/4
Greater Athens	144	10 (6·9)	—	—
Rest of Central Greece and Euboea	23	2 (8·7)	72	17 (23·6)
Peloponnesos	25	2 (8·0)	51	6 (11·8)
Ionian Islands	10	2 (20·0)	30	10 (33·3)
Epirus	18	4 (22·2)	8	0
Thessaly	30	10 (33·3)	19	11 (57·9)
Thessaloniki	32	1 (3·1)	—	—
Rest of Macedonia	12	3 (15·8)	28	4 (14·3)
Thrace	7	1 (14·3)	13	6 (46·1)
Aegean Islands	55	14 (25·5)	54	17 (31·5)
Crete	24	5 (20·8)	12	3 (25·0)
Total	387	54 (14·0)	287	74 (25·8)

Numbers in parentheses indicate percentages.

DISCUSSION

Rubella is generally accepted as a mild infectious disease of infancy. It is important, however, in view of the established teratogenic potential, that rubella is unique among the common infectious diseases in that a significant proportion of young adults has yet to experience infection. This is in contrast to measles and other communicable diseases of childhood from which few persons even in the remotest part of the country escape exposure. In the Naval Training Center of Great Lakes, Ill., U.S.A., rubella is the most common exanthematous disease with an attack rate amongst recruits in a 9-week training period of 3–5 %, which is much higher than measles (Miller *et al.* 1967). This difference is attributed to the lower infectiousness of the virus and to its other poorly understood, special characteristics, which produce epidemic waves at longer intervals. The disease is followed by life-long immunity even though second attacks have been described. Most authors believe, however, that such cases are attributed to wrong clinical or laboratory diagnosis rather than to true second attacks (Brody, 1966). In any case there is no doubt that the immunity lasts at least 20 years (Brody *et al.* 1965). It is obvious therefore that the frequency of antibodies among recruits provides an almost completely accurate picture of cumulative exposure of a population of these ages.

Serological surveys on a national scale, based on serum samples collected from recruits, have been conducted very widely recently. Such a sample is representative of the same age group in the general population; it is almost always available,

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and is easy to work with because the individuals are collected together in one place. It was decided to use such a sample for the study of the frequency of antibodies among adults, after it was shown that there was no significant difference in the sex incidence of the immunity (Table 1). Both in Greater Athens area and the department of Corinthia the percentage of susceptible females was slightly higher, but the difference was without any statistical significance ($P > 0{\cdot}5$).

According to our results 83·2 % of Greek adults at the reproductive age were found immune to rubella. This is consistent with the findings of most workers (Schiff & Sever, 1966; Field, 1967; Rawls *et al.* 1967). Pierce (1967) found that 30 % of the recruits at the Naval Training Center, Great Lakes, Ill., were susceptible to rubella. A study involving 600 pregnant women, ages 14–44, from various States of the U.S.A. estimated the over-all percentage of susceptibles as 17·5 % (Sever, Schiff & Huebner, 1964). In the same study a great variation of the percentage of susceptibles was found in relation to geographic location. We found a

Table 4. *Correlation between the degree of immunity to rubella and the percentage of rural population in the sample examined in each district*

Place of birth	No. examined	Rural (%)	Antibody titre < 1/4 (%)
Greater Athens	266	0	7·9
Rest of Central Greece and Euboea	139	75·5	23·0
Peloponnesos	158	67·0	10·1
Ionian Islands	30	76·6	26·7
Epirus	50	32·0	16·0
Thessaly	99	39·4	39·4
Thessaloniki	74	0	4·1
Rest of Macedonia	196	55·1	11·7
Thrace	51	60·8	31·4
Ionian Islands	68	48·5	26·5
Crete	69	33·3	21·7
Total	1200	40·3	16·8

range from 4·1 % to 39·4 % for the various districts. The lower proportion was found in the conurbations of Thessaloniki (4·1 %) and Greater Athens (7·9 %). In recent years a number of surveys have shown that many factors determine the relative incidence of infectious diseases in different areas. The urban-to-rural proportion of the population is considered as an important factor in the development of the herd immunity. Such a correlation was obvious from our results (Table 4), even though this was not found statistically highly significant (Kendall's S Statistic, $P = 0{\cdot}11$). This was attributed to the residential mobility of the sample examined. It was found that 319 (26·6 %) out of the 1200 studied did not continue to live in their place of birth. Most of them (297 or 93 %) had moved to the conurbations of Athens and Thessaloniki.

The study of the susceptibility among those that had never moved from their place of birth (Table 3) showed a highly significant ($P < 0{\cdot}001$) difference between urban (25·8 %) and rural (14·0 %) population.

The factors responsible for the degree and the characteristics of immunity of a population to an infectious disease are not determined easily. A highly significant correlation between age and proportion with antibody to rubella has been established (Sever *et al.* 1964; Papaevangelou, 1967). In the present study the importance of the urban to rural proportion of the population of an area to its degree of immunity has been shown. It is general knowledge, however, that other factors are responsible too. Sever *et al.* (1964) reported a significant difference between Whites and Negroes. There are also indications (Papaevangelou, 1967) that the communications and easy access to conurbations, as well as the socio-economic conditions and the habits of various population groups, are important for the relative prevalence of immunity.

SUMMARY

No significant sex difference in the incidence of immunity to rubella at the ages of 20–25 was found in a comparative study of young adults from the Greater Athens area as well as from the rural department of Corinthia. The immunity to rubella of Greek adults on a national scale was then studied in a representative sample of 1200 males 20–25 years old. In 83·2 % of them neutralizing antibodies to rubella were detected. A statistically higher proportion of immunes was found among those from urban areas. The factors responsible for the relative prevalence of immunity to rubella in various population groups are discussed.

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