EPIDEMIOLOGICAL AND IMMUNOLOGICAL STUDY OF RECURRENT CHEST INFECTIONS IN INFANTS AND CHILDREN

Thesis

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INTRODUCTION

Recurrent respiratory infections are of common occurrence in early life.

Several investigators stress the important role of adverse environmental factors in inducing recurrent respiratory infections. For example, early injurious social mixing, passive smoking, air pollution, ... etc. **(Galli et al., 1990).**

World wide, malnutrition is certainly one of the most common cause of immune deficiency. Multiple defects in immune function have been described in malnourished individuals, including lymphoma, abnormal delayed type hypersensitivity, hypogammaglobulinemia, impaired bacterial killing, and decreased total hemolytic complement activity **(Sakr et al., 1986).**

With the advent of the WHO program of immunisation against measles, whooping cough, TB, ... etc., there has been marked decrease in the incidence of either acute or chronic respiratory diseases.

Neglect in immunisation will pave the way for respiratory diseases.

Immunological defects have been incriminated in children with recurrent respiratory infections, but it is reasonable to suppose that they are essentially cell mediated immunity **(Galli et al., 1990).**

In all young patients, who have recurrent infections, it is the task of the pediatrician to decide which children have too many and should be evaluated searching for an underlying immunodeficiency disease and a high index of suspicion should be maintained **(Robert et al., 1989).**

A comparative study has been done between 41 children of school age who had recurrent chest infections and treated with antibiotics as prescholars, and followed prospectively for two years through diary reports by parents and medical consultations and compared with 29 children of the same age and socioeconomic background, who had few or no such infections as prescholars.

The annual incidence of bacterial respiratory infections from birth onwards decreased with age, among children with recurrent episodes as prescholars, whereas in the control group, the incidence remained consistently low **(Robert et al., 1989).**

It is suggested that certain children constitute a group of high morbidity, susceptible to respiratory tract infection and other illnesses over a rather long period of years **(Soderstrom et al., 1991).**

In most cases careful history and thourough physical examination allow the pediatrician at least to place the subjects into oneof three categories:

1- Those few patients who need full immunological evaluation.
2- Those who deserve selective screening tests.
3- The vast majority of subjects who can be simply observed over time.

Children with immunodeficiency diseases generally have infections that are characterised not only by increased frequency but also by unusual severity,and unusually prolonged course found,or unexpected complications **(Johnston et al., 1984).**

If however, the child experiences prolonged infections or some bacterial complications with each upper respiratory infection one's index of suspicion should rise sharply. This is particularly true if these complications involve more than one site because recurrent infections involving a single site are most commonly

the result of a structural or anatomical abnormality **(Robert et al., 1989).**

Recurrent infections involving multiple sites are most common in immunodeficiency.

For certain locations, any recurrence of infection should immediately lead one to suspect an underlying immunodeficiency and/or congenital anomalies.

Thus any child with recurrent pneumonia deserves evaluaiton. Similarly infection with certain organisms, particularly those of low pathogenecity should always raise the possibility of a disorder in host defense such as the child with pneumocystis carinii infection or mucovicidosis.

One of the most common presentation of too many infections in infants and children is recurrent respiratory illness. However, this might not indicate impairement of immunodefense mechanisms and the young with recurrent respiratory illness might have an allergic disorder rather than an immunodeficiency **(Rubin, 1985).**

Thus, for recurrent lower respiratory tract infections in any child, allergic disease should be considered as a possible etiology, although the potential

to reduce the frequency of infections by treating the underlying allergic disease has not been fully established.

It is logical to assume that allergen avoidance, and possibly treatment with antihistamines, inhaled steroids and immunotherapy, might play a beneficial role in some patients.

Therefore particularly those requiring surgical intervention for recurrent infection an allergy evaluation is indicated **(Robert et al., 1989).**

Aim of the Study:

The aim of work is to study infants and children who are suffering of recurrent respiratory infections, their epedemiological, and immunological profile, and to investigate thoroughly with particular emphasis on immunity.

It is aimed as well to delineate the most frequently encountered types of recurrent chest infections, and their prevalence amongst other forms of respriatory diseases.

REVIEW OF LITERATURE

A- Epidemiology:

Respiratory infections comprise the main cause of medical consultation and one of two of the first causes of morbidity and mortality in children under five in developing countries **(Pavia Raz et al., 1991).**

The patterns of respiratory tract disease in childhood relate to several modifying factors: age, sex, seasonal variation, geography, socioeconomic conditions, and race.

Among the predisposing conditions for recurrent respiratory infection in children are several host factors, such as environment, infectious agents, and immune mechanisms.

The burden of respiratory infection worldwide indicated 4.5 million children die each year from respiratory infection, representing 30% of all deaths in childhood **(Berman, 1991).** Worldwide 13 million children die annually, 96% of whom are in developing countries, although most of deaths are from diarrhea, fully $\frac{1}{3}$ of children die of pneumonia **(David, 1991).**

Neonatal pneumonia can be acquired during descent through the birth canal, and immediately after birth can be transmitted to the newborn and present after several weeks of life as a severe pneumonitis **(Nelson, 1983).** Beyond the newborn period a lack of specifically directed antibodies against common viral pathogens results in an increased incidence of respiratory tract infections, this peaks at one year of age.

Pneumonic pneumonia is uncommon in small children, and pneumonia due to mycoplasma infection is uncommon during the first 3-4 years of life **(Nelson, 1983).** Another peak in the incidence of respriatory tract infection occurs during the first 2-3 school years because of increased exposure to respiratory infections against which children have not yet developed special immunity.

Epidemiological studies have shown that preschool children contact between four and six respiratory infections in the course of a year without this causing any alarm as a deviation from normality **(Pavia Raz et al., 1991).**

The small size of bronchial and bronchiolar lumina in the first 2 years of life is an important determinant

in the incidence of bronchiolitis from respiratory syncitial and other virus infrections in children.

There is little variation in the incidence of severity of respiratory tract disease on the basis of sex. Lower respriatory tract infections are slightly more common in boys than in girls under 6 years of age, thereafter the infection rates are equal **(Nelson, 1987).**

Seasonal variations in the incidence of respiratory tract infections and bronchial asthma are clinically important. The most common respiratory tract viral pathogens appear in epidemics during the winter and spring months.

Symptoms due to house dust may be more common when children are confined to the house during the cold weather months **(Nelson, 1987).**

The incidence of common viral, mycoplasmal, and bacterial respiratory tract infections varies little with geographic location. In addition areas with high levels of air pollution predispose to frequent respiration infections, and episodes of asthmas.

Although frequency is not different, the severity of lower respiratory tract illness is generally less in middle class than in lower class families, this may reflect the difference in availability of medical care for these groups.

B- Body defence mechanisms:

The normal host is protected against infection by a remarkable interplay of both non-immunologic and immunologic defence mechanisms.

1- Non-immunologic (local) defence mechanisms:

The largest human body surface is the lining of the respiratory tract which is covered by mucous membranes, named for their capacity to secrete mucus. However the constituents that are found in mucus and their roles in human health and disease are still in the initial phase of explanation **(Michael A. Kaliner, 1991).**

Human nasal respiratory secretions provide one convenient source of mucus and include a variety of proteins, which appear to save important functions in host defence.

Nasal airway secretions and their constituent proteins derive from epithelial cells (including goblet

I. PATHOGENESIS OF RESPIRATORY INFECTION

Host Defense Against Respiratory Infections

- Mechanical defenses
- Mucosal integrity
- Competing mouth flora
- Particle filtering and precipitation
- Particle removal
  - Cough
  - Mucociliary transport
- Phagocytic defenses
- Alveolar macrophage
- Polymorphonuclear leukocyte
- Immunologic defenses
  - Humoral
    - IgA
    - IgG
- Nonspecific defenses
  - Surfactant
  - Transfusion
  - Cytokines
  - Complement
  - Lysozyme
  - Fibronectin
  - Glyoproteins

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cells, submucosal glands (including both serous and mucous cells), blood vessels, and secretory cells resident in the mucosa (including plasma cells, mast cells, lymphocytes, and fibroblasts).

Respiratory secretions consist of a mixture of mucus glycoproteins **(Patwo et al., 1984)**, glandular products and plasma proteins.

Baseline resting secretions include the following major proteins:

- Albumin 15% of total proteins.
- Immunoglobulin G 2-4%.
- Secretory IgA 15%.
- Lactoferrin 2-4%.
- Lysozyme 15-30%.
- Non secretory IgA 1%.
- IgM <1%.
- Mucous glycoproteins (10-15%) MGP.

Mucous glycoproteins provide a replaceable, flexible, continuous extracellular surface coating and protecting the mucous membranes, this gelatinous layer insulates the epithelium, water proofs it by trapping an equous layer beneath it, lubricates the surface and humidifies the inspired air. Each MGP molecule absorbs water of

II. ROLES AND FUNCTIONS OF HUMAN NASAL SECRETIONS

- Protective functions
  - Antioxidant (uric acid)
  - Humidification
  - Lubrication
  - Waterproofing
  - Insulation
  - Provide proper medium for ciliary actions
- Barrier functions
  - Macromolecular sieve
  - Entrapment of microorganisms and particulates
  - Transport media for elimination of entrapped materials
- Host defense functions
  - Extracellular source of IgA/IgG
  - Extracellular site for multiple enzyme actions
  - Antimicrobial functions
    - Lysozyme
    - Lactoferrin
    - IgA/IgG
    - Glandulin
    - Rapid deployment of multiple plasma proteins

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hydration onto itself providing a generous source of humidification for inspired air.

Temperature transfer through the airway secretions to inspired air is facilitated by the gel like structure of mucus, which allows for a gradual transfer of heat to inspired air while protecting the underlying mucosa from excessive cooling **(Michael, 1991).**

In a subject breathing nasally at rest, the transit time through the nose is estimated to take about 0.01 second. In this period of time, the inspired air is wormed from room temperature to 30°C.

Humidification is completed by the time inspired air reaches the pharynx, the reverse process takes place during exhalation, air is cooled about 50°C by the time it reaches the nasal vestibule.

The respiratory mucous membrane is constantly exposed to oxygen on its luminal surface, in order to restrict opportunities for oxygen induced injury, nasal secretions include antioxidants **(Peden et al., 1990).**

A number of antioxidants have been found including lactoferrine, glutathione, transferrin, ceruloplasmin and vitamin C, but the major antioxidant was recently

found to be uric acid **(Peden et al., In Press),** although the pricise biochemical mechanism for uric acid production is unknown at this time.

The secretory blanket is thought to consist of two separable layers: the surface mucous (or gel) and a deeper aquous (or serous) layer in which the base of the cilia is located.

In the nose, particles trapped in the surface mucus layer are transported by mucociliary actions to the posterior pharynx at the rate of 1 cm/min., the surface mucous blanket is then swallowed, and it is constantly being replaced about every 10-20 minutes undr resting conditions **(Patow et al., 1984).**

Micro-organisms and particulate material are trapped in the mucus and passively removed by these processes, large particles never reach the mucus membrane as the blanket is selective.

The layer on which the mucus floates and in which the cilia beat is the epithelial lining fluid, which contains most of the aquous and which appear to reconstitute themselves rapidly **(Kaulbach et al., In Press).**

The capacity of nasal secretions to neutralise or eliminate potentially harmful pathogens is evident by the relative health that most of us enjoy as an ordinary part of life.

The major specific mediators of host defence in secretions are the immunoglobulins IgA and IgG.

IgG is found diffusely throughout the mucosa but in highest concentration near the basement membrane **(Meredith et al., 1989).**

The locally produced IgA is dimeric being joined by a J chain before secretion. Dimeric IgA binds to secretory component produced by serous cells and forms secretory IgA, which binds micro-organisms in the airway lumen and preventing attachment of these potential pathogens to the mucosa.

The non-specific antimicrobial properties of mucus are able to compensate for the functions of S. IgA as IgA deficient patients are generally asymptomatic suffering from a normal incidence of infections, by contrast patients deficient in IgG present for medical help because of recurring respiratory infections (Michael A. Kaliner, 1991).

Lysozym is a relatively small protein found in all body secretions, it has a broad spectrum antimicrobial action, kills bacteria found in the air and effectively prevents mucosal infections from most air born bacteria.

Lactoferrin is another antimicrobial protein, which is bacteriostatic and bactericidal, lactoferrin binds iron and it is presumably this action that kills bacteria.

Glandulin is a small potent molecule secreted in glandular secretion that is bactericidal to multiple bacteria particularly gram negative as pseudomonas **(Brayton et al., 1991).**

It has been suggested that this outpouring of plasma proteins might represent the first line of host defense at mucosal surface **(Persson et al.,In Press).**

Thus it may be more useful in the coarse of a self limited upper respriatory infection to increase glandular secretions and stimulating gustatory reflex (by eating hot soup) **(Raphael et al., 1989).**

The mucociliary system forms a primary defense mechanism of the upper respiratory tract and bronchial

tree against inhaled particles including bacteria **(Greenstone et al., 1985).**

In order to colonise the respiratory epithelium, the bacterium must first avoid immediate clearance on the mucous layer, which is constantly moved towards the back of the throat by ciliary beating. It has been shown in vitro that certain bacteria produce factors that slow and disorganise ciliary beating and damage epithelium **(Robert Wilson et al., 1988).**

Cilia are small hair-like structures that are found on the free surface of mucous membranes.

For efficient mucous transport, each individual cilium must not only itself beat in a coordinate manner but must also beat in concert with the other cilia on the same and adjacent cells.

The sequence of beating of cilia produces metachronal waves.

In the larger airways, the majority of the epithelium is normally ciliated, except for small focal areas covered with non ciliated microvillous columnar cells, the normal ratio of ciliated columnar cells to golbet cells is nearly 5/1, the relative numbers of both types decreasing from the trachea to the peripheral airways.

The mucociliary system may malfunction in a number of ways either secondary to a disease process or when a primary defect occurs in one of its component parts.

The characteristic pattern of mucous may change during disease for example becoming less elastic during viral infections **(Sakakura, 1983)**, or more viscous during bacterial infection, the transport of such mucus is impaired, and viscous mucus may become tethered to glandualr ostia, and golbet celis holding back the mucous flow.

In addition to mucociliary clearance, particles that reach the alveoli are removed by lymphatic drainage and blood flow. Clearance takes days to months. As there are no cilia or mucosa cells in the alveoli, it is postulated that particles may reach the cilia by traction on a continued fluid lining or as a result of phagocytosis by alveolar macrophages which then migrate to the broncho alveolar junction.

Alveolar macrophages are activated during infection, once activated they have increased lysozymal enzyme levels, more phagocytic activity and more bactericidal activity **(Peter et al., 1982).**

Non immunologic defenses are comprised primarily of non specific physical and biochemical barriers to invading pathogens that have developed wherever the body interfaces with the external environment **(Robert et al., 1989).**

2- Immunologic defense mechanisms:

The normal immune system is composed of several relatively distinct components, it can be divided arbitrary into:

- Lymphoid system.
- Phagocytic system.
- Complement system.

(Sells, 1987)

1- The lymphoid system:

The major type of the lymphoid system is the lymphocyte, a small mononuclear cell that comprises about 30% of the total circulating white blood cells.

In addition to peripheral blood, lymphocytes are found in lymph nodes, the spleen, tonsils, thymus, gastrointestinal tract and many other tissues.

Lymphocytes can be divided into several separate cell types based on differences in immune function and phenotype markers with T cells and B cells being the most prominent **(Robert et al., 1989).**

Lymphocyte functions can be largely segregated into the activities of T cells (cell mediated), and B cells (antibody mediated), but there may be complex interaction that necessarily between the two cell types.

As general rule, however, cell medaited immunity is most important in the defense against viruses, fungi, and protozoa as well as tumours and foreign tissue grafts, whereas antibody is most important in the defense against bacterial pathogens.

* **Cell mediated immune function**:

The discovery that human T cells, form rosettes with normal sheep erythrocytes provided the first simple marker for the presence of T cells in lymphoid tissues.

Non multiple T cells specific membrane bound glycoproteins also have been identified that can be detected with monoclonal antibodies **(Moller, 1984).**

Major regulatory T cell subtypes are the T helper or inducer cells and the T suppressor or cytotoxic cells **(Romain et al., 1984).** The T helper cells assist in the immune response by producing soluble factors of lymphokines, namely interleukin-2 which is included in the study of this work.

These lymphokines include factors that stimulate the growth and differentiation of B cells, which also bear specific receptors for a particular antigen, thereby leading to the production of specific antibody **(Robert et al., 1989).**

Optimal function of the T cells and B cell system is provided by a regulatory component consisting of macrophages helper T cells, and suppressor cells, these cell to cell interactions are usually mediated by a family of hormonal substances called interleukins.

In humnan, IL-2 is a glycosylated protein encoded by a gene on the long arm of chromosome 4 **(Malkovsky et al., 1987).**

It acts on activated T cells and to a lesser extent B cells as well as with natural killer cells and thymocytes, causing these cells to proliferate and/or manifest differentiated cell function **(Warren Strober et al., 1988).**

Defects of IL-2 production or IL-2 receptor expression have been noted in a number of disease states, but in no instance has it been shown that such abnormalities are a primary features of the disease. Among diseases with IL-2 production abnormalities are

acquired immunodeficiency (AIDS), autoimmune disease such as type I diabetes mellitus, SLE and hypogammaglobulinemia **(Barzy, 1987).**

However, IL-2 receptor expression defects have been seen in immunodeficiency states, multiple sclerosis, and adult T cell leukemia.

IL-2 have a role as a therapeutic agent in infection, auto-immunity and immunodeficiency. In this regard, it has been shown that IL-2 can augment specific antibody responses which are low because of specific primary gene abnormalities, and IL-2 can cause increased antigen non specific cytotoxic function necessary for destruction of potential pathogens **(Warren Strober et al., 1988).**

The kinetics of IL-2 production, showing peak IL-2 concentration at about 24 hours and a subsequent decline. This decline in concentration has been explained by both consumption of IL-2 production through nitrogen induced suppressor cells. These suppressor cells appear in culture after 24 hours and turn off de novo production of IL-2 in fresh cultures **(Manal, 1988).**

* Humoral immunity:

B cells are the second major cell type of the lymphoid system. The B cell precurors arise in bone marrow, but the site of their differentiation into mature B cells is presently unknown. Initially this process may take place in the fetal liver and later in peripheral lymphnodes or in lymphoid tissue in the gastrointestinal tract.

Most B cells differentiate to become plasma cells, the cells that synthesise and secrete immunoglobulins **(Robert et al., 1989).**

Thus the major role of the B cells involves the production of immunoglobulin, a group of structurally similar glycoproteins found in both blood and extracellular fluids. Five major immunoglobulin classes have been identified in man (IgG, IgA, IgM, IgD, IgE).

The antigen driven activation of mature, resting B cells can occur via T cell independent or T cell dependent mechanisms. T cell independent activation can occur with selected polysaccharide antigens, resulting in an IgM response **(Huston et al., 1991).** However most antigens driven B cell responses are T cell dependent. Likewise, amplifications of antibody production and isotype switching are under T cell regulation.

After antigen cross-linking of membrane immunoglobulin, T cell dependent B cell proliferation and differentiation to plasma cells require the appropriate sequential involvement with cytokines. Several cytokines have been demonstrated to affect human B cell activation, proliferation, and differentiation in a specific manner. IL-I affects initial B cell activation by inducing B cell surface receptors for the succession of stimulatory cytokines that frollow **(Jandl et al., 1988).**

IL-2 promotes the growth and differentiation of activated B cells **(Nakagawa et al., 1987).**

The immunoglobulin classes that are important to host defense are IgA, IgM, IgG.

IgG is the predominant serum immunoglobulin, which readily crosses the placenta, and provides passive immunity to the newborn infant.

IgM represents about 10% of the total serum immunoglobulins and is the first immunoglobulin class prodcued in response to primary antigenic stimulus.

IgA is found relatively in low concentration in serum but is present in large amounts in body secretions and mucosal surfaces, it is thus named secretory IgA.

it serves as an important first line of defense against invading pathogens **(Robert et al., 1989).**

As a rule, however, cell mediated immunity is most important in the defense against viruses, fungi and protozoa, as well as tumours and foreign tissue grafts, whereas antibody is more important in the defense against bacterial pathogens.

2- The phagocytic system.

3- Complement system.

C- **Pathogenesis of recurrent respiratory infections**:

Susceptibility to respiratory infection depends on both exposures to microbes and host factors.

People living in poverty experience more crowding in their homes and work places, have larger family sizes and concomitantly, increased exposure to pathogens and increased inoculum size.

Different factors such as poverty, poor nutrition, co-infections,stress, low birth weight, constitute with other factors pathogenic pathways that impair host defense against infection **(David, 1991).**

There is strong association between poverty and increased respiratory disease incidence and morbidity.

In a cross sectional study in Manila in which households were visited weekly for 2 years, researchers found mobidity from respiratory infections to be associated significantly with lower socioeconomic status **(Tupasi et al., 1990).**

A Glasgow study of childhood pertussis and measles showed a strong association between measures of deprivation and hospital admission rates **(Maclure et al., 1984).**

Atmospheric pollution, malnutrition, and immunity: Human exposure to both infectious organisms and atmospheric pollutants occur via the respiratory tract, and it has long been suspected that atmospheric pollutants have the potential to alter host resistance to infection **(Mark et al., 1991).**

Several major historical pollution events serve to remind us of the potential for atmospheric contaminants to cause adverse health effects including death. The most dramatic was in London in 1952, which resulted in more than 4,000 excess deaths, most of deaths were ascribed to cardiorespiratory cause including bronchitis.

The effects on respiratory health of the pollution currently being experienced in cities such as Cracos,

Poland, and in Kuwait from uncontrolled burning of sabotaged oil wells are just beginning to be assessed **(Jerdy Chowski et al., 1989).**

An ongoing study of six eastern and midwestern US cities has shown links between particles exposure and respiratory disease in children **(Ware et al., 1986).**

In a recent study in Philadelphia, **Schwartz and Dockery (1991)** described an association between levels of atmospheric particles and mortality. An increase of 100 ug/m^3 in total suspended particles was projected to increase overall mortality by 7% including an 11% increase in mortality from pneumonia.

In considering the interaction between environmental exposures and respiratory infections, it is appropriate to review the nature and sources of the atmospheric pollutants with the greatest potential for causing adverse health effects related to host defense **(Mare et al., 1991).**

In the United States, the principal outdoor pollutants are generally classified with the framework provided by the environmental protection agency, which identifies two sets of pollutants "hazardous" and "criteria" pollutants.

Hazardous pollutants are predominantly carcinogens (as asbestos). The sources are diverse but principally include industries and waste products.

Criteria pollutants include ozone, lead, combustion related pollutants (sulfur dioxide, nitrogen dioxide, carbon monoxide particles).

Outdoor sources of pollutants include combustion products present in automobile exhaust and emissions from coal and petroleum fired industrial processes.

Residents of London experience a higher mortality rate from bronchitis than did those in surrounding communities, and this mortality has been declining in parallel with improving atmospheric conditions since 1956 **(Waller, 1989).**

In developing countries, the use of coal for home heating and cooking contributes to outdoor air contamination. High sulfur coal is used because it is less costly, provides for even less efficient combustion and greater emissions.

Barker et al. have shown a correlation between infant mortality from bronchitis and pneumonia and subsequent mortality from bronchitis in men 50 years

III. Atmospheric Pollutants With Greatest Potential to Alter Host Defense

Pollutant	Sources	Effects
Acidic aerosols	Power plants Kerosene heaters	Impaired pulmonary function (asthmatics) Altered mucociliary clearance Altered AM function?
Particles	Tobacco smoke Diesel engines Coal or wood stoves Fireplaces	Depend on particles size and active chemical species
NO_2	Automobile exhaust Gas stoves Kerosene heaters	Increased airway reactivity Impaired pulmonary function (asthmatics) Acute respiratory illness in children?
Ozone	Atmospheric photochemical reactions	Altered AM function? Impaired pulmonary function Airway inflammation Increased epithelial permeability
Sulfur dioxide	Power plants Steel smelting plants Kerosene heaters	Increased airway reactivity Impaired pulmonary function Upper airway irritation
Sensitizing antigens	Dust mites Cockroach debris Mouse urine	Asthma

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later. Suggesting that childhood respiratory infections lead to chronic respiratory disease and mortality in adults **(Barker et al., 1986).**

Humans spend more than 85% of their times indoors **(Bolejji, 1989)**, and the importance of indoor air contamination as a factor in susceptibility to infection is being increasingly recognised.

Although most atmospheric pollutants are present at much lower levels indoors than outdoors. NO_2 is often present at higher levels indoors when unvented combustion sources such as gas stoves or kerosene heaters are present. NO_2 has been linked with increased susceptibility to respiratory infections in children **(Samet et al., 1987).**

Energy conservation measures in recent years may have served to increase exposure to infectious organisms in the homes in inner cities are always infested with rodents and cock roches, and sensitization to antigens associated with rodent urine or cock roach debris has been implicated in increasing the incidence of asthma among inner city residents **(Pollart et al., 1987).**

Children living in infested homes may manifest atopy, allergic sensitization and airway obstruction,

placing them at risk for more severe lower respiratory infections.

Extensive literature addresses environmental pollutants and respiratory infections.

Two distinct but complementary hypotheses have been tested in the epidemiologic studies.

- Pollutant exposure increases the incidence of respiratory infections.
- Pollutant exposure increases the severity of respiratory infections **(Graham, 1990).**

Malnutrition increases the risks of morbidity from infection, and conversely, infection even so mild so as not to cause overt disease, promotes malnutrition **(David, 1991).**

These effects are intimately connected in what Tomkins and Watson described as the malnutrition infection cycle: decreased dietary intake depresses immunity and the integrity of epithelial surfaces, these effects promote susceptibility to microbial colonisation and invasion and increase the severity and duration of the resultant infections.

The diseased individual suffers from anorexia and malabsorption with decreased nutrient intake and increased gastrointestinal losses **(Tomkins et al., 1989).**

Concurrently, metabolic demand of calories, protein, and micro-nutients increases with fever. These changes further impair host defenses and the cycle begins a new.

Rapid and complete recovery depends on both treatment of infection and access to adequate nutrition.

The far reaching effects of this malnutrition/infection cycle extend to social, educational, and economic development.

Worldwide 13 million children die annually, 96% of whom are in developing countries, the majority suffer malnutrition.

Although most of the deaths are from diarrhea, fully one third of children die of pneumonia **(David, 1991).**

The risk of infection has been shown to correlate with nutritional status in many longitudinal studies of children in the developing countries.

In their review of children hospitalised in Manila with pneumonia, Tupasi et al. showed a proportionate relationship between nutritional status and mortality with children whose weight for age was above the 90th. The mortality risk ratio was 27 times for children below the 60th percentile. 11 times for those in the 60th to 74th percentile, and 4.4 times for those in the 75 to 89th percentile. These relationships were independent of age, crowding, and parental smoking **(Tupasi, 1990).**

Mechanisms of increased infection risk for the malnourished have been studied extensively, an early evidence for waning cell mediated immunity as consequent to starvation has been noted **(Martin, 1987).**

It was observed that with worsening nutritional status, tuberculin skin-test reactivity was impaired, and the severity of tuberculosis increased.

In fact the cellular immune system seems to be the component of the immune system that is most affected in malnutrition **(Feigin, 1979).**

The impact of chronic moderate protein deficiency on resistance to pulmonary tuberculosis was studied in a guinea pig model. Inbread and outbread quinea pigs

were maintained on isocaloric diets containing 30% or 10% ovalbumin, vaccinated with mycobacterium bovis BCG vaccine and infected by the respiratory route with virulent mycobacterium TB. Protein deficiency was associated with significant loss of dermal tuberculin hypersensivitity, reduced purified Protein derivative (PPD), driven lymphoproliferation in vitro and diminished interleukin-2 production (IL-2) **(Mc Murray, 1992).**

IL-2 levels were consistently low in cultures of stimulated blood and spleen lymphocytes from protein deprived animals. Previous vaccination of malnourished guinea pigs did not consistently enhance the response of PPD-stimulated lymphocytes to added recombinant interleukin-2 (r IL-2) **(Mc Murray, 1989).**

Additionally, allergic phenomenon such as asthma and urticaria improved spontaneously.

Protein energy malnutrition results in atrophy of the thymus and of the T cell areas of lymphoid tissue in the spleen, tonsils, and Payer's patches.

Circulating T cells are decreased in number. Sensitization and recall of cutaneous and delayed hypersensitivity reactions are also impaired. Cell mediated immunity is most severely impaired. T cell

differentiation and maturation in the thymus are arrested, antibody production and macrophage activation are suppressed.

Low levels of lysozym in mucosal immunity may permit colonisation and contract of pathogens with epithelial cells **(David, 1991).**

Antiprotease activity is also reduced, which may reduce recovery from inflammation and predispose to chronic lung disease

The changes in immune function with malnutrition can be so severe so as to mimic the immunologic alterations of AIDS as exemplified by the occurrance of pneumocytis carinii pneumonia.

Indonisian children with xerophtalmia (Vit. A deficiency) had a two to four fold increased incidence of morbidity and mortality from respiratory infections.

In the developing world there is a causal relationship between vitamin A deficiency and increased mortality.

In a study of hospitalised African children with measles, it showed decreased respiratory complications and mortality after vit. A supploementation **(Keutsch, 1990).**

Vitamin A is thought to affect epithelial integrity and repair. Squamous metaplasia of the tracheobronchial tree is the histopathologic marker of vitamin A deficiency.

Vitamin A deficient children are predisposed to secondary bacterial infections because of impaired mucosal cell response to viral infection and decreased glycoproteins and lysozym activity. There may be also increased mucosal vulnerability to colonisation by pathogens.

Skin test reactivity is abnormal, and vitamin A seems to play some role in insuring competent cell mediated immunity **(Mussey et al., 1990).**

Dark skinned immigrants, shortly after arriving in England had an increased rate of tuberculosis reaction, this period coincided with low serum vitamin D levels **(Davis, 1985).**

Vitamin D seems to play an autocrine function by regualting macrophage function. The vitamin is hydroxylated to vitamin D_3 by pulmonary macrophages probably under the control of cytokines and bacterial products and outside the control of parathormone.

Vitamin D_3 enhances the activation of macrophages and their antimycobacterial effects.

Iron, zinc, and copper are micronutrients necessary for both microbial growth and human immunologic function **(Chandra, 1983).**

Mucosal surfaces are clearly affected by iron deficiency (atrophic gastritis) and by zinc deficiency.

Zinc plays a role in carbohydrate and nucleic acid synthesis. It is crucial for rapidly turning over cells like lymphocytes and epithelial mucosal cells.

The effects on bacterial colonisation and invasion are unknown. Both iron and zinc appear to impair skin test reactivity that is reversible with supplementation.

Copper deficiency in experimental animals decreases antibody production **(David, 1991).**

A large number of studies has shown increased risk of respiratory infections among children who never breast fed or who were weaned early **(Victoria et al., 1987).**

In case of respiratory infections, infants who received no breast feeding died at a rate that is 3-6

times higher than those who were exclusively breast fed. The protective effects of breast feeding are many, it is an alternative to potentially contaminated fluids.

It is a rich source of immunocompetent lymphocytes and secretory IgA and initially of IgG as well.

In addition, there is a long lived effect explained by some soluble factors that enhance the development of active secretory immunity **(Stephens, 1986)**, and of increased responsiveness to diphtheria, tetanus, and polio vacciantion.

Children living in poverty have nearly twice the risk of secondary exposure to cigarette smoking **(David, 1991)**.

Smoking is the principal cause of 80% to 90% of chronic obstructive pulmonary disease, 85% of lung cancer, cancer larynx and oral cavity.

It also contributes to higher rates of respiratory infections, more protracted symptoms after mild infections, increased risk for post-operative respiratory failure, and spontaneous pneumothorax.

Children of parents who smoke have more frequent respiratory problems. Extensive epidemiological evidence

now links environmental tobacco smoke exposure to increased occrrence of lower respiratory tract infections in children **(Samet et al., 1987).**

The effects of environmental tobacco smoke exposure are greatest for infants, but school-aged children may also be affected adversely **(Waren et al., 1984).**

Acute exposure to cigarette smoke increases airway resistance and pulmonary epithelial permeability, it interferes with mucociliary transport by stimulating mucus production while disorganising ciliary action **(US Department of Health and Human Services, 1984).**

It also decreases fibrinocetin, a surface glycoprotein that participates with IgA and lysozym to protect against binding and colonisation by virulent microorganisms.

Cigarette smoke affects the macrophage, decreases responsiveness to antigen, increases synthesis of elastase, and decreases production of antiproteases.

The resultant altered enzyme balance increases injury to the pulmonary interstitium.

Immunoglobulin production by B cells is also altered and decreased **(David, 1991).**

The immotile cilia syndrome is a rare autosomal recessive disease characterised by a congenital defect in ciliary function **(Robert et al., 1989).**

Several different ciliary defects have been described all leading to impaired mucus clearance from the respiratory tract.

Patients with immotile cilia syndrome are often seen with atelectasis, or pneumonia.

Bronchiectasis also usually develops over time.

Haemophilus influenza, S. aureus, and P. aeroginosa are frequently cultured from these sites of infection

In children with recurrent lower airway symptoms where other mechanisms of lung injury such as allergy, immunodeficiency, and cystic fibrosis have been ruled out, should have immotile cilia syndrome been considered in the differential diagnosis **(Barlocco et al., 1991).**

There is data to suggest that blacks have a predisposition to tuberculosis and perhaps to other infectious diseases.

In their review of over 26,000 nursing home patients, Stead et al. discovered in their recent epidemiological analysis of TB in Arkansas nursing homes, that black

residents have a 13.5% risk of new infection, nearly twice the risk for white residents **(Stead et al., 1990).**

Social conditions and crowding do not explain the differences in new infection rate.

There is some aspect of the initial host defense, probably at the level of the macrophage, to explain the difference.

The relation between vitamin D deficiency and dark skinned people is also consistent with these data **(David, 1991).**

The incidence of low birth weight term babies is 20% to 40% in underdeveloped countries.

Risk factors include low level of education, late entry into prenatal care, low pregnancy weight gain, smoking and substance abuse **(Department of Health and Human Services, 1990).**

Low birth weight infants often suffered from nutrition deprivation during development and have impaired cell mediated immunity and neutrophil bactericidal activity. In contrast, premature but appropriate for gestation age babies recover immunocompetence within several months.

LBW children also have an under developed respiratory drive system and are prone to apnea, aspiration and pneumonia **(David et al., 1991).**

People living in poverty have higher rates of respiratory diseases and AIDS partly because of increased exposures that result from crowding and high risk behaviours.,

These primary infections in turn can set the stage for secondary infections. These interactions were termed microbial synergism **(Mackiovac, 1978).**

They may injure mechanical or immune defenses directly or indirectly through their effect on host nutritional status.

Measles, pertussis, typhus, influenza, and rubella are among the acute infections that have long been known to suppress cell mediated immunity. More recently measles vaccination has been reported to have similar effects. Measles epidemics have been reported to induce outbreaks of tuberculosis reactivation **(David et al., 1991).**

Phagocytosis also can be affected by coinfections, influenza impairs phagocyte chemotaxis, engulfement and intracellular killing is impaired in chronic homolytic states like malaria and bartonellosis.

Humoral immunity can be affected as well, for example concurrent enteroviral infections impair antibody responsiveness to poliovaccine **(Krober, 1991).**

Respiratory viruses like influenza disturb normal ciliary motions, may denude large areas respiratory epithelium, and impair mucociliary transport.

Growth retardation and concimittant immunologic abnormalities can persist for months after resolution of disease, during this time period, cellular immunity is decreased while humoral immunity appears less severely affected, even in children with marasmus **(David, 1991).**

It seems logical that poor people would be more afflicted than others by stress caused by psychological environmental (crowding, temperature extremes), and physical factors. A potential synergy between infection and emotional illness has been a subject of speculation since 1918 **(King et al., 1989).**

different mediators are involved in the interplay between stress and the components of the immune system: efferent neurotransmitters and neurohormones, cortico-steroids, sympathomimetics, and prostaglandins on one hand, and afferent lymphokines and growth factors on the other **(Dentzer et al., 1989; Bonneau et al., 1990).**

IV. Impairment of Host Defense Under Conditions of Poverty

	Mechanical Defense	Phago-cytic	T Cell	B Cell	Non-specific
Cigarette use	+	+	+	+	++
Protein-energy malnutrition	+	+	+	±	+
Vitamin A deficiency	+	−	−	−	−
Vitamin D deficiency	−	+	+	−	−
Iron deficiency	+	−	+	−	−
Zinc deficiency	+	−	+	−	−
Copper deficiency	−	−	−	+	−
Alcoholism	+	+	+	+	+
Low birth weight	−	+	+	−	−
Breast feeding	−	−	−	+	−
Co-infection	+	+	+	+	+
Diabetes	+	+	±	±	+

Curr. Probl. Pediatr., May, 1989.

Also, stress has been shown to cause reduction in T and B lymphocytes, in T cell reactivity, and salivary IgA secretion.

Grieving individuals have more frequent pneumonia. In their carefully controlled trials in which nearly 400 subjects were exposed to respriatory viruses, Cohen et al. demonstrated increased rates of respiratory illness in proportion to the degree of psychologic stress within the previous year **(Cohen et al., 1991).**

Along with malnutrition, dental and periodontal diseases are among the major health problems of the homeless **(Institute of Medicine, 1988).**

Caries lead to irreversible tooth destruction, periodontal disease is the leading cause of tooth loss. Both conditions are associated with lack of brushing, poor eating habits including use of caries producing food and lack of routine oral health care.

Periodontal disease leads to virulent oropharyngeal flora that is more likely to cuase pneumonia when aspirated **(David et al., 1991).**

It was shown that extreme hypercholestorelemia and hyperlipoproteinemia impair the immune system.

Lymphocyte and granulocyte membranes are altered by excess cholesterol and their functions are impaired.

Delayed cutaneous hypersensitivity reactions, antibody production and phagocytosis by the reticuloendothelial system are also reduced **(Chandra, 1983).**

A study of 196 Soviet children aged 5-14 years (156 obese, 40 healthy) showed obesity to be associated with a reduction in number of T lymphocytes and their function and increase in IgA and a decrease in IgG levels.

The immunity deviations were deemed, probably attributable to the effects of insulin **(Kratets, 1988).**

Others have not found these changes in the absence of diabetes.

Although diabetics have no more frequent respiratory tract infections than the general population, others than tuberculosis, their infections are of greater severity and involve opportunistic organisms.

Impaired neutrophil chemotaxis and phagocytosis are the most reducible problems **(Sherett et al., 1989).**

Disorders of immunity associated with recurrent chest infections:

Types of primary immune deficiency:

The primary immunodeficiency may in turn be classified into several groups depending on the limb of the immune system that is predominantly affected **(Rosen et al., 1984).**

The B cell deficiencies are the most common of the priamry immunodeficiencies, they comprise about 50% of the primary immunodeficiency **(Robert A. Wood, 1989).**

Of the remainder, T cell defects including both pure cellular and combined T cell and B cell deficiencies account for about 40%, phagocytic defects make about 6%, and complement disorders about 4%.

B cell deficiency

X-linked agamma globulinemia (congenital agamma globulinemia) = Bruton's disease:

Most children remain well during the first 6-9 months of life, presumably because of the presence of maternal antibodies, then as these antibodies disappear, affected children begin to contract recurrent infections, particularly those caused by pyogenic bacteria such as pneumococci, streptococci and haemophilus.

V. Classification of Primary Immunodeficiences

B cell deficiencies
X-linked agammaglobulinemia
IgA deficiency
Common variable immunodeficiency
T cell deficiencies
DiGeorge syndrome
Nezelofs syndrome
Chronic mucocutaneous candidiasis
Combined T cell and B cell deficiencies
Severe combined immunodeficiency
Ataxia-telangiectasia
Wiskott-Aldrich syndrome
Phagocytic disorders
Chronic granulomatous disease
Chediak-Higashi syndrome
Hyper IgE syndrome
Complement disorders

Less commonly staphylococci. The most common of infections being pneumonia **(Lederman et al., 1985).**

Infections of the lower respiratory tract may rapidly progress to sepsis with dissiminated infections. Bronchiectasis with respiratory failure is a major cause of morbidity and mortality in patients surviving to middle age **(Steihm et al., 1986).** The diagnosis of this disease is made when a male child is shown to have markedly diminished levels of serum IgG, IgA, IgM, in addition to absent functional antibody.

Peripheral B cells are present in very low number or entirely absent, tonsillar tissue, adenoids and peripheral lymph nodes are scanty or undetectable on physical examination **(Wedgwood, 1986).**

Common variable immunodeficiency: (acquired agamma globulinemia):

This is a heterogenous group of immunologic disorders characterised by panhypogammaglobulinemia and recurrent infections **(Rosen et al., 1984).**

Typically, total Ig levels are below 360 mg/dl and total IgG levels below 250 mg/dl. This disease can have its onset at any age affecting males and females equally, this disease has no pattern of inheritance.

Most patients have chronic progressive bronchiectasis, unfortunately some children may have crippling pulmonary impairment because of delay in making the proper diagnosis **(Robert A. Wood, 1989).**

Pneumonia seems to be the most infectious complication (83%) **(Stiehm et al., 1986).**

Haemophilus influenzae, pneumococcus pneumonia, streptococcus pyogenes, and staphylococcus are the most frequent infecting organisms.

Patients have a high number of immunoglobulin being B lymphocytes, lymphoid cortical follicles are present. Cytokine defects have been documented and implicated in the pathogenesis of a few cases. Defective IL-2 production by T cells has been reported **(Perri et al., 1985; Matheson et al., 1987).**

* Selective IgA deficiency:

IgA deficiency with normal concentrations of other immunoglobulins was the first and is the most immunoglobulin deficiency described **(Morgan et al., 1988).**

It is defined by a serum IgA levels below 5 mg/dl with normal IgG and IgM levels **(Klemola, 1987).**

Some authors report that most patients with selective IgA deficiency are completely asymptomatic, whereas

other authors suggest that many patients are prone to frequent infections that vary in intensity from mild to severe **(Hutson et al., 1991).**

Bacterial infections of the lower respiratory tract are by far the most common, with an increased risk of development of impaired lung function **(Bjorkander et al., 1985).**

Transient selective IgA deficiency is especially common in children but usually reverts to normal before the age of 14 years and may simply be a manifestation of maturational delay in IgA humoral immunity **(Pebani et al., 1986).**

Individuals with IgA deficiency also are reported to be at a significantly increased risk for the development of both autoimmune and allergic disease. The presumed increase in allergy is speculated to be the result of an increase in the absorption of dietary and environmental antigens from mucosal surface because of the absence of secretory IgA **(Robert et al., 1989),** the incidence may be as high as 1 in 100 **(Morgan et al., 1988).**

*** <u>Hyperimmunoglobulin M immunodeficiency</u>:**

This is a syndrome characterised by an elevated or normal serum IgM associated with very low serum IgG and

IgA levels. The syndrome is complicated by pyogenic infection, it affects mainly males and may progress to to panhypogammaglobulinemia **(Hutson et al., 1991).** These patients experience same risks of infections and complications as common variable immunodeficiency syndrome.

* **Selective IgM deficiency**:

This rare disorder is characterised by serum IgM levels below 10% of normal but normal serum levels of other istoypes **(Buckley, 1986).**

The limited studies showed defective helper T cells or excessive suppressor T cells as the cause of selective IgM deficiency **(Ohno et al., 1987).**

Most patients experience recurrent sinopulmonary infections.

* **Transient hypogammaglobulinemia of infancy**:

This disorder is characterised by transiently depressed immuoglobulin levels in infancy and early childhood, its true incidence is not clear, it appears that it is rare, 11 cases among 10.000 patients evaluated for possible immune deficiency.

Normally, all infants experience a fall in total IgG levels during the first 6-8 months of life as

maternally derived IgG is catabolised. There is response to antigenic stimulation, intrinsic immunoglobulin production begins with subsequent increases in IgM followed by IgG and IgA **(Robert A. Wood, 1989).**

This process apparently is delayed in infants with transient hypogamma globulinemia, leading to a prolonged and accentuated nadir in serum immunoglobulin levels, mainly IgG isotype. B cell number is normal.

All patients recover spontaneously by the age of 2-3 years.

B and T cell deficiencies

* Severe combined immunodeficiency:

Infants with severe combined immunodeficiency usually have failure to thrive, and pneumonia is also commonly present at the time of diagnosis. Most often an interstitial process caused by P. carinii.

Viral infections are handled poorly by affected infants and are commonly fatal, specially those caused by respiratory syncitial virus (RSV).

In addition to lymphopenia, infants have cutaneous anergy, low or absent serum immunoglobulin levels, and no specific antibody production.

Eosinophilia is common, the number of mature T cells is low, B cells number may be low, normal, or even elevated **(Rosen et al., 1984; Geha, 1988; Buckley et al., 1986).**

* Ataxia telengiectasia:

This is an autosomal recessive syndrome, characterised by ataxia telengiectasia, and chronic sinopulmonary disease.

Most patients contract recurrent bacterial infections of the lower respriatory tract, and pulmonary insufficiency secondary to progressive bronchiectasis.

Cellualr immunity is commonly impaired and seems to relate in most patients to defects in T helper cell function **(Oxeluis et al., 1982).**

* Wiskott Aldrich syndrome:

This is an X-linked recessive disorder characterised by eczema, thrombocytopenia, and recurrent infections. Infections with pyogenic bacteria usually begin in the first year of life and result in recurrent epidoses of pneumonia and sepsis.

Most commonly, the serum IgM level is low, IgG level is normal or slightly depressed, and the IgA and IgE levels are elevated **(Robert et al., 1989).**

Phagocytic disorders

* **Chronic granulomatous disease**:

Characterised by recurrent infections resulting from an inability of neutrophils and monocytes to kill ingested bacteria and fungi, phagocytosis is entirely normal up to the point of killing.

Patients typically have recurrent abcess of the lungs, lymph nodes, skin, subcutaneous tissue and liver.

The organisms most frequently encountered are staphylococcus aureus, klebsiella, pseudomonas, aspergillus and candida **(White et al., 1986; Ezekowitz et al., 1988).**

* **Chediak Higashi syndrome**:

This is an autosomal recessive diseae characterised by frequent pyogenic infections secondary to abnormality of intracellular killing and neutrophil chemotasis. Symptoms generally begin in early childhood **(White et al., 1986).**

Giant granules are found in the cytoplasm of all white blood cells in infected patients, coupled with abnormal chemotaxis leads to a dramatically increased

susceptibility to infection in patients with this disorder **(Quie, 1986).**

* **Hyperimmunoglobulin E recurrent infection syndrome**:

It is also known as Job's or Buckley's syndrome, it is characterised by high levels of IgE with recurrent skin and sinopulmonary infections, common organisms are staph aureus. Pulmonary abcesses are frequently encountered in association with recurrent pneumonia, and persistant pneumatoceles may result from these infections **(Quie, 1986).**

Serum IgE levels are markedly elevated (more than 2000 IU/ml), and eosinophilia may be encountered in both blood and sputum, levels of serum IgG, and IgA and IgM are usually normal to slightly elevated **(Donabedian et al., 1983).**

Predominant T cell deficiency

* **Di Geroge syndrome**:

It is the result of hypoplasia or aplasia of thymus and parathyroid glands during embryologic development. Immunologic function in these patients is variable. In general T cell numbers are decreased, B cell numbers are normal or elevated, usually with normal serum immunoglobulin levels **(Robert et al., 1989).**

Some children may have profound lymphopenia, virtually absent cell mediated immunity, and extreme susceptibility to infection with viruses and opportunistic pathogens such as candida and P. carinii.

* Nezelof's syndrome:

Characterised by marked deficiency in cell mediated immunity, with normal or elevated immunoglobulin levels, there is lymphopenia with profound deficiencies in total T cell number, peripheral lymphoid tissues are hypoplastic.

Children with this disorder commonly have opportunistic infection, chronic or recurrent pulmonary infections, failure to thrive **(Robert et al., 1989).**

D- Etiologies of Recurrent Chest Infections encountered in the study:

Different causes of recurrent chest infection, are classified according to their importance, they all show common evidence of serious chronic lower respiratory tract disease.

Several signs and symptoms which suggest that a respiratory tract illness may be life threatening, or assocaited with the potential for chronic disability are listed in the next table, if none of these is found by examination, the respiratory process is usually benign.

The following table is explaining history and physical findings suggesting chronic lung disease whatever the etiology.

It was found that chronic lung disease can affect growth and nutritional status, as well as neurological delay. The types the most commonly found of recurrent chest infection were bronchitis, bronchial asthma, Bronchopneumonia, Bronhiectasis, and Tuberculosis.

VI. History and Physical Findings Suggesting Chronic Lung Disease

HISTORY

Chronic cough

Recurrent wheeze

Decreased activity

Malabsorption symptoms

Fever for longer than 3 weeks

Weight loss

Recurrent pneumonia

Chronic sputum production

Multiple serious bacterial infections

PHYSICAL

Poor growth and nutritional status

Tachypnea

Cynosis

Deviated trachea

Increased anteroposterior diameter of chest

Wheezing crackles

Clubbing

Neurological delay

(Feigin et al., 1987)

I- Chronic Bronchitis:

Chronic bronchitis is illdefined in children and reported less frequently. The prevalence of childhood Bronchitis is variable ranging from 2% to 40% in selected series **(Morgan et al., 1984).**

A chronic or frequently recurring productive cough usually indicates an underlying pulmonary or systemic disease. Affected patients should be evaluated for immunedefficiencies, anatomic abnormalities, allergic disorder environmental disease, upper airway infection with postnasal discharge, cystic fibrosis, immotile cilia syndrome, and bronchiectasis **(Nelson et al., 1984).**

There is a significant association between higher levels of air pollution and an elevated incidence of chronic pulmonary disease including bronchitis, but a direct causal relationship has not been established **(Goldsmith, 1975).**

An increased incidence and exacerbations of bronchitis and other forms of acute and chronic lung disease are assocaited with cigarette smoking.

There is increased morbidity from respiratory infectious in teenagers who smoke, as reflected in school and work absence as well as in functional and pathologic evidence of small airway abnormalities, smoking parents, and specially those whose children have chronic lung disease, discussion should be advised that they are subjecting their children's lungs to significant amaounts of "2nd hand" cigarette smoke in the home, they should be urged to stop smoking **(Doyle, 1974).**

Clinically chronic bronchitis is characterised by excessive mucus production by cough that is present on most days for a minimum of 3 months per year, fever can accompany the cough and can range from 37°-39°C.

Chronic Bronchitis can be a clinical manifestation of a number of clinical disorders. Asthma or reversible obstructive airway disease, can be distinguished by clinical resposne to traditional bronchodilators.

Persistant lower respiratory tract infections (Pertussis, chlamydia, and mycobacterial infections) can present with a similar complex of symptoms **(Morgan et al., 1984).**

Anatomic lesions that lead to obstruction of the respiratory tree can mimic chronic bronchitis. Congenital heart disease should be considered in this patient population, and is evaluated best with clinical examination, chest radiograph ECG, and echocardiography. Mediastinal tumours, although uncommon, can produce extrinsic obstruction leading to recurrent cough & wheezing. The infant with chronic cough, poor feeding habits, and failure to thrive should be evaluated for gastro-oesophageal reflux, or tracheo-oesophageal fistula, identified most easily by barium swallow or PH probe monitoring **(FRank A. Oski et al., 1990).**

Treatment of Chronic bronchitis:

Bronchiodialtors (Theophyllin preparations, B-adrenergic agents, cromolyn sodium, corticosteroids) are used when deemed appropriate in the management of chronic cough assocaited with asthma.

It is imperative that patients with chronic pulmonary disease as a result of asthma understand the pulmonary irritant effect, and possibly additive reduction in pulmonary function caused by tobacco smoking, dust exposure, and air pollution.

In addition, parents of these children should be made aware of the effects of passive smoking on the already compromised pulmonary function of their children, and should be encoraged to stop smoking.

Antimicrobial therapy in chronic bronchitis is reserved for patients with severe illness in whom the likelihood of 2ry bacterial infection is great. In those instances, therapy usually consists of Ampicillin (75 mg/Kg/day), Erythromycin (40 mg/kg/day). For patients recieving theophyllin therapy who also have a bacterial infection, it is important to remember that use of certain antibiotics (erythromycin) can be associated with elevated serum concentration of theophyllin, making toxicity to the latter most likely. Sequential monitoring of pulmonary function studies is important.

The prognosis for the chronic bronchitis complex is varied and depends on the specific diagnosis.

II- Bronchial asthma:

It is estiamted that 5-10% of children will at some time during childhood have signs and symptoms compatible with asthma, prior to puberty sex incidence is equal.

Asthma could be defined as diffuse obstructive lung disease with:

- hyperreactivity of the airways to a variety of stimuli.
- high degree of reversibility of the obstructive process, which may occur either spontaneously or as a result of treatment.

Irritability or hyper-reactivity of the airways is manifest as bronchoconstriction after exercise, natural exposure to irritants, fumes and odors, tobacco smoke cold air.

Exacerbations of asthmatic attacks occur during viral respiratory infections, after exposure to air pollutants or allergens **(Blair, 1977).**

About 80-90% of asthmatic children have their first symptoms before 3-5 years of age.

The prognosis for young asthmatic children is generally good, the condition will get better depending in significant part upon growth in the cross sectional diameter of the airways. About half of all asthmatic children will be virtually free of symptoms by the time they reach adulthood **(Nelson, 1984).**

The etiological causes of Asthma are biochemical, autonomic, immunologic, infectious, endocrine, and psychologic factors in varying degrees in different individuals.

The onset of an attack of asthma may be acute or insidious. Recurrent episodes of coughing and wheezing, particularly accentuated by exercise are features of asthma. Some patients present with persistent chronic non-productive cough, particularly at night after going to bed.

When the attacks of asthma are due to exposure to allergenic environmental factors (dust, pollen, and food), most often these patients have increased concentrations both of total IgE, and of specific IgE against the allergen.

RSV is the most important productive factor of asthma, as well as para-influenza virus, in older children rhinovirus has been implicated **(Doushey et al., 1980).**

Morbidity from asthma in childhood and adolescense is considerable.

Despite the good level of awareness of asthma yet regular preventive therapy was reduced by $^{3}/_{4}$ in

those suffering from distrurbed sleep due to severe asthma.

Conversely there is over treatment with prophylactic drugs of many children suffering from mild infrequent asthma, this signifies the discripincy of managing cases of asthma in different localities and different studies **(Robertson et al., 1993).**

As regards treatment of asthma: oxygen given at a rate of 2-3 L/mn is indicated in most cases. Injection of epinephrine has been the treatment of choice, but bronchodilator aerosols are being increasingly used.

Some forms of theophyllin might be used in severe cases, However, in certain cases the prescription of prednisone in decreasing doses over a few days may be useful in hastening resolution of the exacerbation and causes no harm **(Narrish et al., 1977).**

III- Pneumonia:

The various clinical forms of pneumonia are often classified by their anatomic distribution, or by the agents which cause them, such as viral, bacterial, or aspiration pneumonia. Most bacterial infections are susceptible to antibiotic threapy, in contrast to viral pneumonia.

Pneumoncoccal pneumonia produces an inflammatory lesion of the mucosa and an alveolar exudate, usually without destruction of mucosal cells or extensive involvement of interstitial tissues. The gross lesion is a consolidation of all or part of a lobe in the lobar variety or of scattered lobules in the pneumonic variety.

In contrast viral agents H. influenza, and certain strains of the viridans group of streoptococci invade or destroy the mucous membrane and may produce principally bronchiolitis, peribronchiolitis, and interstitial lesions **(Nelson et al., 1984).**

Both staphylococcus and Klebsiella tend to destroy tissue and to produce multiple small abcesses.

The following classification is helpful in considering pneumonia in children:

1- Viral or probable viral pneumonia:

- Interstitial pneumonitis and bronchiolitis.
- Giant cell pneumonia.
- Influenza.

2- Bacterial infections:

- Pneumococcus.
- Streptococcus.
- Staphylococcus.
- H. influenza.
- Klebsiella.
- Tubercle bacillus.

3- Other infections:

- Pneumocystis carinii pneumonia.
- Q fever.
- Mycoplasma pneumoniae.
- Treponema pallidum.
- Nocardiosis.
- Actinomycosis.
- Chlamydia.
- Ornithosis.
- Psittacosis.

4- Myocotic infections:

- Aspergillosis.
- Coccidioidomycosis.
- Histoplasmosis.
- Blastomycosis.
- Mucomycosis.
- Sporotrichosis.
- Thrush.

5- Aspiration of:

- Amniotic contents (Fetal anoxia).
- Food.
- Foreign bodies.
- Zinc stearate.
- Dust.
- Hydrocarbons.
- Lipoid substance.

6- Loeffler syndrome.

7- Hypostatic pneumonia.

Bacterial pneumonia during childhood and recurrent pneumonia is the absence of an underlying chronic illness, such as cystic fibrosis, or immunologic deficiency, is quite unusual. In infants and children with lower respiratory tract infection signs and symptoms of pulmonary involvement are often non-specific, and findings of physical examiantion may be surprisingly few.

The most common event disturbing the defense mechanisms of the lung is a viral infection which alters the properties of normal secretions, inhibits phagocytosis, modifies the bacterial flora, and may temporarily disrupt the normal epithelial layer of the respiratory passages.

A viral respiratory disease often precedes the development of bacteiral pneumonia by a few days. Once pneumonia has occurred, a series of intricate mechanisms brings about resolution of infection and recovery.

Children with defects in defense mechanisms ,or in the chain of events involved in recovery from infection, experience recurrent pneumonia, or failure to resolve the disease completely. These defects occur with abnormalities of antibody function (agamma globulinemia), cystic fibrosis, cleft palate, congenital bronchiectasis, immotile cilia syndrome, tracheo-oesophageal fistula, abnormalities of the polymorphonuclear leukocytes, neutropenia, increased pulmonary blood flow, deficient gag reflex, ...etc. Among iatrogenic factors promoting pulmonary infection are trauma, anesthesia, and aspiration.

A- Viral pneumonia:

The type and severity of the illness are influenced by several factors including age, sex, season of the year, and crowding.

Pneumonia is most commonly due to RSV virus, less commonly rhinovirus, influenza virus, hewrpes simplex. Pneumonia might be preceded by rhinitis fever and

cough. Dyspnea with retraction and nasal flaring is more common in younger children and infants.

Viral pneumonia might be difficult to distinguish from bacterial pneumonia.

There is no specific treatment, in case of suspicion antibiotics are given initially, intravenous fluids, oxygen and even assisted ventillation might be needed.

Infections of the upper respiratory tract are the most common infections of humans, and concern that a child with a cold will "catch pneumonia" is widespread, the true relationship between these two infections is obscure. However, when examining children with respiratory complaints for evidence of pneumonia, most clinicians depend as much on breathing patterns, particularly tachypnea and flaring of the alae nasi as on auscultratory findings, rales may be heard, but signs of consolidation are infrequent. An elevated white blood cell count suggests a bacterial process, if the illness is persistent, although not necessarily progressive evidence of mycoplasma infection should be suspected. tuberculin test should be performed if encounter with M. tuberculosis has been at all likely **(Rubin, 1985).**

A chest radiograph is certainely helpful in identifying the presence and extent of pneumonia, but unless the child is severely ill or has a classic syndrome, the decision to treat with an antibiotic is usually made clinically.

Expectorants have not been shown to be of benefit at recommended dosages, and mist therapy as commonly used is ineffective.

In some children, pneumonia will be recurrent, and further investigation is then required, considerations include anatomic disorders such as right middle lobe syndrome, immunodeficiency and cystic fibrosis **(Kenneth B. Roberts, 1990).**

B- Bacterial pneumonia:

1- Pneumococcal pneumonia:

A mild upper respiratory tract infection characterised by stuffy nose, anorexia, precede the onset of pneumonia, this lasts for few days then ends by abrupt onset of fever 39°C, restelessness, apprehension and respiratory distrress, often cyanosis.

Respiratory distress is manifest by grunting, flaring of alae nasi, supraclavicular, intercostal, and subcostal retraction, tachypnea and tachycardia.

On auscultation decreased breath sounds, presence of pleural effusion or empyema should be suspected. Maningismus, paralytic ileus may be present.

Physical findings in the lung usually change little during the coarse of illness, although moist rales may be audible during resolution **(Nelson et al., 1983).**

Penicillin G is the drug of choice 50.000 IU/Kg/24 hrs. or procain penicillin 600.000 units single injection in older childrne, followed by oral penicillin V [50.000 IU/Kg/24 hrs.] Adjuncts to therapy include liberal oral fluids and aspirin for fever, oxygen administration should be given before cyanosis, as it will greatly reduce the need for sedation.

Polyvalent pneumonoccal polysaccharide vaccine has proved efficient in certain populations, such as patients with sickel cell anemia. However, its routine use in healthy children is not indicated **(Ammann et al., 1977).**

2- Streptococcal pneumonia:

Streptococcal pneumonia, and tracheobronchitis are uncommon but certain viral infections, particularly the exanthems and epidemic influenza predispose to these

diseases, which are most frequently encountered in children 3-5 years old, and very rarely in infants.

Clinical picture is similar to that of pneumonococcal pneumonia. Penicillin G is the drug of choice (100.000 IU/Kg/24 hrs), by parenteral route for 2-3 weeks, can be continued orally after clinical improvement.

In case of empyema, thoracocentheses should be imposed. Intrathoracic administration of antibiotics or enzymes to liquify pus or dissolve fibrin is ineffective **(Jay et al., 1975).**

3- Staphylococcal pneumonia:

S aureus pneumonia is a serious and rapidly progressive infection which, unless recognised early and treated carefully, is associted with prolonged morbidity ane mortality, it is more common in infants than in children.

Staphylococcus cause confluent bronchopneumonia which is often unilateral or more prominent on one side than the other, and is characterised by the presence of extensive areas of haemorrhagic necrosis and irregular areas of cavitation.

Most commonly the patient is an infant under 8 years of age with a history of staphylococcal skin lesion, with signs and symptoms of an upper or lower respiratory tract infection for several days to 8 weeks, then the condition changes with the onset of fever, cough, and respiratory disress. The patient is lethargic, but upon arousal is irritable and toxic. Sometimes assocaited vomiting, diarrhea, anorexia and abdominal distension secondary to paralytic ileus **(Rebban et al., 1960).**

Treatment:

Oxygen therapy, semisitting position, intravenous fluids and good nutrition, blood transfusion may be needed, and assisted ventillation might be indicated in severe cases.

Penicillin G is the drug of choice (100.000 IU/Kg/24 hrs).

IV- Suppurative lung syndrome: Bronchiectasis:

Bronchiectasis refers to dilatation of the bronchi associated with inflammatory destruction of bronchial and peribronchial tissue, accumulation of exudative material in dependent bronchi, and in some istances, distension of dependent bronchi.

Bronchiectasis might be congenital, or acquired after birth, usually the result of chronic pulmonary infection. Measles, pertussis, pneumonia, once regarded as frequent antecedent infections, are at present rare causes of bronchiectasis.

Cystic fibrosis is the most common underlying disease abroad in children with generalised bronchial involvement **(Camner et al., 1975).**

Other predisposing factors include inhalation of foreign body, often a nonopaque one, enlarged broncho-pulmonary nodes due to tuberculosis, asthma, allergy, emphysema, chronic lung infections, lung abcess, neoplasm and localised cysts.

Patients with immunodeficiency syndromes may have bronchiectasis usually after repeated attacks of bacterial pneumonia and bronchitis. The immotile cilia

syndrome results in chronic pulmonary infectin which eventually leads to bronchiectasis، Gastro-oesohageal reflux with chronic aspiration may be a cause of bronchiectasis **(Clark, 1963).**

Clinically:

Cough with copious mucopurulent sputum during acute respiratory infections.

Physical activity or change in position initiate a bout of coughing.

Recurring infections of the lower respiratory tract are common, they tend to persist and are difficult to control, anorexia, poor weight gain are common, fever is less common, hemoptysis might exist with variable severity, and bronchiectasis follows an intermittently improving and relapsing coarse **(Clark, 1963).**

V- Middle lobe syndrome:

This syndrome consists of subacute or chronic pneumonitis, bronchial obstruction, and atelectasis. This is generally due to extrinsic compression of the middle lobe by hilar nodes followed by peribronchitis and chronic infection. Clubbing fingers, moist rales may be present.

For every patient with suspected or diagnosed bronchiectasis the following causative factors must be looked for:

Agammalgobulinemia, immotile cilia syndrome, asthma, tuberculosis, or other respiratory allergy, and cystic fibrosis.

Bronchopscopy might be indicated to exlude stenosis, structures, tumours, foreign body, and then bronchography to determine the extense and severity of bronchiectasis.

A familial deficiency of bronchial cartilage has also been proposed **(Dees, 1966).**

Treatment consists of effective postural drainage, elimination of all septic foci, antibiotic therapy, prolonged antibiotic therapy might cause resistance, the antibiotic is selected according to culture and sensitivity of sputum got by bronchoscope.

Segmental or lobar resection should be considered in severe cases, and when a foreign body is inhaled, or an intrinsic anatomic obstruction exists **(Miller et al., 1972).**

VI- Immotile cilia syndrome : (Kartagener syndrome):

Kartagener initially described a group of patients all of whom had situs inversus, chronic sinusitis, and chronic bronchitis with bronchiectasis. The disease appears to be transmitted as an autosomal recessive with an incidence of about 1/3000 persons.

Bronchiectasis is a late complication, does not appear until early adult years, wheezing is common.

The disease should be suspected in children who have chronic sinusitis and otitis media in addition to bronchitis, in presence of situs inversus the diagnosis becomes certain, but definitive testing should be done **(Elrasson et al., 1977).**

Bronchoscopy may visualise decreased ciliary movements, another diagnostic test involves scraping the nasal mucosa about the first turbinate with an ear curette, brush, or swab, immediate suspension of mucosal cells in Hank saline and light microscope examination of ciliary activity.

Treatment is symptomatic, consists of close medical supervision with agressive antibiotic treatment of pulmonary infection, chest physiotherapy and broncho-dilators.

Early infection involves pneumonoccus and haemophilus **(Recklin et al., 1980).**

VII- Empyema (Purulent pleuresy):

This is defined as accumulation of pus in the pleural spaces. It is most often associated with pneumonia due to staphylococci, less frequently with pneumococci (especially type 1 and 3) and H-influenza.

In pediatrics, empyema is most frequently encountered in infants and preschool children **(Bechamps et al., 1970).** Most commonly purulent pleuresy consists of a series of loculated areas involving a large portion of one or both pleural cavities. If the pus is not drained it may dissect through the chest wall and into lung parenchyma producing bronchopleural fistula.

The clinical manifestations mostly occur during the coarse of pneumonia, the initial signs and symptoms are preliminary those of the underlying disease. In case of inappropriate antibiotic therapy, an interval of a few days may occur between the clinical phase of pneumonia and the evidence of empyema with fever toxemia, respiratory distress, chest pain. Thus empyema may be synpneumonic or post pneumonic.

Culture of pus should be done to recognise the microorganism.

Management consists of drainage of pus by thoracocenthesis, adequate draiange by underwater seal or by continuous suction **(Murphy et al., 1980).** Sometimes several tubes are needed to drain loculated areas. The local instillation of proteolytic substances or fibrinolytics is harmful in children as it may cause systemic reactions. Local antibiotics are not preferered as they produce local reactions.

Systemic antibiotics are given according to culture and sensitivity **(Siegel et al., 1978).**

VIII- Tubreculosis:

Tuberculosis is acquired by inhaling small droplet nuclei contaminated with mycobacterium tuberculosis. The usual source is an infected adult, coughing with sufficient force to expel and propel 5-u particles, small children with tuberculosis are unable to propel particles with much force and so are rarely infectious to others **(Starke, 1988).**

M. tuberculosis once inhaled into the lung, elicits an inflammatory response, producing a small area of pneumonia that is rarely recognised cliniclaly.

After 3-8 weeks, the tuberculin reaction becomes positive, signaling a host response to the infection, at this stage it is still unusual for clinical signs of illness to be recognised, except in infants, nearly half of whom may be symptomatic **(Koch, 1982).**

The area of pulmonary involvement is usually not identified on a chest X-ray, but M. tuberculosis organisms may be recorded from early morning gastric aspirates in 10-25% of children, if a lesion is demonstrable on an X-ray film the rate of bacteriologic confirmation is increased to as high as 80-90%.

In some infants and childrne, the primary infection is not well contained, and an area of caseation enlarges, ultimately spilling into the bronchi and leaving a cavity (progressive primary pulmonary tuberculosis).

If the bronchus is occluded, eithre by endobronchial disease or by extrinsic compression from enlarged nodes, the so called collapse consolidation lesion is formed **(Kenneth B. Roberts, 1990).**

A segmental or lobar opacity seen on chest radiograph is often termed epituberculosis, it represents a consolidated area resulting from erosion of bronchus and local spread of tuberuclous material.

The caseous material may trigger hypersensitive reaction, in additions to the mechanical one.

During the initial phase of infection, prior to the development of hypersensitivity to tuberculin, the bacilli gain access to the circulation and are distributed throughout the body. The majority of infants and children contain their primary infection well, but distant foci persist in a dormant stage.

Miliary tuberculosis is not synonymous with the early bacteremia but represents a massive hematogenous seeding, usually of a large pulmonary vein by a caseous focus.

Despite the extensive characteristic pulmonary invovement seen on the chest X-ray, auscultation may give few clues to the degree of involvement. Organomegaly is often present **(Snider et al., 1988).**

Once the diagnoss of tuberculosis is considered clinically, additional support is provided by the demonstration of a positive reaction of 5 tuberculin units (TU) of intracutaneously administered tuberculin (PPD-S, purified protein derivative standard).

10 mm of induratin 48 hours after inoculation is considered a positive reaction, but under certain

circumstances, such as recent exposure to tuberculosis or severe illness compatible with tuberculosis, 5 mm and 10 mm may be difficult to determine, the response may be caused by mycobacterium other than M. tuberculosis, such as bacillus calmette-Guerin (BCG) strain, or the so called atypicals, often the history or the simultaneous administration of different mycobacterial antigens as skin test along with PPD-S will help resolve confusion **(Snider, 1985).**

The treatment is largely determined by the extent of the disease.

For the child with a positive tuberculin reaction but no evidence of active disease, isoniazid for 9 months as the sole therapy prevents the development of active disease, the protection appears to be long lasting, and toxicity, including hepatitis, is rare in children **(Keneth B. Roberts, 1990).**

Mild pulmonary disease demonstrable by a chest X-ray prompts the addition of a second oral medication.

For more advanced disease, a third drug, classically streptomycin, previously was recommended, at present, the combination of isoniazid and rifampin appears to be at least as effective as the older three drug regimens,

and has the advantage of better entry into the CSF. Currently recommended duration of therapy for children not suspected of having drug resistant organisms is 9 months.

Isoniazid and rifampin are prescribed for daily administration for the entire course or more commonly now, for the first 1-2 months, followed by twice weekly doses for the remaining 7 to 9 months.

Because the duration of therapy is shorter than formerly recommended and supervised administration on an ambulatory basis is feasible, "short course" therapy offers the potential of maximising compliance **(Keneth B. Roberts, 1990).**

Accurate diagnosis and treatment are necessary not only for the individual child but also as an integral part of tuberculoosis eradication, since the child, once infected, is at life-long risk for developing the disease and for infecting others **(Starke, 1988).**

Public health investigation of new cases remains an important activity in the control of tubrculosis. Household contacts of a person with newly diagnosed active disease have about a 3% risk of the development

of active tuberculosis within 1 year if not treated: the rate is twice that high for infants and young childrne.

Since 3 to 8 weeks are required after exposure before hypersensitivity to tuberculin develops, the tuberculin test must be repeated in exposed persons if there is a negative reaction at the time contact with the source of infection is broken.

The administration of isoniazid is a logical preventive measure while waiting for the 8 weeks to elapse before determining whether or not infection has occurred **(Snider et al., 1989).**

i- Cystic fibrosis:

Cystic fibrosis is a multisystem disorder of children and adults characterised chiefly by chronic obstruction and infection of airways and by maldigestion and its squences.

Abraod, cystic fibrosis is an important pediatric problem for a number of reasons, it is the major cause of severe chronic lung disease of childrne. It is responsible for most exocrine pancreatic insufficiency

during early life, it is also responsible for many cases of childhood nasal polyposis, pansinusitis, rectal prolapse, and hyperglycemia unrelated to diabetes mellitus.

In addition cystic fibrosis may present as failure to thrive and occasionally as cirrhosis or other forms of hepatic dysfunction. Therefore, this disorder enters into the differential diagnosis of many pediatric conditions.

The sweat test: using pilocarpin to colelct sweat, and chemical analysis of its chloride content (Q), stimulating the skin of the forearm after washing the arm with distilled water., sweat is collected on filter paper which has been placed on the stimulated skin and covered to prevent evaporation.
After 30-60 min, the filter paper is removed, weighed and eluted in distilled water.
For reliable results at least 50 and preferably 100 mg of sweat should be collected.
In infants, it may be necessary to use the upper back to obtain enough sweat, the test is difficult in 1st 2 wks due to low ant of sweat.
up to 20 yrs, >60 mEq/l of chloride in sweat is diagnostic of cystic fibrosis, 40-60 mEq/l are suggestive.

SUBJECTS AND METHODS

The subjects of study consisted of 43 males, 25 females aged 14 months - 12 years. All targets were suffering from recurrent chest infection, they were randomly selected from Out Patient Clinic of Chest Diseases, Children'sd Hospital, Cairo University, during a period of 3 years.

Criteria for selection of patients depended on the following:

- History of at least 4-5 attacks of prolonged chest infection per year.

- Inadequate response to rational treatment of lower respriatory airway infections.

Collective Table Showing first group (46 patients) with laboratory investigations.

Nbr.	Sex	Age	Diagnosis
1	M	4 yrs	Bronchiectasis
2	M	2 yrs	Bronchiectasis
3	M	12 yrs	Br. pneumonia
4	M	9 yrs	Bronchitis
5	F	3 yrs	Bronchiectasis
6	M	14 mo	Bronchitis
7	M	2.5 yrs	Br. pneumonia
8	M	4 yrs	Bronchitis
9	F	10 yrs	Br. pneumonia
10	F	3 yrs	Br. pneumonia
11	M	12 yrs	Bronchiectasis
12	M	3.5 yrs	Br. pneumonia
13	F	6 yrs	Bronchiectasis
14	F	3 yrs	Br. pneumonia
15	M	4 yrs	TB
16	F	8 yrs	Br. pneumonia
17	F	3 yrs	Br. pneumonia
18	F	5 yrs	Br. pneumonia
19	F	11 yrs	Br. pneumonia
20	M	3 yrs	Bronchitis
21	F	8 yrs	Br. pneumonia
22	M	3 yrs	Br. pneumonia
23	F	6 yrs	Bronchiectasis
24	M	2 yrs	Bronchitis
25	F	12 yrs	TB
26	M	11 yrs	Bronchiectasis
27	M	9 yrs	TB
28	M	11 yrs	TB
29	F	11 yrs	Br. pneumonia
30	M	16 mo	Br. pneumonia
31	M	6 mo	Bronchopneumonia
32	F	6 mo	Bronchitis
33	M	2 yrs	Bronchitis
34	M	1.5 yrs	Br. pneumonia
35	M	5 yrs	Bronchitis
36	F	4 mo	Br. pneumonia
37	M	6 yrs	Bronchitis
38	F	11 yrs	Bronchitis
39	M	1.5 mo	Br. pneumonia
40	M	4 yrs	Bronchitis
41	M	2.5 yrs	Bronchitis
42	M	4.5 yrs	Br. pneumonia
43	F	1.5 yrs	Bronchitis
44	M	3.5 mo	Bronchitis
45	F	6 mo	Br. pneumonia
46	F	9 mo	Bronchuectasis

50 normal childrens aged 6 months to 12 years: 35 males, 15 females, not suffering from any past or present disease living under the same socioeconomic and hygienic conditions were selected as controls, they were selected from healthy associates of Out Patient Clientels or from there coming for routine check up.

Patients were subjected to careful detailed history, thorough clinical examination with patients stress on past history, vaccination, family history.

Patients with secondry recurrent chest diseases associated with other elements (congenital or acquired), and their final respiratory diagnosis, sex, and age.

Nbr.	Sex	Age	Chest problem
47	F	11 years	Right lobar pneumonia
48	F	1 year	Bronchopneumonia, consolidation
49	M	6 months	Lung abcess
50	F	16 months	Suppurative lung syndrome
51	M	8 months	Bronchopneumonia
52	M	9 years	Kartagnar syndrome
53	M	4 months	Pneumonia
54	M	12 years	Pneumonia, lung abcess
55	M	6 months	Pneumonia
56	M	7 months	Bronchitis
57	M	1 year	Pneumonia consolidation collapse
58	M	5 years	Lung abcess
59	M	9 months	Pneumonia
60	F	2 years	Pneumonia
61	M	1½ year	Suppurative lung syndrome
62	M	1½ year	Lobar pneumonia
63	M	1½ year	Bronchopneumonia
64	M	2 years	Chronic bronchitis
65	M	4 months	Bronchopneumonia
66	F	4 years	Bronchopneumonia
67	M	11 Months	Pneumonia
68	F	18 Months	Pneumonia

Controls (50) were devided as well into 3 age groups:

Age group	Number	M	F
up to 2 years	10	5	5
2 - 5 years	15	15	-
5 - 12 years	25	15	10

Patients who were randomly chosen were subjected to careful detailed history, thorough clinical examination, the history includes the presenting complaint, present history: fever, cough, expectoration, hemoptysis, dyspnea, cyanosis and any other complaint related to other system.

Past History: of previous illness with special stress on TB, whooping cough, tonsillitis, or similar conditions, and any other history of admission to hospital.

History of vaccination: specially BCG vaccine for TB.

Family History: of any respiratory complaint with particular stress on contageous diseases (Whooping cough, TB), any history of tuberculous contact, allergy, smoker parent, similar conditions ....etc.

Nutritional History: According to (Menu) different food items in 24 hours for 7 successive days in order to recognise the main types of nutrients in the patient's food. Accordingly patients were categorised into: inqdequate protein intake, adequate protein intake, good protein intake.

Socioeconomic study was found essential for these patients to assess any correlation between the recurrence of chest infection and the socioeconomic status of the patient.

The following parameters were used:

1) Father's work.
2) Paternal educational level.
3) Mean monthly income/capitum.
4) Maternal educatinal level.

Paternal educational level was excluded as it does not affect the accuracy of results, in the presence of least possible number of parameters.

From a study done by Abdel Ghaffar and Kashkoush (1978) that included 5000 families:

(1) Father's Work A_1:

1st level: Industrial and agricultural common workers, and similars (Labourers).

2nd level: Technicians, government employmees, with below average standard graduation and similars.

3rd level: Co-directors, in governmental units and similars.

5th level: Business men, commercials, and similars.

6th level: University graduate employees, and junior military persons and similars.

7th level: Chief governmental directors, doctors, engineers, lawyers, senior military persons and similars.

8th level: Directors of city council, university professors, consultants, and similars.

9th level: Co-ministers, and governorers.

(2) Mean monthly income/member A_2:

less than 5 pound	1
5- less than 10 pounds	2
10-15 pounds	3
15-20 pounds	4
20-25 pounds	5
25-30 pounds	6
30-35 pounds	7
35-40 pounds	8
40-45 pounds	9
above 45 pounds	10

These levels are variable according to the economy of the family.

(3) Mother's educational level A_3:

Grade 1: Ignorant	1 point
Grade 2: Writes and reads	2 points
Grade 3: Primary school certificate	3 points
Grade 4: Preparatory school	4 points
Grade 5: Secondary school graduate	5 points
Grade 6: University graduate	6 points
Grade 7: High studies	7 points

The equation used to predict the socioeconomic scoring for each patient is:

$$B = 0.16 + (A_1 \times 0.44) + (A_2 \times 0.45) + (A_3 \times 0.15)$$

Scoring is 1.2 - 9.67.

In order to facilitate the use of this equation, results were mutliplied x 10.

Thus B x 10 will make results ranging between 12-97, and socioeconomic scoring was classified as follows:

Very low	12-20
Low	21-29
Below average	30-42
Average	43-60
Over average	61-71
High	72-84
Very high	85-97

For simplicity and clarity, these different classes are further categoriesed into only 3 groups:

Poor	12-29
Moderate	30-60
Rich	61-97

Blood samples: were got by sterile syringe from patients and controls, after cleansing the skin with antiseptic.

The sample was obtained in plastic dry tubes in order to do the following tests; serum should be as fresh as possible.

- Serum immunoglobulins: IgA, IgG, IgM, IgE.
- Soluble interleukin-2 receptors in serum.

5 ml of the blood sample was put in test tube with EDTA in order to do CBC.

The following is a description of the technical principle for the laboratory tests which have been done:

IgA, IgG, IgM were calculated in serum by radioimmunodiffusion, IgE by ELISA technique as well as IL-2 R.

(1) IgA:

The technique used is Nor-Partigen IgA (Behring): (Immunodiffusion plate for determination of human IgA).

Nor Partigen IgA contains monospecific antiserum to human IgA/chain in a ready for use agarose-gel layer, the antiserum is obtained by immunisation of rabbits.

We use serum or plasma samples which are as fresh as possible or have been stored deep frozen.

With Nor Partigen IgA both control serum and standard solutions, and the specimens to be examined are applied undiluted, the volume required per well is 0.005 ml.

For checking the accuracy of Nor Partigen IgA, introduce control serum for Nor Partigen well 1. Wells 2-12 are intended for the specimens to be examined.

After expiration of a diffusion period of 2 days measure the diameters of the precipitates to an accuracy of 0-immusing a suitable dévice such as a scaled magnifying glass against a black background with lateral illumination **(Geiger et al., 1970).**

(2) IgG, IgM:

Same previous technique for IgA is used for both IgG and IgM, same principle by the use of Nor Partigen immunodiffusion plate for determination of human IgG and IgM doses are explained in mg/ml.

(3) IgE: Enzygnost - IgE monoclonal (Boehring).

IgE is calculated by the IgE enzyme immunoassay (EIA) test kit for the in vitro quantitative measurement of human immunoglobulin E in human serum, also described as sandwich immunoassay: an anti-IgE, which is coupled to a solid phase (paper disc, plastic bead, etc.(, binds the patient IgE molecule.

The IgE bound is then identified with an enzyme or isotope labelled anti IgE reagent.

The IgE in the patient's serum is bound to a bead coated with an anti-IgE antibody. An enzyme labelled anti-IgE also binds the IgE and completes the sandwich. Next the bead is washed which carries away any unbound antibody enzyme conjugate. The bead is then incubated with a substrate for the enzyme.

The product of the enzyme substrate reaction forms a colored complex when the stopping agent is added to the tube, the greater the amount of IgE in the patient sample, the greater the amount of enzyme conjugate bound to the bead and, therefore, more of the colored complex will be produced. The intensity of the color is measured spectrophotometrically.

An IgE standard calibration is prespared relating intensity of the color to the concentration of IgE, the concentration of IgE in the patient's sample is calculated from this calibration.

Serum samples should be separated and immediately stored tightly capped.

IgE results are expressed in IU/ml.

(Eriqui et al., 1987)

(4) Interleukin:

This is measured by the intertest-2X™ human interleukin-2 ELISA Kit, which is an immunoassay for the quantitation of natural or recombinant human interleukin (IL-2) levels in serum.

This test is a solid phase enzyme immunoassay employing the multiple antibody sandwich principle.

A 96-well microtiter plate, precoated with mouse monoclonal antibody specific for human IL-2, is used to capture IL-2 present in standard and unknown samples.

An anti-IL-2 polyclonal antibody which binds to multiple epitopes on captured IL-2 is added.

Next, a peroxidase, conjugated goat anti-rabbit polyclonal antibody is added to each well. Addition of peroxidase/TMB substrate solution initiates a peroxidase catalyzed color change which is stopped within 5 minutes by acidification with stop solution.

The absorbance measured at 450 nm is proportional to the concentration of IL-2 present in the samples.

A standard curve is obtained by plotting the IL-1 standards versus absorbance. The IL-2 concentration in experimental sample are then determined from the standard curve **(Enders et al., 1989).**

The 22 patients out of the 68 patients included in this work were diagnosed as recurrent chest infection secondary to a predisposing factor diagnosed already by radiological investigations, and laboratory tests, these factors included: mental retardation, cerebral palsy IgA deficiency, FB inhalation, Down's Syndrome, immotile cilia syndrome, etc ...

So when the etiology of recurrent chest infection is evident, for example, as in Down's Sydnrome, no need for invasive laboratory investigations, this will save both time and cost.

These cases were also categorised according to their clinical diagnosis into:

Chronic Bronchitis	2 cases
Bronchopneumonia	16 cases
Tuberculosis	2 cases
Cystic fibrosis	2 cases

Every subject was submitted to very careful clinical examination with particular stress on respiratory system according to the following sheet:

Date: Serial No.:

Patient's name: Serial order in family:

Father's name : Work:

Mcther's name : Educational level:

Date of birth : Sex:

No. of family members: Mean monthly income/member

Adress:

Nutritional assessment: 24 hours food intake for 7 following days:

Time	Type of food	Amount	Mode of preparation
Breakfast			
Before lunch			
Lunch			
Before dinner			
Dinner			

History:

* Complaint:

- Cough Productive Dry Relation to posture
- Fever Diurnal Nocturnal
- Dyspnea At rest Exertional Orthopnea
- Chest pain Location
- Anorexia Vomiting
- Loss of weight Constipation
- Pallor Abdominal pain

- Cyanosis Central Peripheral
- Bone pains Site
- Irritability Headache Convulsions
- Allergic manifestations
- Other complaints

* Present history:
  - Onset:
  - Duration:
  - Course:

* Past history:
  - Similar condition:
  - Related to seasons:
  - Drug intake:
  - Foreign body inhalation:
  - Admission to sanatorium or chest hospital:
  - Other diseases:

* Family history:
  - Health of father Mother
  - TB: Allergy:
  - Smoker parent:
  - Health of sisters Brothers

- Neighbours & contacts:

* Milestones (developmental history):

Sitting Crowling

Talking Teething

Stool continence Urine continence

* Vaccinations:

- BCG: Time Scar No scar
- Booster BCG
- DPT Boosters
- Polio Boosters
- Measles

* Examination:

Anthropometry:

Body weight Height - Length

Mid arm circumferance Head circumferance

Skinfold thickness

Subscapular

Triceps

Biceps

* General examination:

Temperature Heart rate: Respiratory rate:

Blood pressure:

Toxemia

Cyanosis Pallor

Oral thrush Angular stomatitis

Puffed eyelids Conjunctivitis

Working alae nasi

Neck: Lymph nodes Vessels Thyroid

Lymphadenopathy

Clubbing fingers

Oedema of lower limbs

Vertebral column

* Chest examination:

* Chest examination:

Inspection:

- Shape — Movements
- Retraction — Bulging — Dilated veins
- Sinuses or fistula — Costal margin
- Apex beat — Position
- Scar or site of operation

Palpation

- Movements
- Tactile vocal rhonchi
- Palpable rhonchi
- Apex beat
- Trachea: central
  shifted: to R
  - L

Percussion:

- Normal resonance
- Hyper resonance
- Impaired note
- Stony dullness

Auscultation:

Breath sounds

- Normal
- Diminished
- Bronchial

Adventitious sounds

- Rhonchi
- Sibilant
- Sonorous
- Crepitations
  - Fine
  - MSC
  - GGG

Right		Left	
Front	Back	Front	Back

Heart	Abdomen	CNS

Provisional diagnosis

Lab. investigations:

(1) X-ray chest.

(2) Complete blood picture

(3) IgA IgM

IgG IgE

(4) SIL - 2 R

Anthropometric measurements including body weight, height or length, head circumference, triceps skin fold, mid arm circumference, and arm muscle area were done.

* Stature (height in standing position) is usually measured for children aged above 3 years.

Length (height in recumbant position) is usually used to measure children below 3 years old. So in this study we use both methods.

In the recumbant length the child lies on the supine length table after removing his shoes and socks, with the head in the supinated Frankfurt plane (the eyes looking directly upward and the lower border of the eyes in the same vertical plane as the upper margin of the external auditory meatus), we apply downward pressure on the shoulders to prevent arching of the back and to bring the head into contact with the fixed head board.

We also apply slight pressure on the knee while maintaining a firm grip to the child's foot to ensure that the legs are straight, ankles at right angles, and toes pointing directly upwards.

Then, we bring the movable foot board into firm contact with the child's heals, and measure the distance between the two boards in centimeters.

* Triceps skinfold: The child stands with his back to the measurer and his arm relaxed with the palm facing the lateral thigh. The skinfold is picked up over the posterior surface of the triceps muscle 1 cm above the mark (which is midway between the olecranon and acromion processes) and the caliper jaws are applied at the marked level.

* Arm muscle area:

Frisancho (1981) recommended that assesment of nutritional status can be made on the basis of area of fat and areas of muscle rather than direct skinfold thickness and arm circumference.

To obtain indices of fat area, or of muscle area in cross section of the arm, we can measure arm circumference and triceps skinfold thickness **(Alex P. Roche, 1985).**

The equation used for calculation of arm muscle area is:

$$AMA = \frac{MAC - (3.14 \times TSF)^2}{4}$$

AMA = arm muscle area TSF = triceps skinfold

MAC = midarm circumference.

46 Patients out of 66 patients included in this work have been submitted to radiological investigations and to the following laboratory investigations:

- Complete blood picture
- Immunoglobulins IgA, IgG, IgM, IgE
- Interleukin-2-receptors in serum.

At times, different laboratory procedures were carried out according to clinical state of the subject: Chromosomal study for Down's Syndrome, sweat test for cystic fibrosis.

The 46 patients for whom laboratory tests were done, were categorised according to their presenting diagnosis, signs and symptoms into 5 subgroups:

- Chronic Bronchitis 7 patients
- Bronchial asthma 7 patients
- Bronchopneumonia 20 patients
    * Pneumonia
    * Empyema
    * Pleural effusion
    * Consolidation collapse
    * Lung abscess
- Bronchiectasis 8 patients
- History of pulmonary TB 4 patients

Full laboratory investigations were also performed for controls.

RESULTS

Table (1): Sex, Age socioeconomic standard of the subject of study diseased and controls.

Variable	Patients		Controls	
1- Sex	**Number**	**%**	**Number**	**%**
Male	43	63.23	35	70%
Female	25	36.77	15	30%
Total	68		50	
2- Age				
< 2 years	22	32.35	10	20%
2-5 years	21	30.88	15	30%
5-12 years	25	36.77	25	50%
3- Socioeconomic state				
Poor	29	42.65	15	30%
Moderate	33	48.53	35	70%
Rich	6	8.82	-	-
4- Parental smoking				
Smoking	43	63.23	5	10%
Not smoking	25	36.77	45	90%

Figure (1): Sex disribution of the studied patients and their parallel control

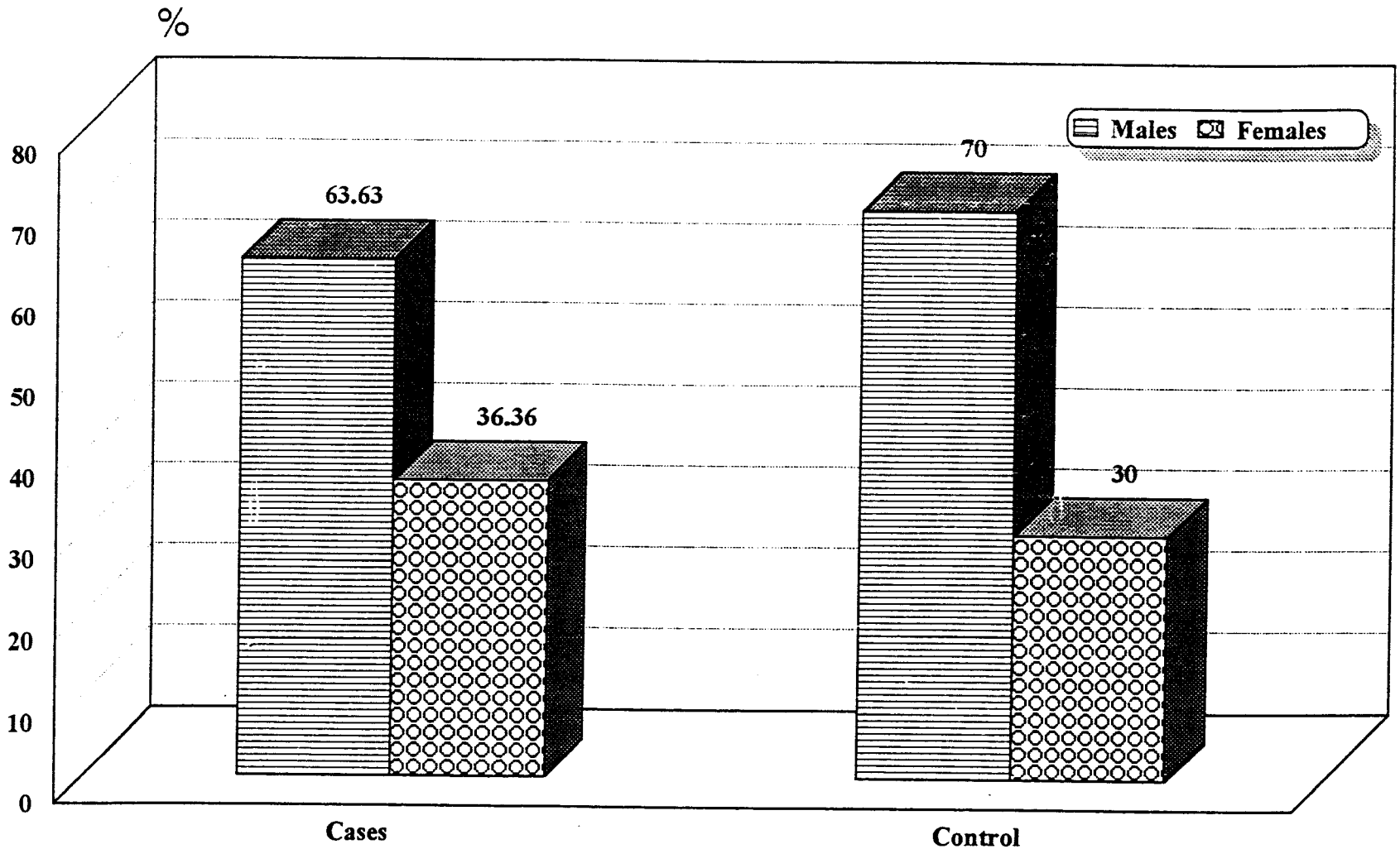


Figure (2): Age distribution of the studied patients and their parallel controls.

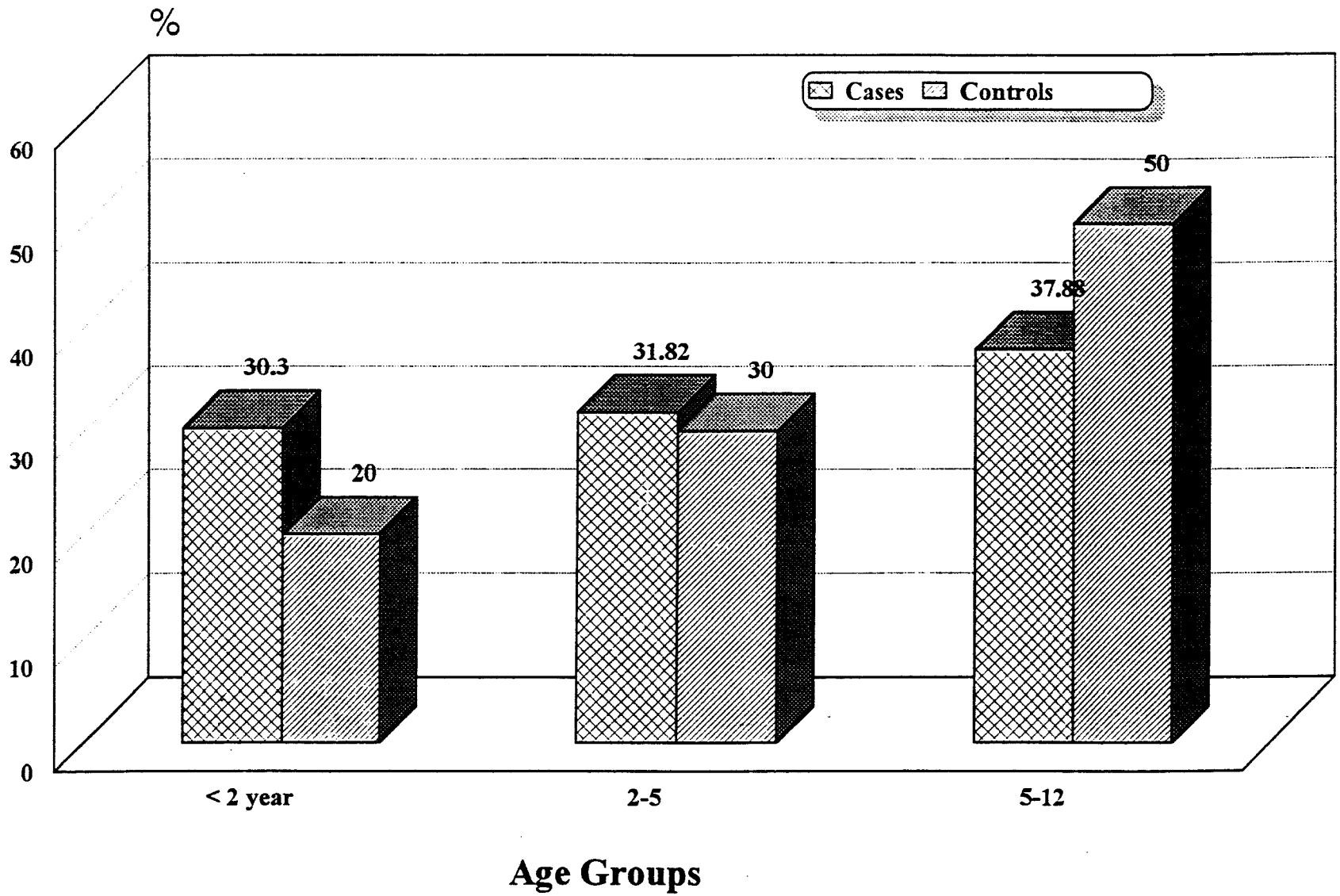


Table (2): Sex and age distribution among patients.

Age group	Male	Female	Total
< 2 years	5	6	11
2-5 years	4	13	17
5-12 years	10	8	18
Total	19	27	46

Table (3): Comparative points in patient's sheet.

Variable	Number	Percentage
1- Family history		
No	50	73.53%
Yes	18	26.47%
2- Vaccination		
Yes	66	97.05%
No	2	2.94%
3- Animal Protein intake		
deficient	31	45.59%
proper	28	41.18%
ample	9	13.23%

Table (4): Anthropometric measures.

Nbr.	Age	Sex	B.W.	Higher	MAC	HC	TSF	AMA
1	4 yrs	M	11 kg	100 cm	16 cm	49	2.4 mm	5.7 cm^2
2	2 yrs	M	8 kg	74 cm	12 cm	45	32 mm	9.6 cm^2
3	12 yrs	M	22 kg	123 cm	19 cm	53	5.5 mm	25 cm^2
4	9 yrs	M	36 kg	134 cm	22 cm	52	8 mm	30 cm^2
5	3 yrs	F	10 kg	87 cm	12.5 cm	47	5 mm	9.5 cm^2
6	14 mo	M	12 kg	82 cm	16 cm	45	7.5 mm	14.8 cm^2
7	2.5 yrs	M	12 kg	91 cm	14 cm	49	6 mm	11.7 cm^2
8	4 yrs	M	15 kg	103 cm	15.5 cm	52	7 mm	14 cm^2
9	10 yrs	F	23 kg	138 cm	16 cm	53	5 mm	16.6 cm^2
10	3 yrs	F	11 kg	92 cm	14 cm	48	7 mm	11 cm^2
11	12 yrs	M	25 kg	129 cm	20 cm	51.5	6.5 mm	25.7 cm^2
12	3.5 yrs	M	9 kg	82 cm	11½ cm	48	4 mm	8.4 cm^2
13	6 yrs	F	15 kg	108 cm	16 cm	49	7 mm	15 cm^2
14	3 yrs	F	13 kg	95 cm	16 cm	47	9 mm	13.8 cm^2
15	4 yrs	M	20 kg	107 cm	17 cm	55	7 mm	17.4 cm^2
16	8 yrs	F	23 kg	127 cm	18 cm	51	7.5 mm	19.5 cm^2
17	3 yrs	F	11 kg	90 cm	15 cm	49	7 mm	13 cm^2
18	5 yrs	F	17 kg	105 cm	16 cm	49	6 mm	15.8 cm^2
19	11 yrs	F	33 kg	143 cm	20 cm	52	11 mm	30.8 cm^2
20	3 yrs	M	16 kg	101 cm	16 cm	50	6 mm	15.8 cm^2
21	8 yrs	F	32 kg	124 cm	21 cm	53	13 mm	33.8 cm^2
22	3 yrs	M	10 kg	85 cm	13.5 cm	49.5	5 mm	11 cm^2
23	6 yrs	F	12 kg	104 cm	12.5 cm	49	4.5 mm	9.8 cm^2
24	2 yrs	M	10 kg	81 cm	15 cm	49	6 mm	13.7 cm^2
25	13 yrs	F	43 kg	148 cm	22.5 cm	54	13 mm	38.7 cm^2
26	11 yrs	M	20 kg	126 cm	15 cm	51	4 mm	15 cm^2
27	9 yrs	M	20 kg	130 cm	14.5 cm	49	4 mm	14 cm^2
28	11 yrs	M	32 kg	141 cm	18.5 cm	54.5	6 mm	22 cm^2
29	11 yrs	F	32 kg	145 cm	19 cm	51	6 mm	23 cm^2
30	16 mo	M	10 kg	80 cm	12 cm	46	5 mm	8.7 cm^2
31	6 mo	M	7 kg	63 cm	5 cm	45	3 mm	7 cm^2
32	6 mo	F	6 kg	62 cm	4.5 cm	43	3 mm	6.5 cm^2
33	2 yrs	M	8 kg	74 cm	12 cm	45	3.2 mm	9.6 cm^2
34	1.5 yrs	M	10 kg	80 cm	12 cm	46	5 mm	8.7 cm^2
35	5 yrs	M	17 kg	105 cm	16 cm	49	6 mm	15.8 cm^2
36	4 mo	F	5.5 kg	59 cm	4	38	2 mm	5 cm^2
37	5 yrs	M	15 kg	108 cm	16 cm	47	9 mm	13.8 cm^2
38	11 yrs	F	33 kg	143 cm	30 cm	52	11 mm	30.8 cm^2
39	1.5 mo	M	4.5 kg	54 cm	3 cm	38	2 mm	4 cm^2
40	4 yrs	M	11 kg	100 cm	16 cm	49	2.4 mm	5.7 cm^2
41	2.5 yrs	M	12 kg	91 cm	14 cm	49	6 mm	11.7 cm^2
42	4.5 yrs	M	20 kg	107 cm	17 cm	55	7 mm	17.4 cm^2
43	1.5 yrs	F	10 kg	78 cm	12 cm	47	4.8 mm	9 cm^2
44	3.5 mo	M	16 kg	61 cm	4 cm	40	3 mm	5 cm^2
45	6 mo	F	5.5 kg	68 cm	5 cm	43	3 mm	7.5 cm^2
46	9 mo	F	8 kg	71 cm	7 cm	48	4 mm	9 cm^2

B.W. = body weight
HC = head circumferance
MAC = mid arm circumferance
L = Length
AMA = arm muscle area
TSF = triceps skin fold.

These are patients for whom laboratory tests were done.

Table (5): Weight/height % in patients in relation to age of subjects.

Frequency	%
15	5th %
4	10th %
10	25th %
6	50th %
8	75th %
2	90th %
3	95th %

According to National Center for Health Statistic (NCHS), Health Resources Administration.

(Nelson, 1983, p. 32-33).

Any patient below 50th % in weight/height % is considered malnourished.

72% of patients are < 50th percentile.

Table (6): Showing percentage distribution for each type of respiratory infections in patients in relation to age.

Diagnosis	Age group			
	2 years	2-5 years	5-12 years	%
Chronic bronchitis	2	3	2	15.22
Bronchial asthma	1	4	2	15.22
Bronchopneumonia	6	7	7	43.48
Bronchiectasis	1	3	4	17.39
Tuberculosis	-	1	3	8.69

Table (7): Mean and SD of laboratory results in patients and paralell controls.

	IgA	IgG	IgM	IgE	IL-2
Patients					
Mean	164.4	1587.78	252.45	246.30	601.96
±SD	115.48	687.6	138.06	281.43	256.72
Controls					
Mean	57.0	1274.7	202.20	136.5	550.5
±SD	41.92	447.21	87.29	257.76	232.85
Significance	significant	non significant	significant	non significant	non significant
P	<0.05	>0.05	<0.05	>0.05	>0.05

Table (8): Mean and standard devaitoin of laboratory results in patients and parallel controls in different socioeconomic classes.

Socioeconomic level	number	IgA		IgG		IgM		IgE		IL-2	
		X	SD	X	SD	X	SD	X	SD	X	SD
Poor	19	135.42	85.25	1365.63	584.09	238.37	153.15	175.97	221.93	546.84	176.55
Moderate	23	178.43	127.40	1780.83	760.84	255.83	131.06	274.28	310.25	619.13	204.82
Rich	4	221.25	162.09	1535.50	443.26	300	121.94	419.50	330.66	765	661.03
Controls	50	50	41.92	1274.70	447.21	202.20	87.29	136.50	257.76	550.50	235.85

Figure (3): Mean values of different immunoglobulins among studied patients and their parallel controls.

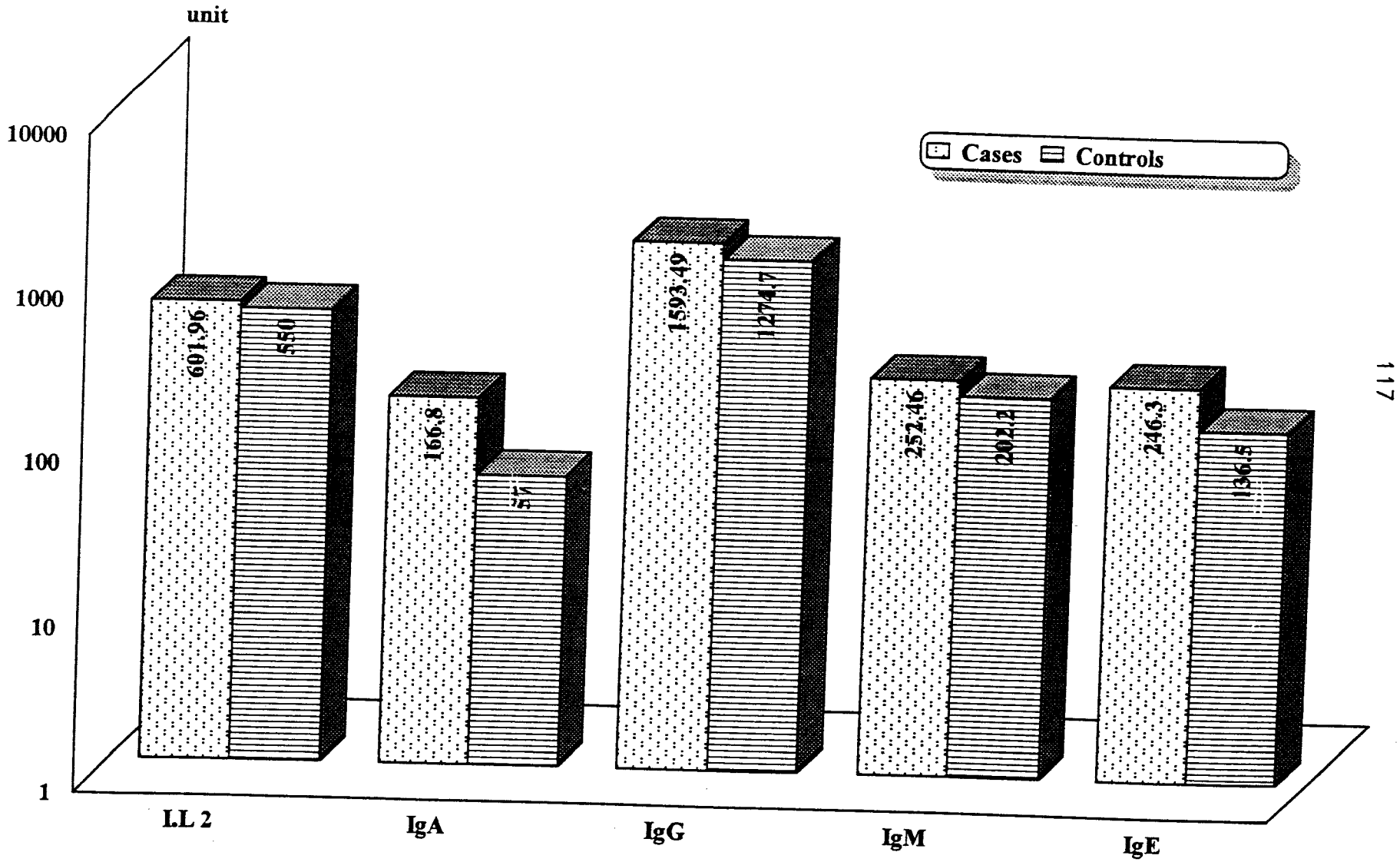


Table (9): Mean values of different studied immunoglobulins in relation to different diseases.

Diagnosis	number	IgA $\bar{X}$	IgA SD	IgG $\bar{X}$	IgG SD	IgM $\bar{X}$	IgM SD	IgE $\bar{X}$	IgE SD	IL-2 $\bar{X}$	IL-2 SD
Chronic and Asthmatic bronchitis	14	146.36	108.22	1616	746	270.20	154.58	300.29	297.80	649.29	189.63
Bronch-pneumonia	20	177.04	107.01	1506.70	499.48	237.75	114.82	263.38	292.29	544.25	162.10
Bronchiectasis	8	141.38	145.86	1342	601.47	284.25	180.56	209.64	282.18	671.88	486.72
Tuberculosis	4	208.50	143.10	2386	1094.66	200.05	116.50	45.31	62.29	585	259.94
Total patients	46	164.04	115.48	1587.78	687.06	252.45	138.06	246.30	281.43	601.96	256.72

IgA : immunoglobulin A
IgG : " G
IgM : " M
IgE : " E
IL.2 : interleukin 2

$\bar{X}$: mean value
SD : standard deviation

Figure (5): Mean value of Different studied Immunoglobulins
In relation to different diagnosis.

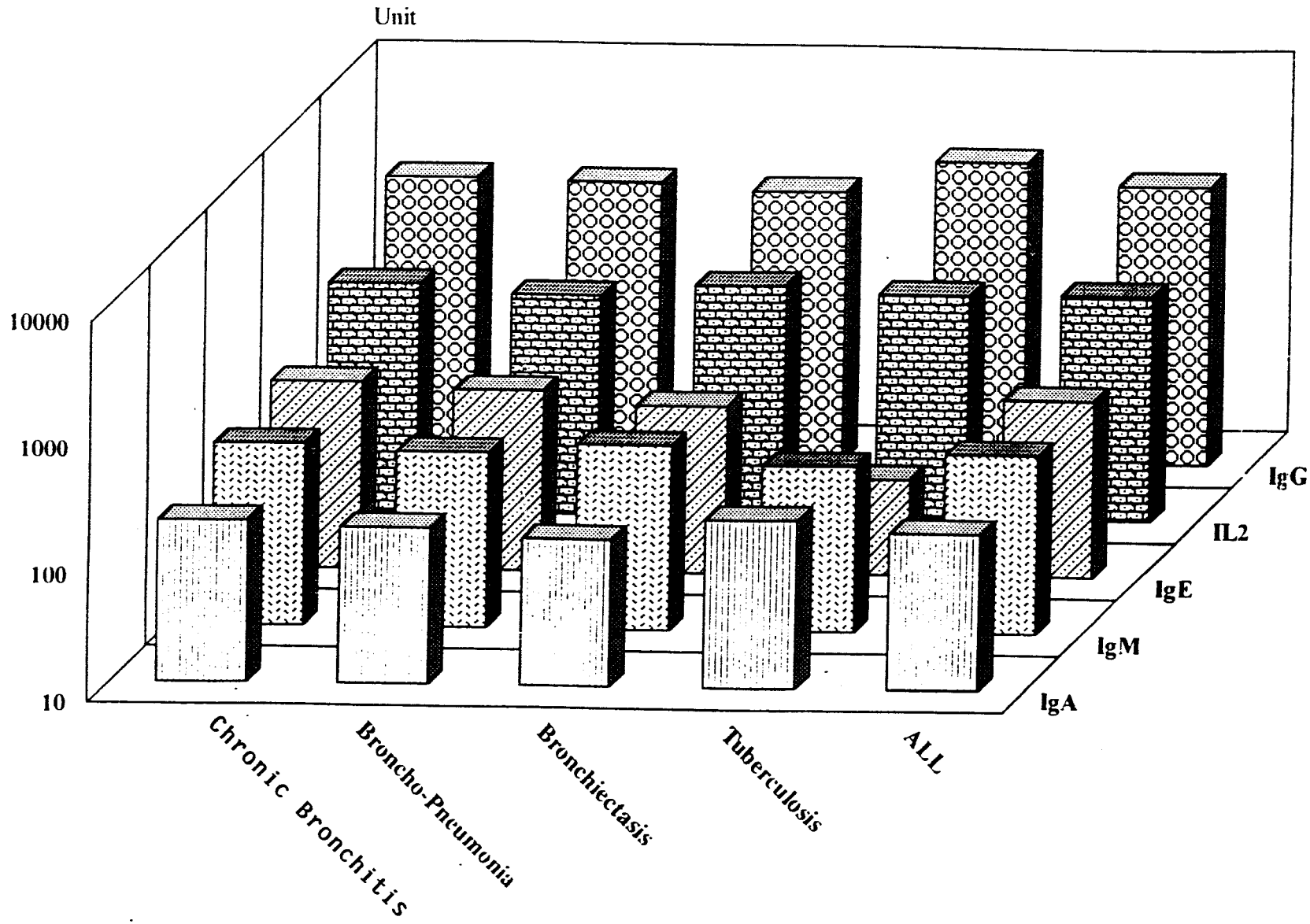


Table (10): Normal range for Immunoglobulins, and mean values for patients in different age groups.

Variable	Patient		Normal Value	
(1) IgA	number	$\bar{X}$	Range	
< 2 years	11	88	50±24	mg/dl
2-5 years	17	155.24	93±27	
5-12 years	18	219.72	148±63	
(2) IgG				
< 2 years	11	1244.8	762±209	mg/dl
2-5 years	17	1515.59	929±228	
5-12 years	18	1865.56	946±124	
(3) IgM				
< 2 years	11	215.9	58±23	mg/dl
2-5 years	17	223	56±18	
5-12 years	18	302.6	59±20	
(4) IgE				
< 2 years	11	96.36	11-15	IU/ml
2-5 years	17	287.48	15-60	IU/ml
5-12 years	18	299	60-90	IU/ml

References:

1- Geiger and Moffman, 1970.

2- Eriqui et al., 1987.

3- Enders et al., 1989.

Table (11): Mean and SD of laboratory results in male and female patients in relation to age.

Variable	Male		Female	
(1) IgA	$\bar{X}$	SD	$\bar{X}$	SD
< 2 years	82.3	27.12	94.8	49.02
2-5 years	158.77	72.04	143.75	130.72
5-12 years	199.25	184.69	236	108.86
(2) IgG				
< 2 years	1178.5	312.86	1324.4	365.96
2-5 years	1479	353.34	1634.5	445.93
5-12 years	1688.75	1326.53	2007	525.43
(3) IgM				
< 2 years	281.3	116.35	137.4	27.57
2-5 years	207.23	122.43	274.25	86.1
5-12 years	291	214.5	311.9	113.49
(4) IgE				
< 2 years	96.17	96.56	96.6	55.29
2-5 years	221.33	229.8	502.5	400.28
5-12 years	394.38	402.5	222.76	248.08
(5) IL-2				
< 2 years	655	157.83	510	224.28
2-5 years	661.54	203.38	530	192.14
5-12 years	530.63	213.75	624.5	413.82

Figure (4): Age Distribution of the studied patients
In relation to different diagnosis.

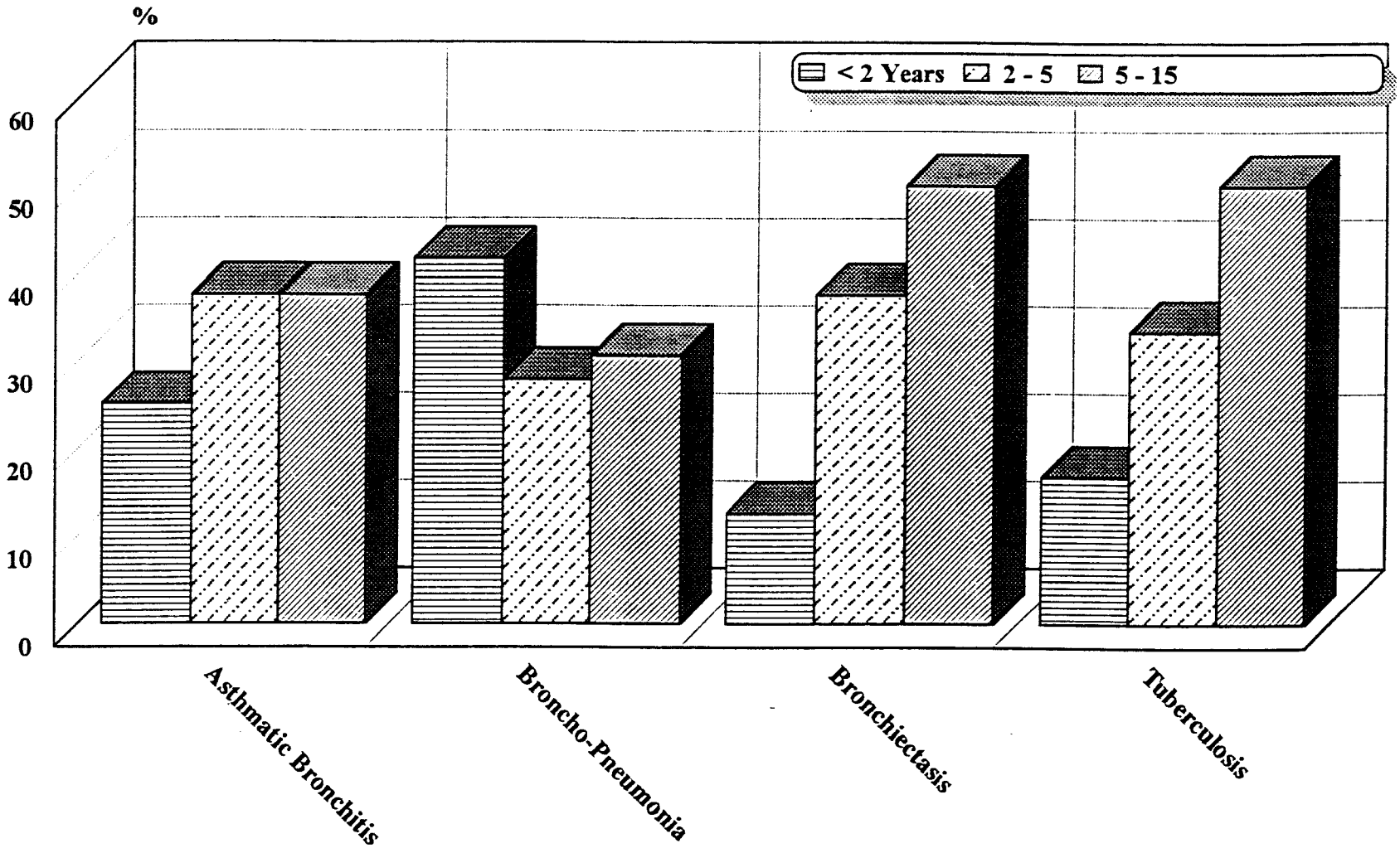


Figure (6) Scatter diagram showing the relation between IgA level and patient's age in both sexes

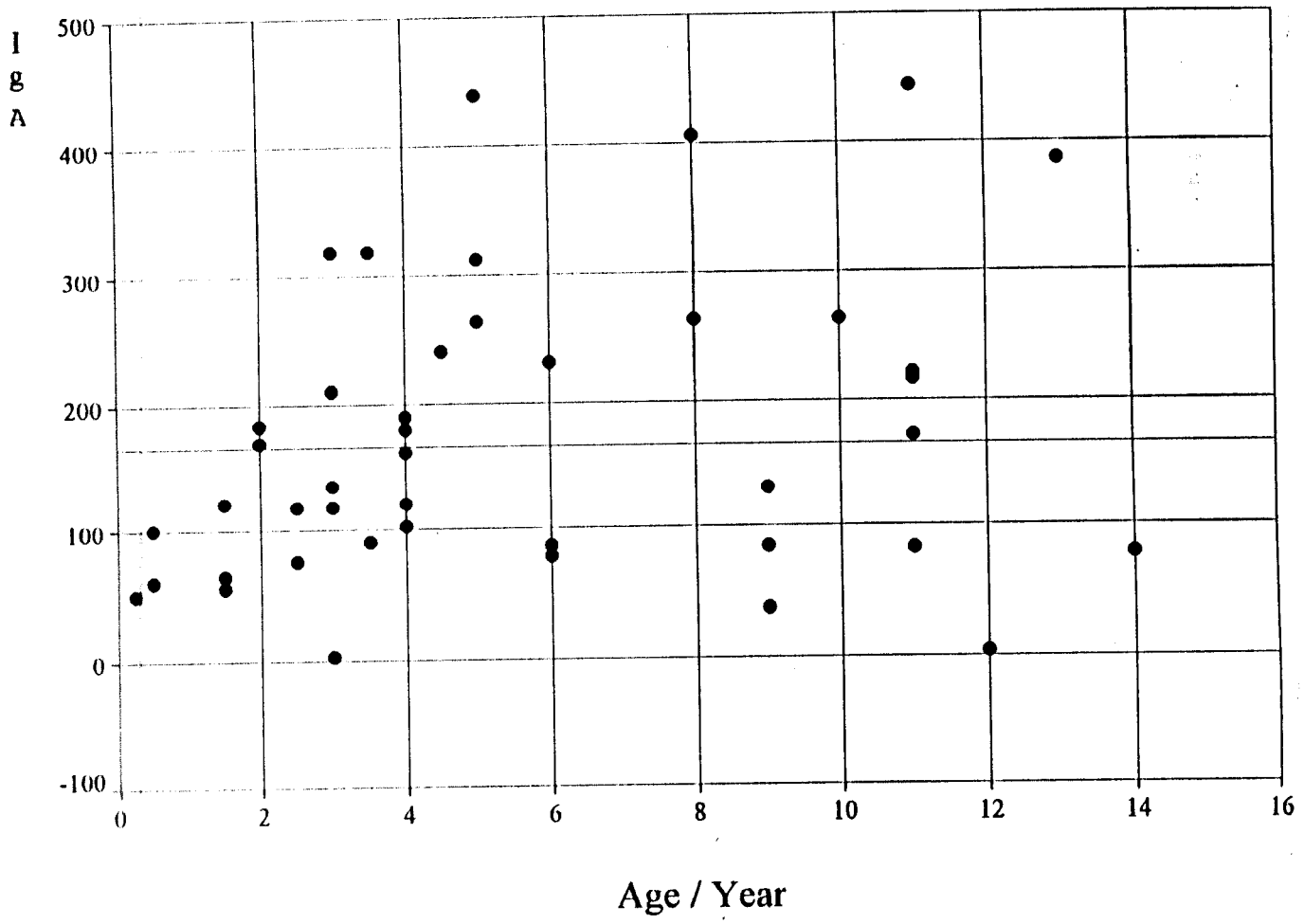


Figure (7) Scatter diagram showing the relation between IgG level and patient's age in both sexes

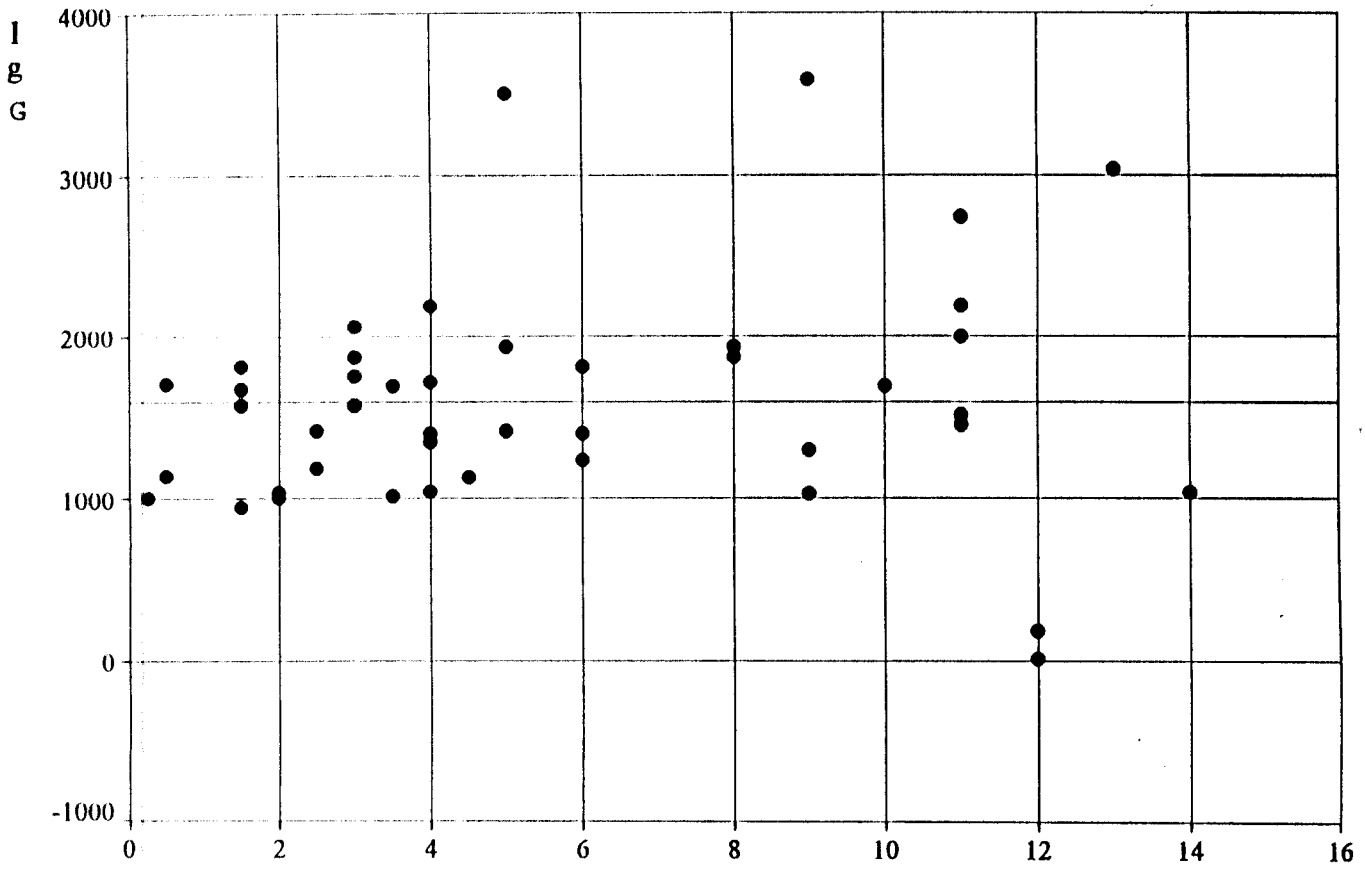


Figure (8) Scatter diagram showing the relation between IgM level and patient's age in both sexes

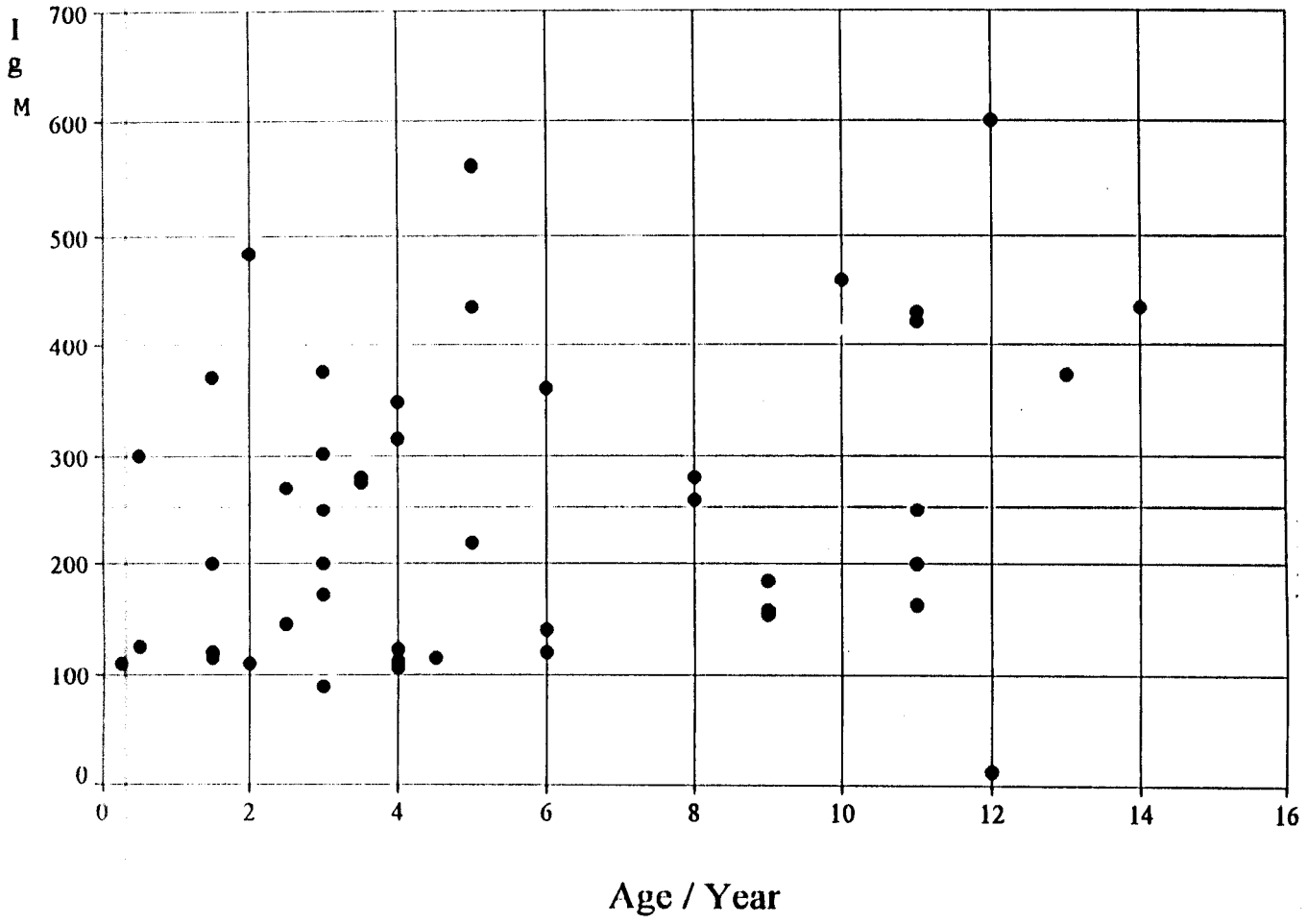


Figure (9) Scatter diagram showing the relation between IgE level and patient's age in both sexes

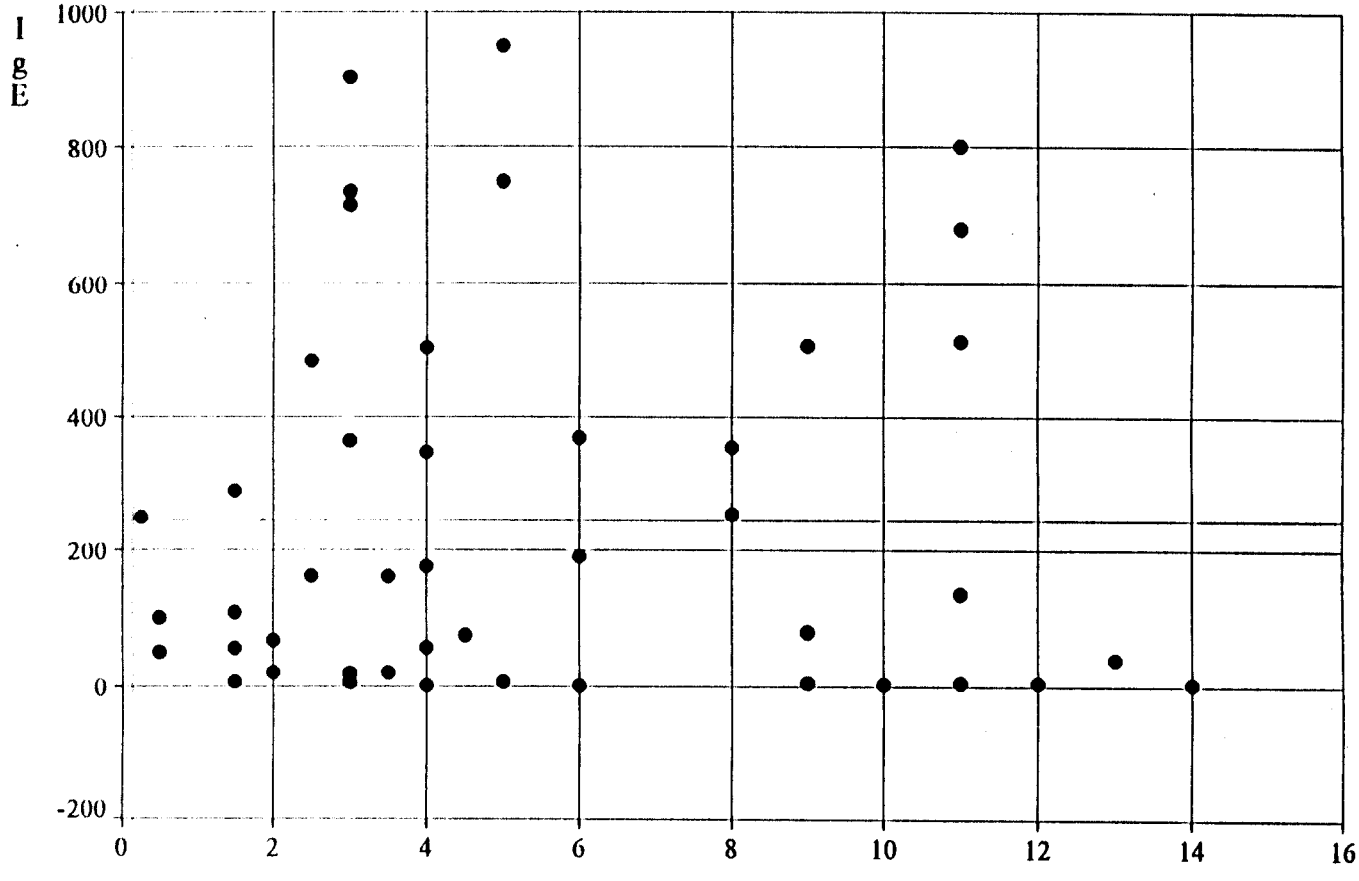
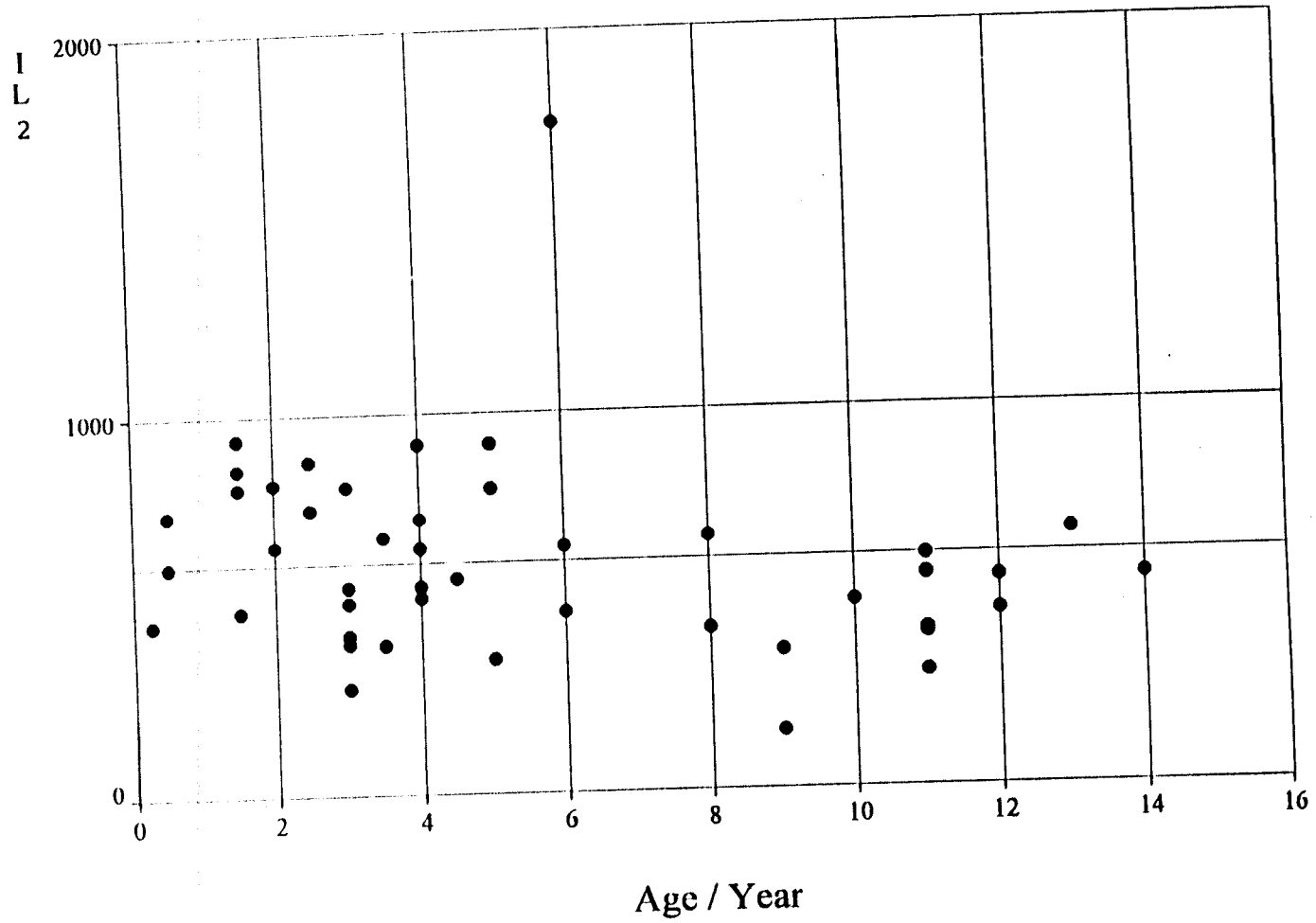


Figure (10) Scatter diagram showing the relation between Inter-Leukin2 level and patient's age in both sexes



DISCUSSION

Recurrent chest infections comprise one of the main causes of medical consultation and one of two of the first causes of morbidity and mortality in children under five in developing countries **(Pavia Raz, 1991).**

The burden of respiratory infection worldwide includes 4.5 million children who die yearly from respiratory infections, and represents 30% of yearly deaths in childhood **(Berman, 1991).**

This work is a trial to study the etiology and back- ground of recurrent chest infections amongst infants and children attending the Outpatient Clinic of Respiratory diseases in Cairo University, Children's hospital. The subjects of study comprised 68 patients aged up to 12 years, and they were 43 males, 25 females of different socioeconomic classes The study included as well 50 parallel age and sex matched heatlhy controls of the same socioeconomic class as the patients, (Table 1 Figure 1) 35 males and15 females Patients were subjected to thorough history taking according to special sheet, careful clinical examination with particular stress on respriatory system according to special sheet. All were suffering from recurrent chest infection and were admitted to hospital and investigated and followed up.

Investigations include: Complete blood picture, serum level of immunoglobulions A,G,M,E, and serum level of soluble interleukin-2 receptors, Chest X-Ray, and when needed specific laboratory procedures were used, according the etiology of different categories of recurrent chest infection was approached.

As regards age distribution in our patients 30-30% were below 2 years of age, 31.82% from 2-5 years, and 37.88% from 5.12 years with approximately equal distribution in the 3 age groups, and the numbr of patient with below 5 years age equal 62.12% of all patients, this agrees with what wrote by **(Pavia Raz et al., 1991),** who stated that respiratory infections comprise the main cause of morbidity and mortality in children under five in developing countries (Tables 1,2 & Figure 2).

It can be observed that recurrent chest infections can be met with at any age period and seem to be related to environment, general health of the individual, nutritional status, and absence or presence of congenital malformations wether respiratory or otherwise.

Concerning sex prevalence (table 1). The whole number of patients showed that among the 68 patients, 43 were males, and 25 were females, males constitute

63.63% of the whole number of patients, while females represent 36.36% with obvious prevalence of males over females.

Regarding the family history of recurrent chest infection, 75.8% of our patients had no positive family history, while 24% were having positive family history (which is already a high percentage) (Table 3).

This is in concordance with the result obtained by other investigtors **(Soderstrom et al., 1991)**, who revealed that children with recurrent respiratory tract infections as prescholars tend to belong to families with health problems, also it is with what was stated by **(Diane et al., 1989)** who said that recurrent chest infection is more likely to have a positive family history of allergy, other atopic symptoms, and a cyclic seasonal exposure pattern.

The number of patients with positive family history were mainly suffering of congenital bronchiectasis, asthmatic Bronchitis, and cystic fibrosis.

These types of recurrent chest infection usually have a genetic background, this shows the importance of proper family history, and genetic counselling.

Concerning the environmental factors and family habits 36.36% of the subjects of study had positive history of parental smoking (Cigarette, Goza), and 63.63% had negative history, it is considered as a significant difference, concerning controls, 10% had positive family history (table 1).indicating the role of parental smoking as an important adjuvant factor in occurance of recurrent lower respiratory tract infections as stated **(Metzola Ziegler et al., 1991)**, that fifty four patients aged from 1-6 years who had recurrent attacks of wheezy bronchitis were prospectively followed up for 3 months to find out if there is an association between different viral respiratory infections and episodes of wheezing.

Of the 115 episodes of upper or lower respiratory tract symptoms, virus or mycoplasma pneumonia infections were diagnosed in 52 episodes (45%), 34 of rhinovirus, the incidence of wheezing was not associated with IgE mediated atopy, with positive virological tests, or with fever during virus infection, but was associated with parental smoking **(Samet et al., 1987)** this admitted that smoking is the principal cause of 80% to 90% of chronic obstructive pulmonary disease, it also contributes to higher rates of respriatory infections, more

protracted symptoms after mild infections, and that children of parents who smoke have more frequent respiratory problems, extensive epidemiological evidence now links environmental tobacco smoke exposure to increased occurance of lower respiratory tract infections in children.

Concerning the programme of compulsory vaccination against the six most common diseases. It really, added much to the protection against recurrent chest infection episodes.

In the past ,complications of measles, whooping cough, tuberculosis, together with Influenza were associates of recurrent chest infection wether specific or non specific (Table 3).

At present, at birth, environmental conditions, overcrowding, malnutrition, bad parental habits, and other factors wether congenital or acquired pave the way for occurence of recurrent chest infection amongst infants and children.

Despite what has been wrote by **(David, 1991)** about reactivation of TB (tuberculosis) by administration of measles vaccine should be taken with preservation,

mealses disease was famous for it's pulmonary complications, chronic bronchitis, suppurative lung disease and reactivation of tuberculosis.

At present, we see in practice good results of immunisation against measles, whoopin cough, and tuberculosis.

Concerning the assessment of nutritional state of patients comparable with controls, the follow up of 24 hours regimen (Menu) for 7 successive days enabled us to categories patients according to their intake of animal protein in their diet into 3 categories according to protein intake, the first group comprised those who take ample animal protein (12.12%), 2nd group those who take proper protein in diet (42.42%), and those who their diet were deficient in protein (45.45%), Table (3)

Anthropometry of patients in comparison to healthy control revealed that patients with recurrent chest infection are inferior to their parallel controls, thus dietetic insufficiency particularly protein intake and resulting decrement in the parameters utilised in assessment of nutritional status are contributary

factors to the occurance of recurrent chest infection Table (4).

The same conclusion is also found when compairing the mean table of different anthropometric parameters and when calculating the wheight/height pecentage for each patients, we find that 72% of patients are below the 50th percentile according to National Center for health statistics (Table 5). NCHS health resources administration **(Nelson, 1983).**

This means that 72% of our patients are malnourished which is a high rate, which indicates that malnutrition can be considered as an important predisposing factor to recurrent lower respriatory infections in infants and children, this is with what's written by **(Robert A. Wood et al., 1989)**, who stated [that warldwide, malnutrition is certainly the most common cause of immunodeficiency, multiple defects in the immune function have been described in malnourished individuals including lymphopenia, abnormal delayed hypersensitivity, hypogammaglobulinemia, and impaired bacterial killing].

Also, **(Buyukgebiz et al., 1990),** made a study on preschool children who have a history of recurrent acute respiratory infections, and proved that malnutri-

tion especially Vitamin A deficiency is the contributing factor, although infections also have a negative effect on serum Vitamin A levels, it was also found that subclinical Vitamin A deficiency is a problem of public health importance, since 64% of the children examined wer found to have low levels of serum Vitamin A (Vitamin A is thought to affect epithelial integrity and rapair).

This agrees with what **(David, 1991)**, declared that malnutrition increases the risks of morbidity from infection, and conversely infection even so mild so as not to cause overt diseae promotes malnutrition.

Feigin, (1979), proved that the cellular immune-system seems to be the component of the immune system that is most affected in malnutrition.

Watson (1989), described the malnutrition infection cycle by the fact that decreased dietary intake depresses immunity and the integrity of epithelial surfaces, these effects promote susceptibility to microbial colonisation and invasion, and increase the severity and duration of the resultant infections, this is the case of our patients who were suffering of malnutrition which promoted infection, with recurrence of attacks of

infection due to impaired epithelial surface of the airways and depressed immunity.

In a study made by **(Chandra, 1983)**, it was found that Iron, Zinc, and Copper are micronutrients necessary for both microbial growth and human immunologic funciton.

Mucosal surfaces are deerly affected by Iron deficiency and Zinc deficiency, Zinc is crucial for rapidly turningover cells like lymphocytes and epithelial mucosal cells.

Copper deficiency was proved to cause decreased antibody prodcution in experimental animals **(David, 1991)**.

All these micronutrients could be deficient in malnourished patients, with secondry affection of respiratory mucosal integrity.

As regards the socioeconomic profile of patiants, according to the equation used in this study to calculate the socioeconomic standard of patients, it was found that 40.9% of patients are poor, 50% are of moderate economic level, and only 9% were well off (Table 1). The socioeconomic study revealed the importance of the low mean montly income/member due to the big number of

family members, and indicated the importance of the educational standard of patients and especially of the mother.

Other important factors include poor water supply, bad housing, poor electrical supply, unstable social life, all were found of significance among materials of study as evident from table (1) thus pave the way for recurrent respiratory infections.

Non educated mother does not know to take care of her child, how to feed him properly, to make him live in good hygien, to protect him from infection, to seek medical advice immediately when her baby gets' ill. This is in agreement with what's declaired by the (Department of health and human service, 1990), that risk factors for recurrent respiratory infections include low level of parental education, also this agrees with what **(Stead, 1985)** wrote that a number of disease manifest marked differences in their clinical manifestations under various conditions of poverty. 50% of our patients lived in rural areas, 25% in public crowded badly aerated small homes, and 25% lived in industrial district mainly Helwan and Tebbin and nearby Cairo were air pollution with cement and dust is highly evident and clear.

In rural shelters, where lack of hygien is evident and indoor polution due to burning kerosine, rabbis, and wood to produce fire to cook and get warmth, are considered as responsible for air pollution.

Also, in public low social life shelters, crowding is a very important factor that makes habitants mainly children targets for recurrent chest infection.

Badly aerated homes together with the presence of any infected person in the family may get the chance for spread of infection and creates respiratory problems, this was specially noted in cases of tuberculosis in this study, this is in agreement with what **(Bolejj, 1989)** stated that humans spend more than 85% of their times indoors and the importance of indoor air contamination as a factor of susceptibility to infection is being increasingly recognised.

Samet, (1987) declared that although most atmospheric pollutants are present at much lower levels indoors than outdoors. NO_2 is often present at higher levels indoors when unvented combustion sources such as gas stoves or kerosene heaters are present. NO_2 has been linked with increased susceptibility to respiratory

infections in children, 25% of our patients were living in industrial districts, mainly Helwan and Tebbin, where air is highly enriched with pollution particles mainly cement.

Waller, (1989) stated that outdoor sources of pollutants include combustion products present in automobile exhaust and emissions from coal and petroleum fired industrial processes. So it is not surprising that 30.43% of our patients where presenting with asthmatic Bronchitis due to persistant exposure to allergens

Laboratory investigations in our study included:

Complete blood picture, which was of great importance in delineating different categories of respiratgory infections particularly those who are suffering from infections from other categories. This is especially important in chronic chest infection, as the hemogram is of paramount importance especially in allergic patients.

Patients with bronchial asthma showed eosinophilia in their hemogram, those with chronic chest infection presented with leucocytosis in bactreial insult, while those with rural infection showed leucopenia.

80% of patients showed with hypochromic microcytic anemia, due to chronic infection, and associated malnutrition. The mean value for whole patients for red cells, hemoglobin and leucocytes is lower than the corresponding in parallel controls, these mean values added to other laboratory investigations and clinical pictures of subjects were helpful in delineating the different diseases.

The total Immunoglobulin A (IgA) mean value was 166.8 and ranged from 3-445 mg/dl table (7) controls had a range of 4-114 mg/dl with a mean value of 57 mg/dl these values show significant difference between patients and controls, in spite of the presence of individual cases among our patients who have IgA level below normal range but they are very few, tables (6),(12).

Nbr	Patient age	Sex	IgA level	Normal X / age
3	12 years	M	4	219.72 mg/dl
5	3 years	F	3	88 mg/dl
11	12 years	M	4	219.72 mg/dl
27	9 years	M	37	219.72 mg/dl

and if we devide our patients according to their age, into the main 3 age groups (below 2 years, 2-5 years,

5-12 years), the mean value for each age group will be found higher than the normal range of IgA regardless the etiology of recurrent chest infection **(Geiger and Hoffman, 1970), (Eriqui et al., 1987), (Enders et al., 1989),** This is an astonishing finding in our study, as we were expecting the IgA level to be low in all patients with recurrent chest infection.

So when compairing mean value of differentage groups among patients and controls it was evident, the role of different epidemiological and genetic factors in inducing recurrent chest infections.

The few cases with selective IgA deficiency are explained by what **(Pebani, 1986)** said that transient selective IgA deficiency is especially common in children, but usually reverts to normal before the age of 14 years, and may simply be a manifestation of maturational delay in IgA humoral immunity.

Also, we have in table (12) 8 cases presenting with IgA deficiency, and clinically are diagnosed as Down's syndrome (3), Rickets with IgA deficiency (1), immotile cilia syndrome (1), and cystic fibrosis (2), and a case of immunodeficiency.

So as a whole we get 12 patients with selective IgA deficiency 4 famels and 8 males, equivalent to 17.6%, 7 patients of this group were aged less than 2 years, 4 patients were aged from 9-12 years. 1 patient aged 3 years thus the majority are diagnosed during infancy due to the evident clinical manifestations and diagnosis of recurrent chest infection, they constitute 58% of this group.

The total IgG (Immunoglobulin(G) mean value was 1593.49 mg/dl with a range from 1000-3588 which is higher than the normal range reported in tables, also there is no significant difference between patients and controls, table (7) as the mean value for controls was 1274.7 with a range of 940-1809 mg/dl. Also there is no great difference between values for different types of respiratory infections, this finding supports the fact that irrespective of the nature of triggering factors for repeated respiratory infections, the involved pathogenic mechanisms are the same for all patients.

As regards Immunoglobulin M (IgM): The mean value for all patients was 252.46 mg/dl with a range from 106-484 mg/dl with a significant difference with controls. The mean value for controls was 202.20 mg/dl with a range from 112-421 mg/dl (Tables).

The mean value for total IgM is higher than the normal range reported in tables, and nearly equal values of IgM for different respiratory diseases. In revising the available literature, This IgM was not investigated in recurrent chest infection.

The total Immunoglobulin E mean value was 246.30 Iu/ml with a range from 1-950 Iu/ml, with no significant difference with controls, the mean value for controls was 136.5 Iu/ml, and a range from 4-835 Iu/ml.

The mean value for IgE was higher than the normal range, and with no great difference in values as shown in tables as regards different types of recurrent chest infection.

The IgE level differs between acute asthmatic attack (high value), and during recovery (low value).

Also soluble interleukin-2 [SIL-2] did not show significant difference between patients and controls in values. The mean value for S1L-2 in patients was 601.96 Pc/ml with a range from 150-1750, the mean value for controls was 550.5 with a range between 325-990 Pc/ml, there was no great difference between values of S1L-2 in different respiratory diseases as shown in tables [6,7,8,9,10,11] & Figure (3).

Regardless the few number of patients with low levels of immunoglobulins, generally we can not say that immunodeficiency is an evident diganosis as a precipitating factor for recurrent respiratory infection in our patients.

This indicate the preponderance of subjects of recurrent chest infection not suffering from immune-deficiency.

This is in harmony with the findings of **(Diane, 1989)** who stated that [recurrent respiratory infections most frequently occur in children who do not have a primary immunodeficiency diseases, and can be viewed as a consequence of impaired flow of secretions of fluids and that recurrent lower respiratory illness is a good example, as it is more likely to have an allergic pattern, and may be a cyclic seasonal pattern].

The study of our patients revealed that recurrent chest infection occured most frequently in spring and winter.

Robert et al. (1989), reported that [if however the child experiences prolonged infections or some bacterial complications with each upper respiratory infection, one's index of suspicion should rise sharply]; this is

particularly true if these complications involve more than one site, because recurrent infections involving a single site (as the case of our patients) might be associated with structural or anatomical abnormality **(Armengot et al., 1991).**

Finally, some children are referred because of too many infections but a healthy toddler may have 7-8 infections per year that may be increased if day care centers and siblings in preschool are part of the social setting.

These infections are usually brief and without sequale indicating an intact immune system.

As regards different diagnosis of recurrent respiratory infections before discussing the commonest types of recurrent chest infection in infants and children mainly chronic bronchitis, it should be mentioned that it is difficult to separate those having wheezy bronchitis from those considered to have asthma, both groups have family history of atopy, eosinophilia, and shows remarkable improvement after giving treatment specific for asthma **(Doushey, 1980).**

CHRONIC BRONCHITIS: Shoult not be accepted as a final diagnosis, frequently recurring productive cough in children usually indicates an underlying pulmonary or systemic disease. Patients should be evaluated for allergic disorders, environmental hasards, upper airway post nasal discharge, immune deficiency, anatomic abnormality, Immotile cilia syndrome, bronchiectasis, and cystic fibrosis. This was followed in the present study, according to the special sheet utilised, the results showed that 7 cases out of 68 in whom diagnosis of chronic bronchitis is valid. Tables [9 - 6_A- 6_B] Figure 5.

Cough and wheezing are suggestive of allergy, tobacco smoking with positive or negative smokers is obviously related to their form of disease.

The chief clinical manifestations in chronic bronchitis are cough with or without expectoration. Chest soreness specially at night, wheezing, and the common physical findings of acute bronchitis, the course and prognosis of the condition depend upon erradication of any underlying cause and symptomatic management.

The complications are those of the undrelying illness.

Treatment comprises appropriate management, and dealing with allergy, vaccines, and inhalation of antibiotics are not effective.

In our study subjects from chronic bronchitis were investigated and results showed that cases constitute 15% of all patients, 78% of these patients are males, concerning the 3 age groups that we are dealing in the study, there is nearly equal distribution of number of patients in the 3 age groups. with slight increase in number in the preschool age.

As regards socioeconomic standard of patients 14% of patients were poor, 58% of patients were of moderate socioeconomic level, 28% were well off.

These results lead us to the conclusion that males are predominant than females with no effect of age on the prevalence of the disease (possible preschool age is more prone to this type of disease), the majority of patients are of moderate socioeconomic level, not well off.

The mean value of IgA in chronic bronchitis was 187-29 mg/dl (Table 9), IgG mean value was 1616 mg/dl, IgM mean values was 270.20, IgE mean value 300.29 Iu/ml, IL-2 mean value is 649.29 Pc/dl (Table 9, Figure 5).

As regards ASTHMATIC BRONCHITIS: Asthma is the most common chronic disease of childhood and it affects about 10% of school children **(Valman, 1994)**, about 80% of children with asthma have the first symptoms before the age of 5 years and at least half will stop having attacks when they become adults, in contrast, we found about 60% of our patients to have recurrent attacks of asthma at the age group 2-5 years.

Asthmatic patients represents 15% of all our patients, males are predominant to females, 58% of asthmatic patients are of moderate socioeconomic standard, 14% were poor, and 28% were well off.

Bronchical asthma should be suspected if there is recurrent cough, wheezing. or shortness of breath, especially after exercise or during the night, these symptoms are caused by narrowing of the bronchi and bronchioles by mucosal swelling and contraction of the muscle in their walls, with viscid secretion obstructing the lumen.

The first attack may occur at any age, there is no clinical or laboratory method of distinguishing between acute bronchial infection and asthma.

In the case of our patients, we met them for clinical examination when they have repeated attacks of bronchial asthma and inbetween attacks where they showed typical findings of bronchial asthma, but recurrent cough at night might be the only feature at times.

The length of absence from school, extent of poor growh, and chest deformity, as well as the number of hospital admissions give an indication of the severity of the problem.

A detailed history should be taken of exposure to household pets or other animals which may belong to friends or relatives, exposure to tobacco smoke is associated with an increase in symptoms and should be avoided.

The importance of psychological factors in inducing attacks of asthma is commonly difficult to assess, although stresses caused by absence from school, disruption of the family and conflicting advice are inevitable in the severely affected child.

Finally, viral infections are the most important precipitating factor for attacks of asthma.

For the mean values of immunoglobulins in bronchial asthma refer to tables (6_a , 6_b, 9) Figure (5).

Nasal mucociliary function has been studied in 21 children suffering recurrent airway infection (after exclusion of cystic fibrosis, immune deficits, and allergy). 38% of these patients had alteration in the mucociliary transport and increased incidence of bronchiectasis was observed in this group **(Armengot et al., 1991)**, this is in agreement with the fact that recurrent respiratory infections are not necessarily and primarily due to immune deficiency.

In our study, it was found that 17.39% of all our patients were presenting with BRONCHIECTASIS, they comprised 8 patients, 4 males, 4 females: 4 of these patients were aged over 5 years, 3 patients aged between 2-5 years, and one patient below 2 years age. Interrogation of these patients revealed positive family history of similar disease, and diagnosis was confirmed by bronchography, microscopical analysis of the bronchial mucosa was not necessary, the disease showed equal sex distribution in boys and girls, 50% of these patients were poor, 25% were of moderate socioeconomic level, and 25% were well off, this shows

that the etiology of bronchiectasis in these cases is multifactorial.

The mean values for immunoglobulins in Bronchiectasis are present in table (9), Figure (5).

In our cases, diagnosis was confirmed by bronchogrpahy, other cases might need to be investigated for the etiology by a series of investigations including high microscope, for evaluation of ciliary activity, if there is absence of ciliary contractility for more than 2 occasions this necessitates more testing.

At present diagnosis still depends on electromicroscopic examination of cilia obtained either by brushing and biopsy of the trachea at bronchoscopy, or by nasal mucosal biopsy

In the evaluation of a child with recurrent pneumonia , most pediatricians just think of conditions such as immunodeficiency, or cystic fibrosis, although it is certainly important to rule out these diseases, this was the reason for which our patients who suffered of recurrent pneumonia were subjected to immunoglobulin essay to check up the humoral immunity, as well as the cellular immunity which was presented by soluble Inter Leukin-2 Receptors.

It should be mentioned that several studies have shown reactive airway disease to be the most common cause of recurrent pulmonary infiltrates through increased mucus prodcution, decreased mucociliary clearance, low elastic recoil pressure or impaired collateral ventillation, particularly of the right middle lobe, although most of these infiltrates actually represent atelectasis rather than pneumonia **(Robert et al., 1989).**

In our study 43.38% of our patients were presenting with Bronchopneumonia complicated by consolidation collapse or atelectasis.

In the first groups of patients (46) Table (6A) about 20 patients presenting with pneumonia, 6 were below 2 years age, 7 patients were aged from 2-5 years, and 7 patients were aged from 5-12 years, this shows nearly equal distribution in the 3 age groups.

As for sex prevalence, there is equality between boys and girls, also the socioeconomic standard showed equal distribution between poor and moderate socio-economic level.

The mean values for Immunoglobulins in Broncho-pneumonia are listed in Table (9), Figure (5).

In the second group of patients (22), who have secondary recurrent chest disease there are (13) patients diagnosed as being Bronchopenumonia, out of these patients (Table 12) we have 2 cases of Pneumonia due to foreign body inhalation ,the first patient is a male 6 months, and the second is a male 9 months, these 2 cases presented with history of inhalation pneumonia with occurance of sudden onset of paroxysmal cough, dyspnea, cyanosis ... that suggest inhalation of foreign body.

Over 90% of patients suffering from inhalation pneumonia present their symptoms within 1 hour, and almost all have fever, tachypnea, also apnea, and shock may occur.

Examination usually reveals diffuse rales and wheezes, chest X-Ray is essential, suction of airways and oxygen administration are indicated, Endotracheal intubation and ventillation are essential..

Among, this second group of patients suffering from secondary chest disease, we have 3 cases of Down's syndrome trisomy 21 (generalised hypotonia) and 2 cases of cerebral palsy 2 cases of hiatus hernia, and one case

of tracheomalacia, all of these patients get recurrent attacks of schocking and are considered as cases of foreign body inhalation, shocking can occur even with saliva, most of patients (cerebral palsy, and Down's syndrome) suffer neuromuscular incoordination with deficient swallowing mechanism while congenital anomalies as hiatus hernia and tracheomalacia cause recrrent pneumonia through another different mechanism.

A study performed on 25 control, and 183 children suffering from recurrent, lower respiratory tract infections (by radionucleide gastrooesophageal scientigraphy), gastrooesophageal reflux was observed in 135 patients, the severity of clinical symptoms in the patients was found to be directly related to the severity of reflux observed by scintigraphy **(Padhy et al.,1 990).** It seems to be a strong assocaition between gastrooesophageal reflux and recurrent lower respiratory infections, this is the problem with hiatus hernia in the subjects of the present study.

Finally, in the evaluation of a child with recurrent pneumonia most pediatricians first exclude conditions such as immuno-deficiency, it should be known that several studies have shown reactive airway disease to

be the most common cause of recurrent pulmonary infitlrates through increased mucus produciton, decreased mucociliary clearance, low elastic recoil pressure or impaired collateral ventillation, particularly of the right middle lobe, although most of these infiltrates actuaily represent atelectasis rather than pneumonia **(Robert et al., 1989),** in the present study 43.48% of patients were presenting with Bronchopenumonia complicated by consolidation collapse or atelactasis.

TUBERCULOUS patients were encountered in our study, they represented 6% of all patients, which is a high rate among the study group when compared to the rate in whole population of 1-2%, it is a high rate, besides tuberculous patients usually are referred to TB clinics, but we can not drow solid conclusions for this limited number of tuberculous subjects in the study.

It is worth to say that mean values for IgA, IgG, IgM, IgE, and S1L-2R for patients did not show great deifference from values obtained in other diseases (Table 6_a-6_b), Figure (5), this is in agreement with the fact that irrespective of the nature of triggering

factors for repeated wheezing the involved pathogenic mechanisms are the same.

Tuberculosis is a systemic disease affecting every organ of the body, accordingly it has different modes of presentation according to many factors including genetic predisposition, environmental factors, socio-economic standard and associated diseases especially human immunodeficiency virus (HIV).

CYSTIC FIBROSIS was presented by 2 caes in this study a brother and a sister, the brother died from failure to thrive, diarrhea, and recurrent pneumonia, and died before 1 year of age.

The sister was still living, aged 1½ years, the first attack of pneumonia happened at the age of 4 months, at examination, she had a very low body weight 4 Kg with features of malnutrition, steatorrhea recurrent pneumonia, hyperbilirubinemia, generalised oedema, and 2 attacks of suppurative otitis media.

Laboratory investigations shows normal complete blood picture, normal levels of immunoglobulins. X-Rays chest and CT chest (during pneumonic attack) showed clear pneumonia sweat chloride test was very positive.

Investigators and clinicians have been intrigued by the elusive basic defect in cystic fibrosis, by problems relating to prenatal diagnosis and heterozygote detection, and by the challenge of designing therapies to combat the broad range of manifestations. Cystic fibrosis is most probably inherited as an autosomal recessive trait.

Infection especially with S.aureus and P.aeruginosa plays a major role in the pathogenesis of lung disease in cystic fibrosis. Infection is continued to the lung, infection appear to be expressed selectively at the airway surface.

Humoral and cellular immunity as well as complement activity are generally normal, although functional deficits may occur in cellular immunity and in the alternative pathway of complement as lung infection progresses to an advanced stage.

Common pulmonary complications include atelectasis, hemoptysis, pneumothorax, and cor pulmonale. These complications usually appear in the second or third decade of life as the lung lesion progresses.

X-Ray chest was done for all patients included in the first group, anteroposterior and lateral views. Roentegenography of chest is very helpful in diagnosing recurrent chest disease, prominant X-Ray findings were found in about 20 of patients, the following table shows the radiological details.

There are 2 patients with chronic bronchitis, 6 patients diagnosed as bronchiectasis by bronchography, with a sister and her brother. 10 patients have bronchopneumonia with consolidation collapse, atelectasis or synpneumonic pleural effusion, 1 case of prominant hilar shadows, with right atelectatic band proved to be a cae of tuberculosis by isolation of TB bacilli from the patient, the other 2 cases of tuberculosis were diagnosed as bronchiectasis by repeated compression by tuberculous lymph nodes. A case of corpulmonal, with recurrent chest infection, hyperinflation, with emphysema of the chest.

In the following page a list of these patients is represented.

No. of Patients	Sex	Age	Diagnosis	Radiological Findings
1	M	4 yr	Bronchiectasis	Bilateral Bronchiectasis
3	M	12 yr	Pneumonia	Corpulmonal, emphysema, pneumonia
7	M	2.5 yr	Bronchopneumonia	Consolidation collapse of lingular lobe
8	M	4 yr	Bronchitis	Increased bronchovascular markings
9	F	10 yr	Bronchopneumonia	Increased bronchovascular markings, reactive pleural effusion
10	F	3 yr	Bronchopneumonia	Pneumonic consolidation collapse of left lower lobe mediastinal shift
12	M	3.5 yr	Bronchopenumonia	Extensive pneumonic consolidation of the right lung left pleural effusion
13	F	6 yr	Bronchiectasis	Right lower lobe consolidation, Bronchiectatic changes
17	F	3 yr	Bronchopneumonia	Pneumonic infiltrates, partial lower lobe collapse, left compensatory hyperinflation
18	F	5 yr	Bronchopenumonia	Right patchy opacities
19	F	11 yr	Bronchopenumonia	Right patchy opacities
21	F	8 yr	Bronchopenumonia	Pneumonic infiltrates
22	M	3 yr	Bronchopenumonia	Consolidation collapse of Right middle and lower lobe
23	F	6 yr	Bronchiectasis	Honey coomb appearance, patchy diffuse opacities compensatory emphysema, Bronchiectatic changes
25	F	12 yr	Tuberculosis	Prominant hilar shadows, Right atelectatic band
26	M	11 yr	Bronchiectasis	Bronchiectatic changes
27	M	9 yr	Tuberculosis	Tuberculosis bronchiectasis
28	M	11 yr	Tuberculosis	Tuberculosis bronchiectasis
29	F	11 yr	Bronchopenumonia	Reactive pleural effusion
30	M	16 mo	Bronchopneumonia	Reactive pleural effusion.

M : Male , F : Female yr : year , mo : month

RECOMMENDATIONS

Recurrent chest infection in infants and children was found to be not uncommon amongst the clientels of Outpatient's Clinic of Chest Disease, Cairo University Children's Hospital, this recurrence and chronicity of disease reflects the relactancy with which these people manage their lives.

Early detection and diagnosis of chest disease, although laborious but it is cost effective, it is rewarding via teaching parents, paramedicals and medicals informations about the features of recurrent chest infections through (television, press, curricula societies ....).

Erradication of chest diseases in infants and children is the responsibility of all organisations, and all those who care far health, prosperity and healthy upbringing of the young, ikt entailes aid and support of all available efforts.

The role of family is very important in the prevention and ameleoration of recurrent chest infection, breast feeding and good nutrition, immunisation against

infectious diseases, healthy environment specially pure water supply, sewage disposal, avoidance of parental smoking, and family planning, all contribute in minimising recurrence of chest infection.

Genetic study for hereditary chest disease, and clinical examinations of all members of the family in the presence of diseases as Bronchiectasis, bronchial asthma, Tuberculosis, cystic fibrosis.

Follow up of escaping cases from immunisation, and reimmunisation at entry of school.

As many green areas as possible should be available for children to give healthy environment and good atmosphere.

Lessons explaining the importance of early visit to doctors, taking medications with respect, getting rid of bad non hygienic habits as smoking, using other's utensils, isolation of diseased children from playmates.

Avoid indoor pollution by stopping smoking, burning wood rabbish, kerosene ... at home, out door pollution

is limited by avoiding building factories inside cities just next to houses, that produce pollutants as Helwan, Tebbin, and Shobra El-Khema, this is also achieved by using special filters of chimneys to prevent spread of pollutants.

SUMMARY AND CONCLUSION

The work is a trial to study the etiology and background of commonly encountered recurrent chest infections among infants and children attending Outpatient Clinic of chest diseases, Cairo University Children's Hospital.

The study included 68 patients who were randomly selected from Outpatient Clinic: 43 males, 25 females aged 45 days up to 12 years. All were sufferers of recurrent chest infections. The study included as well 50 healthy age and sex matched parallel controls, 35 males, 15 females of the same socioeconomic level of targets of the study. In our series patients and controls were carefully interrogated, thoroughly examined and properly investigated. All patients were followed while under treatment for about 2 years.

According to clinical, radiological, and laboratory findings, patients were subdivided into two categories.

* First group comprised those patients for whom investigations were needed to arrive at the Etiology of recurrent chest infection.

This group consisted of 46 patients: 7 patients diagnosed chronic Bronchitis, another 7 patients were asthmatics,

recurrent attacks of Pneumonia and Bronchopneumonia were found in 20 patients, the remaining patients were 8 patients of Bronchiectasis, and 4 of documented pulmonary tuberculosis.

* Second group: included 22 patients, who were evidently associated with predisposing factors wether congenital or otherwise that made these targets candidates of recurrent chest infection. They included 2 patients suffering from chronic Bronchitis, 13 patients suffering from Pneumonia and Bronchopneumonia, 2 cases of lung abscess, 2 cases empyema, 2 patients diagnosed cystic fibrosis, 1 patient kartagner syndrome.

The study entailed assessment of nutritional status of all subjects of study (patients and controls), it included body weight, height or length, head circumference, triceps skinfold, mid arm circumference, and arm muscle area.

Laboratory investigations were carried out to all subjects of the first group (46 patients) and 50 parallel controls, they included complete blood picture, level of Immunoglobulins IgA, IgG, IgM, IgE, laboratory procedures were carried out by ELISA technique. SIL-2R (soluble interleukin 2 receptors) were carried out by ELISA technique.

When needed other specific laboratory investigations were done (Tuberculin test, analysis of effusion...)

Roentgenography of chest anteroposterior and lateral views were done to all patients.

Socioeconomic scoring for all patients and parallel controls were done by the use of an equation based on 3 parameters which are father's work, mother's educational level, and mean monthly income per member of family, after which patients and controls were classified into 3 main groups: Poor, Moderate, and well off. Interrogation, examination, and investigations showed that:

In many patients of recurrent chest infection, the etiology is multifactorial, and not a single cause. Bad environment, poor socioeconomic standard seem to run in harmony with infection as a triad leading to recurrence of chest infection.

Laboratory investigations for Immunoglobulins and Interleukin showed that inspite of the presence of few cases of selective immunoglobulin deficiency, immunodeficiency perse is not solely responsible as a prevalent cause of recurrent chest infection in the subjects of this study.

On the other hand low socioeconomic standard, big family number, small badly aerated houses, environmental

pollution especially parental smoking, last but not least malnutrition, seemed to be the prominant etiological cause paving the way for recurrence of chest disease.

Congenital anomalies did show a prominent role in the series of this study, and by chance Down's syndrome, tracheomalacia, gastro-oesophageal reflux, Hiatus Hernia, cerebral palsy, and mental retardation were evident causes together with acquired etiological factors as foreign body inhalation.

It can be concluded that recurrent chest infection in infancy and childhood is a real problem, it should recieve good attention by all those who are concerned with the health and uprising of the young.

Early diagnosis is a must specially in high risk groups suffering from congenital malformations, malnutrition, and bad environment.

Follow up of patients for a period of about 2 years showed how tedious and expensive is the management of these sufferers.

The sequelae of recurrent chest infection did affect the growth and well-being of these sufferers.

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ARABIC SUMMARY

دراسة وبائية ومناعيـــة لحالات عدوى الصدر المتكررة
فى الرضع والاطفال

ملخـــص البحـــث

يعتبر هذا العمل محاولة لدراسة اسباب تكرار عدوى الصدر فى الاطفال والرضـع الذين يتم فحصهم فى عيادة الامراض الصدرية بمستشفى الاطفال الجديد ـ جامعـــــة القاهرة ٠

لقد تكون هذا العمل من ٦٨ طفل وطفلة حتى سن الثانية عشر، ٤٣ مـــن الذكور ، و ٢٥ من الاناث الذين يعانون من عدوى صدرية متكررة، كما يتضمن ٥٠ طفلا وطفلة سليمة فى نفس المرحلة السنية للحالات المنتقاه وفى نفس الظـــــروف الاجتماعية والاقتصادية لهم و ٣٥ من الذكور و ١٥ من الاناث٠

لقد تم استجواب المرضى بعناية فائقة وفحصهم اكلينيكيا بدقة، كما تم عمل بعض الفحوص المعملية والاشعات، وتم متابعة الاطفال لمدة عامين متتاليين ولقد تم تقسيم مجموعة المرضى الى مجموعتين كبار :

ـ المجموعة الاولى: وزالتى تم عمل الفحوصات المعملية والاشعات لهم لتبيـــــن نوع وسبب عدوى الصدر المتكررة لديهم٠
وقد تكونت هذه المجموعة من ٤٦ مريض ومريضة

ـ المجموعة الثالثة: المكونة من ٢٢ مريض ومريضة والتى تم تشخيصها بـــــدون اللجوء الى الفحوصات المعملية او الاشعات لان هنـــــاك سببا واضحا ويعتبر سببا مباشرا لعدوى الصدر المتكررة٠

كما تم عمل قياسات لاجسام الاطفال المرضى والاصحاء فيما يختص بالطول والـوزن ودوران الرأس لتتبين درجة النمو الجسمانى للأطفال ٠

وتم عمل دراسة المستوى الاجتماعى والاقتصادى للاطفال المرضى والاصحـــــاء باستخدام معادلة تتكون من ثلاثة اجزاء هى: درجة تعليم الام، طبيعـــــة وظيفة الاب، والدخل الشهرى لكل فرد فى الاسرة حيث تم تقسيم المرضـــى والاصحاء الى ثلاثة مجاميع اساسية حسب المستوى الاقتصادى والاجتماعـــى :
فقير ـ متوسط ـ مقتـــدر

التحاليل المعملية التى تم القيام بها فى البحث تشتمل على صورة دم كاملة ، قياس للاجسام المناعية فى الدم بانواعها باستخدام طريقة اليزا وقد تم تجميع النتائج فى جداول ورسومات بيانية ملحقة بالبحث .

وقد توصلنا من خلال البحث للاتى : بعد اختبار المرضى بطريقة عشوائية من عيادة الامراض الصدرية وبعد القيام بهذا البحث كما سبق شرحه نتبين ان هناك انواع من أمراض الصدر المتكررة أكثر انتشارا بين هؤلاء الاطفال عن أمراض اخرى (مثل التهاب الشعب المزمن ، حساسية الشعب ،الالتهاب الرئوى ، تليف الرئة ، السل الرئوى) ، كما أن النتائج المعملية اثبتت للمصادفة أن نقص المناعة لايمثل السبب الرئيسى لتكرار العدوى الصدرية فى الأطفال كما كنا نتوقع (وانما يعود السبب الى مجموعة عوامل متضافرة تشكل البيئة المحيطة بهؤلاء الاطفال مثل انخفاض المستوى الاجتماعى والاقتصادى لهؤلاء الأسر ازدياد عدد أفراد الأسرة الواحدة ـ المنازل الصغيرة المعتمة المكدسة وسيئة التهوية ، سوء التغذية فى الأطفال سواء كان سببه الجهل بأصول التغذية أو انخفاض مستوى المعيشة، الجهل ، تلوث الهواء بداخل المنزل عن طريق حرق الخشب والكيروسين والقمامة للحصول على الوقود وتحمية الأفران والتدخين أو خارج المنزل مثل عادم السيارات ومخلفات المصانع ، كما وجد أن بعض أنواع التشوهات الخلقية فى الرضع والاطفال لها دور أساسى فى تكرار عدوى الصدر مثل الطفل المنغولى، ارتجاع المرئ ، فناء الحجاب الحاجز ، التخلف العقلى وهناك أسباب غير خلقية مثل الشرقة وابتلاع الأجسام الغريبة التى تحتجز فى القصبة الهوائية أو الشعب ، سوء التغذية الشديد، لين العظام .

ولقد دعم هذا البحث بشرائح للاشعات الصدرية للمرضى وأيضا شرائح توضيحية لمكونات البحث .

الكلية :

شكر

اشكر السادة الاساتذه الذين قاموا بالاشراف

وهم : ١) .....

٢) .....

٣) .....

٤) .....

ثم الاشخاص الذين تعاونوا معي في البحث

وهم : ١) .....

٢) .....

٣) .....

وكذلك الهيئات : ١) .....

٢) .....

٣) .....

لجنة المناقشة والحكم

وافق الاستاذ الدكتور/ نائب رئيس الجامعة لشئون الدراسات العليا والبحوث بتاريخ / / ١٩٩ ، على تشكيل لجنة لمناقشة الطالب/

. . . . . محمد

من السادة الاساتذه :

١ - أ.د/ . . . . . استاذ طب الأطفال . . . . . رئيسا ١٩٩٧/١٠/٤

٢ - أ.د/ . . . . . استاذ . . . . . عضوا . . . . . .

٣ - أ.د/ . . . . . استاذ . . . . . عضوا . . . . . .

٤ - . . . . . .

. . . . . عضوا . . . . . .

بيان بحالة الباحث

الأسم : .....

قسم : .....

موضوع الرسالـــه : .....

للحصول على درجة : .....

الوظيفـــة : .....

مكان العمل : .....

الشهادات الحاصل عليها الطالب :

١- .....

٢- .....

٣- .....

٤- .....

تاريخ التسجيل : .....

تاريخ المناقشة : .....

التقديـــر : .....

رسالـــــه ماجســـتير / دكتـــوراه

اســـم الطـــالب :

عنـــوان الرسالـــه :

اســـم الدرجـــه : ~~ماجستير~~ / دكتـــوراه

لجنـــة الاشـــراف

١- الاســـم / الوظيفـــة /

٢- أ.د/

٣- أ.د/

تاريـــخ البحـــث : / / ١٩

الدراســـات العليـــا

اجيزت الرسالـــه بتاريخ / / ١٩

موافقـــة مجلـــس الجامعـــة

/ / ١٩٩

جامعة عين شمس

الكلية : .....

صفحة العنوان

إسم الطالب : .....

الدرجة العلمية : .....

القسم التابع له : .....

إسم الكلية : .....

الجامعة : .....

سنة التخرج : .....

سنة المنح : .....

شروط عامة

يوضع شعار الجامعة على الغلاف الخارجى على (الكعب وملون)

دراسة وبائية ومناعية لحالات العـــــدوى الصدرية المتكررة للرضع والأطفال

رسالـــــــة

مقدمة للوفاء بمطالب درجة دكتوراه الفلسفـة

فى طـــــب الأطفـــال

قدمتهـــــا

سلوى تمام حســـــــان

بكالوريوس فى الطب والجراحة وماجستير أطفال

تحت اشراف

الاستاذ الدكتور رشاد صقـــــر

أستاذ طب الأطفـــال

بكلية الطـــب ـ جامعة القاهرة

الاستاذة الدكتورة تغريد جعفـــر

استاذ مساعد التحاليل الاكلينيكيـة

كلية الطب جامعة القاهـرة

الدكتـور جمال سامـــى

محاضر طب الأطفـــال

معهد الدراسات العليـا للطفولـــة

جامعة عيـن شمـس

جامعة عين شمـس

معهد الدراسات العليا للطفولة

قسم الدراسات الطبية

١٩٩٥