DETECTION OF RUBELLA VIRUS ANTIBODIES IN NORMAL EGYPTIAN GIRLS AND BILHARZIAL GIRLS OF AGE 15-18 YEARS OLD

THESIS

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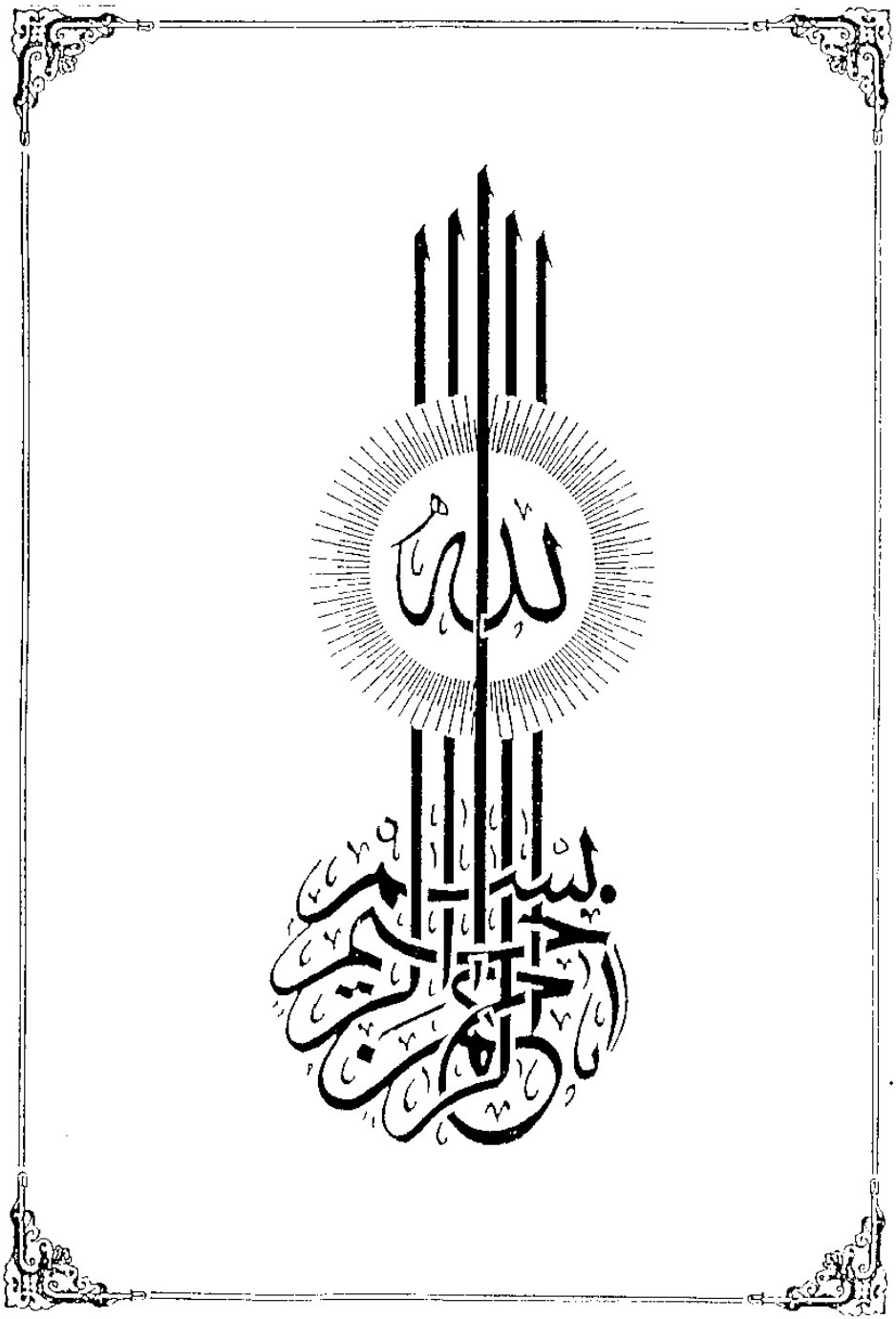
I N D E X



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Introduction
&
Aim of the work

I INTRODUCTION AND AIM OF THE WORK

The rubella was firstly considered as a distinct and specific entity in 1881 by the International Congress of Medicine in London (Forbes, 1969).

Then, Sir Norman Greegs discovered the association of rubella in early pregnancy with characteristic congenital anomalies in the infant (Gregg, 1941).

As a result of the observation, rubella was thrust from its position as a mild inconsequential disease of childhood and became a major medical problem. Then Weller and Neva, 1962 and Parkman et al., 1962 succeeded in isolation of the virus in tissue culture.

This event was followed by the rapid evolution of the serological and virological methods for studying the infection, as with other diseases, an understanding of the epidemiological features of rubella helps to provide a key for prevention. (Ingalls, 1967).

Also, more attention has been given to establishing the risk of foetal abnormality when infection occurs during pregnancy. (Lundstrom, 1962).

The aim of this work is to carry out a serological survey for detection of rubella antibodies in Egyptian school girls at age of 15-18 years old.

Two groups were examined, the first one of 25 girls complaining of bilharziasis, The second group of 25 girls free from bilharziasis.

This survey gives an idea about prevalence of immunity in Egyptian school girls which is of special importance particularly after marriage and pregnancy to avoid the risk of foetal infection, also we shall detect the relation between the prevalence of bilharziasis and the presence of rubella antibodies in the serum i.e. immunity to rubella in bilharzial patients.

Review of the literature

II REVIEW OF THE LITERATURE

(A) History and Clinical Picture of rubella

The history of rubella encompasses a period of about 150 years, from the early 18th century, German descriptions of a new entity called "Rotheln" were viewed with slowly diminishing scepticism.

In 1866, Veale reflected the growing acceptance of Rotheln or german measles as an epidemic entity in his paper in the Edinburgh Medical Journal, he described 30 cases and formally proposed the name rubella (Veale, 1866).

The broad characteristics of the disease, with the notable exception of joint pains were defined in 1930 as : spots which are pink macules appear first behind the ears and on the forehead then spread rapidly, first to the trunk and then to the limbs, minor degree of conjunctival effusion is common, tender enlargement of the suboccipital lymph nodes, sometimes many groups of lymph nodes are affected, the tip of the spleen may be palpable.

In adolescents and adults the onset may be acute with fever. In 1938, Hiro and Tosaka established the

viral nature of german measles and its transmissability by the injection of throat washing. (Forbes, et al., 1969). The frequency of joint pains in natural rubella is a diagnostic feature, although generally described as an occasional complication. It has recently been assumed of importance in relation to the assessment of vaccine side effects. (Simpson, 1940).

In 1941, Greeg was an ophthalmologist, observed congenital defects in infants, of mothers who had suffered rubella early in pregnancy, he noted an epidemic of congenital cataracts, the frequent association of congenital heart diseases. (Gregg, 1941).

Despite the techniques devised by Enders and his colleagues in 1949, isolation of rubella virus was to be delayed until 1962 when two teams, Parkman's team, and Weller's team published their techniques at the same time. They mad possible the isolation of the rubella virus in culture (Parkman et al., 1962) and (Weller & Neva, 1962).

The therapeutic abortion rates and the overdiagnosis of rubella appear to have initiated many studies of the risk of **maternal** rubella which have necessarily depended on the diagnosis made by a multitude of observers.

The introduction of the haemagglutination-inhibition antibody test in 1967 by Steward enabled rapid and reliable assessment of immunity and was an important advance. This has ameliorated the situation for those women have circulating antibodies, but the problems persist for the sizeable minority of women who are still susceptible.

This test facilitated rapid confirmation of diagnosis during the 10-12 days period after the rash when rising antibody tites may be detected. (Steward, et al., 1967).

(B) Characters and Structure of the Rubella Virus

Several years of effort were required before the virus could be grown to sufficiently high titers so that purified preparation could be obtained and the agent could be characterized.

In electron micrographs of thin sections of infected cells, the virions are seen as spherical enveloped particles measuring 70 nm in diameter and containing electron dense cores that are 35 nm in diameter (Murphy et al., 1968). Negatively stained preparations of cell-free virus contain particles that are 70-75 nm in diameter, irregular in shape through roughly spherical and appear to have roughened surfaces suggesting the presence of projections (Liebhaber et al., 1969).

Rubella virus contains RNA and protein, while the presence of lipid is infered from the buoyant density of the particle, which is 1.18 gm/ml and from its sensitivity to lipid solvents. (Liebheber et al., 1969).

The RNA which has been extracted has been shown to be infectious and is estimated to have a molecular weight of 3 X 10^6 daltons (Sedwick & Sokol, 1970).

This would provide sufficient genetic information for 20 virus-specified proteins, each containing an average of 150 amino-acid residues. Haemagglutinin, one or more complement-Fixing antigens, and two precipitinogens are structural components of the purified intact virion.

There are also large quantities of these substances produced during infection, which are not associated with particulate virus and appear as "soluble" or more correctly non-sedimentable antigens. (Le Bouvier; 1969). It has thus far not been possible to disrupt purified rubella virus in a controlled manner so as to yield a nucleoprotein core and a lipoprotein envelope fraction. The virus is extremely sensitive and in general, if it is affected at all by treatment with a particular detergent or surface active reagent, it is totally degraded (Duesberg, 1970).

Duesberg, 1970 said that the place of rubella in the taxonomy of viruses is not yet fixed, it is not a myxovirus and is totally unlike measles virus.

Recently Linda Ho-Terry, 1986 proved that rubella virus is an enveloped, positive-stranded RNA virus and is classified in the family togaviridae.

The virus contains a single non-glycosylated capsid protein, C, and two glycosylated envelope proteins E_1 and E_2. E_1 and E_2 proteins can only be separated by employing strong denaturating agents and reducing conditions, this results in removal of all biological activity and almost all immunological activity, and suggests that in rubella E_1 and E_2 are linked by disulphide bonds as well as non- covalent bonds, to form the envelop spikes.

Three epitopes have been identified on rubella virion envelop polypeptide E_1 using monoclonal antibodies. Antibodies to two of the epitopes, $E_{1_{EP1}}$ and $E_{1_{EP2}}$ show both haemagglutination inhibition and neutralization activities, wherease antibodies to the remaining epitope , $E_{1_{EP3}}$, show neutralization activity only. (Linda, et al., 1986).

(C) The Congenital Rubella Syndrome

During the incubation period of rubella the virus circulates in the maternal blood and can pass the placenta to enter and multiply in the foetal tissues; it produces an antimitotic effect leading to retardation in the cell division and sometimes to foetal malformation. The foetal abnormality and the particular malformations depends upon the period of gestation at which viraemia occurs and thus upon the stage of organogenesis which has been reached. Once differentiation has taken place in any organ, it is no longer susceptible to the teratogenic effect of the virus (Potter, 1957).

The earlier in pregnancy, virarmia occurs the higher is the incidence of Foetal malformation and the more numerous the defects. When the infection is in the first two weeks after conception, before the blastocyst has become embeded, death of the embryo and abortion is likely to result rather than teratogenesis. Between the fourth and sixth week of gestation, infection most commonly causes ocular abnormalities which consist of bilateral central cataract, microphthalmos and buphthalmos (Gregg, 1941).

In the fifth to ninth week, the congenital cardiac