MODE OF INHERITANCE IN INFANTILE ECZEMA

THESIS

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Master Degree in Human Genetics

BY

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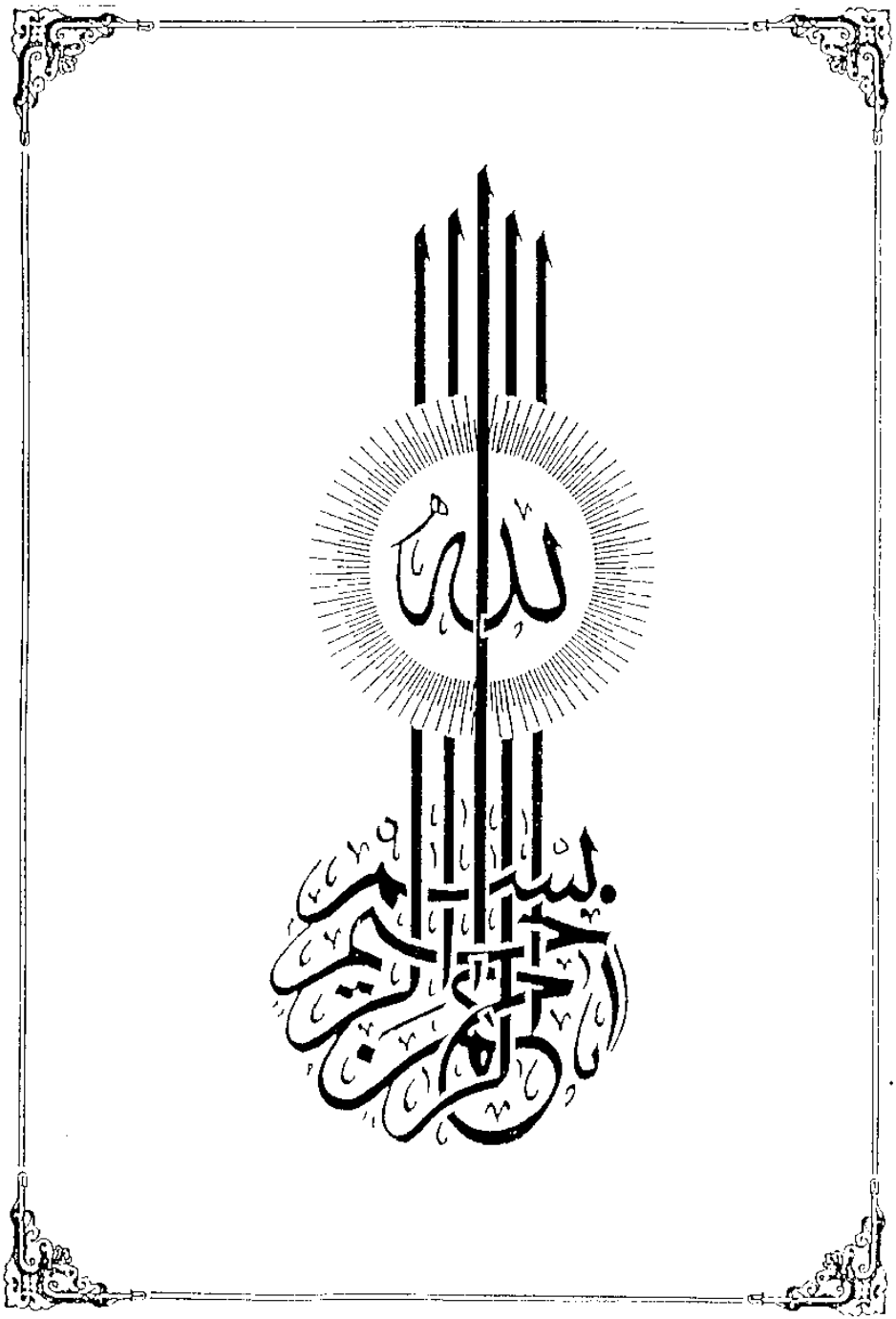

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AIM OF THE WORK

Many workers reported positive family history in infantile eczema (Rajka, 1975; Levine, 1976; Chenwith et al., 1977 and Rasmussen and Provost, 1978), but a definite mode of inheritance has not been reported. For this purpose we planned to study the role of inheritance in this disease using the advanced methodology of population Genetics.

Introduction

Atopy is genetically determined disorder in which there is an increased liability to form antibodes (IgE) and an increased susceptibility to certain diseases especially asthma, atopic dermatitis, hay fever in which such antibodies may play arole.

The word atopy was introduced by Coca (1923) as a convenient collective term for a group of diseases, chief among which were asthma and atopic dermatitis, which occured spontaneously in individuals who had a family history of susceptibility.

Later on Coca and Grove (1925) detected reagin antibodies in these individuals and could be transferred to normal individuals by the prausinitz - Kustner (P.K.) test.

Atopic dermatitis "eczema" is a common, chronic or chronically relapsing severely pruritic eczematous skin disease, occuring in individuals with a personal or family history of atopic diseases such as asthma or allergic rhinitis. The exact cause of atopic dermatitis is unknown, both hereditary and environmental factors may be operative, the exact mode of inheritance has not been established (Mark, 1981).

Zeiss (1981) cleared that eczema is ageneral term of cutaneous response to various stimuli which may be internal or external characterized in acute stages by vesiculation

and erythema and in chronic stages by Scaling and thickening of the skin. Atopic dermatitis comes under the general heading of eczema and the term atopic dermatitis and atopic eczema can be used inter changeably. Atopic dermatitis is set a part from the other forms of eczema by its association with a personal or family history of allergic rhinitis or asthma (Mark, 1981). The clinical features of atopic dermatitis have been described by numerous authors, Mark (1981) and Oakes et al (1983) who divided its course clinically into 3 stages; infantile (infantile eczema), childhood and adult. The infantile form (infantile eczema): it may first appear soon after birth often by the third month of life (Stewart et al 1970).

It affects commonly the cheek, scalp and intertriginous areas such as the neck, axillae and infraauricular folds. It is usually limited to localized involvement of the cheeks and flexural areas. The skin may be red, dry, slightly scaly, cracked and excoriated or it may be moist and Oozing, Pruritis is the major complaint, secondary infection may occur (Rostenberg et al, 1971, Rasmussen and Provost 1978 and Vasarnish, 1982).

Incidence.

The incidence of all atopic manifestations is variously assesed between 2 and 20% (Carr, 1964).

Walker Warine (1956) and Gleich and Muller (1980) demonstrated that about 3% of all infants suffer from atopic dermatitis according to the criteria used for the diagnosis. What proportion of the population is capable of manifesting atopic diseases under suitable conditions is unkown.

Rajka (1960) cleared that the latent atopy can exist and is well shown in identical twins, in only about half do the diseases run a parallel course.

Age Incidence :

The age of on-set is under the age of 6 months (between 2 - 6 months) in 75% of cases (Sedlis, 1965),but it my be delayed to childhood or adult life.onset before the age of 2 months is exceptional but may occur.

Sex incidence :

Champion and Parish (1972) recorded that it is slight Common in males than females.

Happle et al study (1982) showed increased incidence among males. In our study the sex ratio males to females is 1.8 : 1.

Familial Incidence :

Rajka (1960) reported a Positive faimly history of atopy in the form of asthma, hayfever, allergic rhinits in about 70% of patients with atopic dermatitis. Pasternak (1965) found that cases without a family history do not differ materially from the remainder, although the Prognosis is less favourable if both parents are affected.

Kara-Kim et al (1979) done a study to elecit the incidence & heriditary background of atopic dermatitis in the selected urban area, where a relatively inbred Population lives because of low migration from other areas. A total of 516 infants and children under 6 years were examined the incidence of atopic dermatits was 11.2% and 67.3% of patients with atopic dermatitis had a family history of atopic dermatits, asthma, urticaria.

Stewart et al (1970) reported a positive family history of atopy in 70% of cases of atopic dermatitis. West et al (1962) found that 40% of symptomsfree relatives of patients with atopic dermatitis show an abnormal cutaneons reaction to methacholine similar to that seen in atopic dermatitis patients.

Racial Incidence :

Walker and warine (1956) had reported a 3.1% incidence of infantile eczema in Britain and 4.3% in the united states.

Hellerstrom and Hjordis (1956) stated that atopic dermatits Constitutes one-sixth to one-fifth of all cases of skin disease seen at Karolinska institute & stockholm. Brereton et al (1959) recorded that 1.1% of the children in the area of combridge, England had eczema.

Climate and environment :

Champion and Parish(1972) demonstrated that it is Present in temperate regions. Seasonal exacerbations in spring and autmn are frequent.

Exacerbating factors in atopic dermatitis :

Solomon (1975) has incriminated various factors which lead to exacerbations & flare up of atopic dermatitis, the following factors play a Prominent role :-

a) Food allergies :

1) Solid food : Children exposed to any early solid food diet had increased risks of eczema(Fergusson et al 1982). Arecent study done by Sampson (1983) to elecit the role of immediate food hypersensitivity in the pathogenesis of atopic dermatitis on 26 children with atopic dermatitis & marked elevation of serum IgE. The study demonstrated that in some childern with atopic dermatitis, immediate food hypersensitivity can provoke cutaneous pruritis and erythema which lead to scratching and subsequent eczematous lesions.

2) Breast feeding and Cow's milk : There was no evidence to suggest that breast feeding practices had any effect on rates of eczema. Analysis of the data suggested that the apparent association between exclusive breast-feeding and reduced rates of eczema reported in previous studies may be because breast-fed infants were not exposed to early solid feeding rather than to any beneficial effect of the breast milk itself (Fergusson et al, 1982). Also, in another study done by Kramer et al (1981) cleared that breast-feeding was not associated with any reduction in the estimated relative risk of developing atopic eczema. No significant relationship was found among the cases between severity of disease and breast-feeding nor between the age of onset of the disease and duration of breast-feeding or age at which introduction of solid foods occur.

They concluded that breast feeding and delayed introduction of solids not protect against atopic eczema. Infants started on cow's milk formala, develop allergy early.

b) Contactant :

Such as wool aggrevates the dermatitis (Solomon, 1975).

c) Psychological Stress :

Ullman et al (1977) reported that preciptant stress could be identified at the times of onset and exacerbations of the dermatitis and that significant psychiatric pathology was found in 60% of their patients.

d) Temperature :

Intolerance to extreme temperature, humidity especially in the dry winter & hot summer months, show much exacerbations of the skin lesion. soit is prevalent in temperate region with seasonal exacerbations (Gleich et al, 1980).

e) Excersise :

Atopics tolerate excersise Poorly because their cutaneous vessels are unable to adapt to changes in the skin temperature quickly (Solomon, 1975).

Genetic factors :

The observations that allergic rhinitis, asthma and atopic dermatitis tend to run in families dates back to the latter part of the last century and has been confirmed by numerous subsequent studies (Rajka 1975; Chenowith et al, 1977; and Rasmussen and Provost 1978). There is no agreement about the pattern of inheritance, most authors considered atopic dermatitis to be an inherited disease but the exact

mode of inheritance is not clear. A family history is obtained in about 70% of all cases (Rajka, 1960), those cases without a family history donot differ materially from the remainder although the prognosis is less favourable if both parents are affected (Pasternak, 1963). Cooke et al (1916) and Edfors (1971) thought the defect to be carried by autosomal dominant gene while Adkinson (1920) and Berrard et al (1976) Suggested autosomal recessive inheritance.

However, Weiner et al (1936) asserted that it cannot be single pairs of genes. Tips (1954) felt that different genes may be responsible for allergic rhinitis, asthma and atopic dermatitis. Twin studies don't favour any particular type of transmission (Edfors, 1971), more recent twin study done by Zeiss (1981) revealed that monozygotic twins have 10 folds greater concordance for the disease than do dizygotic twins, Kjellman (1977) beleived that his data pointed to a polygenic transmission as well as genetic infleunces on specificity of the symptoms. Parish and CHampion (1972) tryto relate atopy to single dominant or polygenic, they found that clinicaly normal parents may have affected childern which exclude a simple dominant inheritance. In other families both parents may be affected but the childern are normal excluding simple recessive mode of inheritance. It has been tought for some years that it is atopic diasthesis rather than particular manifestations that inherited. Parents

with any of the manifestations of atopy may transmitt any of the components of the Syndrome to the offsprings but with a tendency to transmitt the same pattern of the disease (Mark, 1981).

A recent investigation done by Kjellman (1977) showed the Occurrance of atopic disease in Swedish childern revealed that when both parents had an identical type of atopic disease e.g. respiratory or cutaneous, the incidence of atopic disease was higher (72%) than when non-identical type occured in parents (21%).

Zeiss (1981) cleared that most authorities agree that there is a polygenic inheritance with environmental factors needed to have the gene express itself.

A more recent study done by Happle and his colleagues (1982) showed an evidence of the carter effect in atopy. In atopy, the sex ratio deviates markedly from unity when the specific organ manifestations are considered Separately. In atopic asthma, the male to female ratio is about 2 : 1. In childern of patients affected with atopic asthma, they determined that the incidence of atopic dermatitis, atopic asthma and atopic rhinitis. Among childern of women affected with atopic asthma, was found larger than the incidence among childern of men affected with atopic asthma. This phenomenon called the

carter effect, can be explained by multifactorial mode of inheritance; a certain number of genes is necessary for clinical signs of atopy to become manifest. Women with atopic asthma have a higher threshold and therefore transmitt more predisposing genes to their childern. This demonestration of the Carter effect is a further argument in favour of polygenic inheritance of atopy.

Another study on the occurrence of atopic diseases in three generations was done by Luoma and Koivikko (1982), The incidence of asthma, hay fever and atopic dermatitis was assessed in three generations in 2820 families by questionnaire. 35% of the families were atopic when the histories of parents and grand parents were included. 64% of atopic childern had atopy in probands and the corresponding figure for non-atopic individuals was 31%. The highest prevelance of atopy was found in the parent's generation (13.5%) but it did not differ significantly from that childern (10.8%) when compared with grand parents (7.6%). The influence of heredity was apparent.

An approach to demonestrate the role of genetic factors in the aetiology of a disorder is to determine if there is any association with an inherited marker trait such as a particular blood group or HLA type.

If a disorder is found to be associated with particular