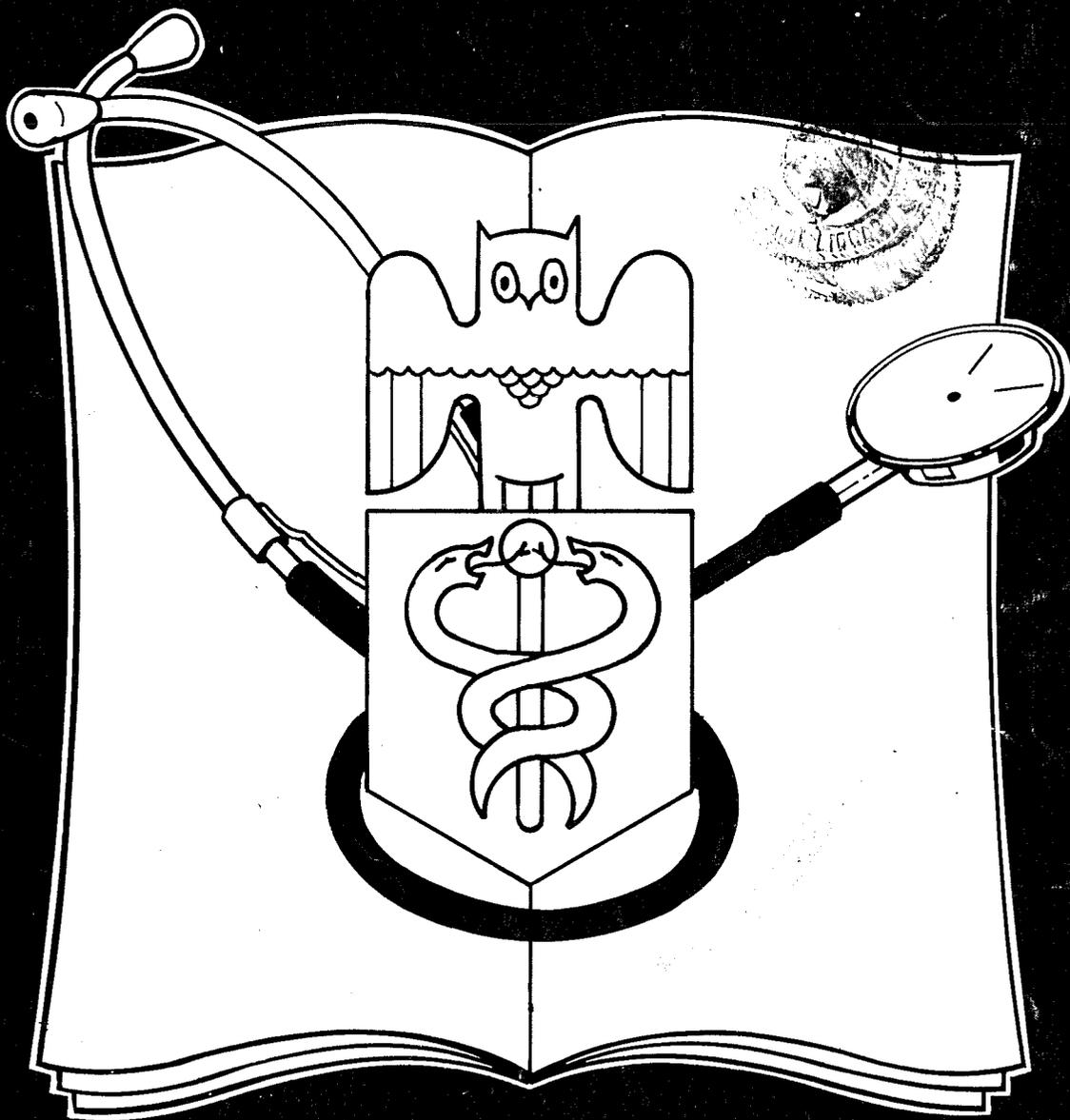


# Medi-Scope

ISSUE NO.6 1984



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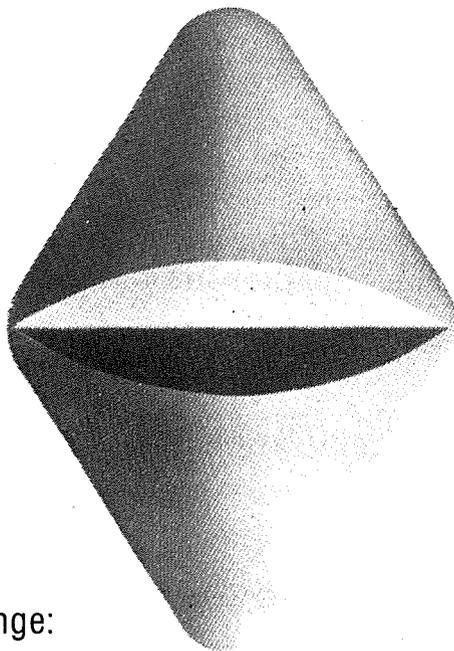
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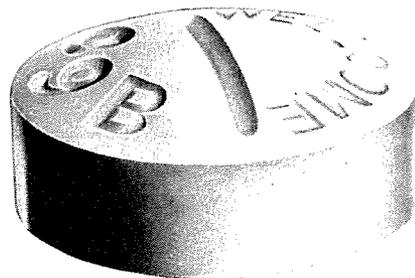


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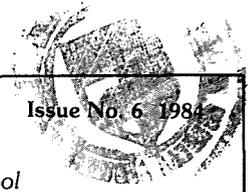
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# Editor's Letter



## Medi-Scope

Issue No. 6 1984

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Times change and people change with them. Mediscope is no exception and whilst the old editorial board passes into history, into its shoes step younger feet.

I wish to thank the previous editor Mark Bugeja and the previous sterling services rendered to the magazine, in setting it up (a difficult enough task), putting it on an even keel and keeping the magazine well above the water level. Its success is much due to their hard work. We all hope to be able to keep up the standards attained so far and even reach higher levels.

The new editorial board whilst hoping that readers past and present will continue reading this magazine in the future, also wishes to point out that for its continuing success, this magazine depends a lot upon the articles presented to us from various contributors, this ranging from the professorial to the student level.

Being the Maltese magazine that has the greatest circulation amongst the medical students and doctors in Malta, the board has seen it fit to branch out slightly more and include occasional topics as Dentistry, and later on we hope various others.

In this edition of Mediscope, no clinical diagnosis quiz is being presented due to the short interval between the previous publication and this one to give better chance for all to reply this popular quiz that yields rich rewards for little troubles. This will be resumed in the next edition.

Having said my share I will leave you to read this magazine, hoping that you will find the articles interesting and useful.

THE EDITOR

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# Hyperglycaemic, hyperosmolar, nonketotic coma

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## Introduction

As mentioned in the previous article, the 'diabetic-related' comas listed in order of their probable frequency are

- 1 hypoglycaemia coma
- 2 diabetic ketoacidosis
- 3 hyperglycaemic hyperosmolar non-ketotic coma; and
- 4 lactic acidosis

A combination of disorders may be often seen, and it must also be appreciated that ketoacidosis can be met with in alcoholic individuals who are not necessarily diabetic, which alcoholic ketoacidosis might also be complicated by hypoglycaemia.

It must be remembered that a great variety of diseases that could induce coma can be present in diabetics as well as in non-diabetics, and hence one must avoid the pitfall of always equating a coma problem in a diabetic with one of the so-called 'diabetes-related' comas.

Among the commoner possibilities of coma-inducing conditions one finds alcohol, epilepsy, insulin (too much or too little), opium and narcotics, uraemia, trauma (head...), infections of the C.N.S., C.V.A., and shock.

In view of the relatively high incidence of type II diabetics in Malta, it could well be that a not insignificant number of hyperglycaemic hyperosmolar non-ketotic coma cases (especially in older persons) might be occasionally missed, diagnosed late or misdiagnosed — this creating a potentially serious state, especially in view of the high frequency of both complications (including thrombosis) and mortality in this condition, especially in the elderly.

The following is an account of this important condition based on works by Arieff, Podolsky, Kozak and Rolla.

This is a life-threatening emergency with an extremely high mortality rate. It is a clinical syndrome with four major features:

- (a) severe hyperglycaemia (blood glucose > 600mg/dl)
- (b) lack of significant ketoacidosis (plasma Acetest < 2 at 1:1 dilution)
- (c) extreme hypertonic dehydration
- (d) variable neurological signs - such as depressed sensorium or frank coma

## Non-ketotic hyperosmolar coma with hyperglycaemia

Non-ketotic coma has been reported to occur in association with a wide variety of clinical situations, including: pancreatitis, severe infections, pulmonary embolism, burns, myocardial infarction, dialysis (peritoneal &/or haemo-), hyperalimentation, hyperthyroidism and chronic renal failure. In addition, different drugs, including thiazide diuretics, frusemide, propranolol, cimetidine, chlorpromazine, diphenylhydantoin, steroids and diazoxide and immunosuppressive agents have also been implicated.

The common denominator of all appears to be either (a) a decrease in insulin effect possibly via drugs or hormones that either antagonise insulin or interfere with insulin action and/or release and/or (b) excessive carbohydrate administration to a 'stressed' patient. The marked hyperglycaemia causes metabolic derangements leading to increasing loss of sodium salts and particularly water, in the urine. This, together with hyperglycaemia, increases extracellular hyperosmolality with consequent increasing thirst. Drinking water freely could for a while moderate the hyperosmolality, however when plasma osmolality reaches high levels, impairment of sensorium develops. This, eventually causes interference with the patient's ability to replenish water losses, and leads to a fall in glomerular filtration rate, azotemia and hyperglycaemia with further elevation of plasma osmolality, and rapid deterioration of mental function from somnolence to coma.

"The seriousness of the problem may not be apparent because of the relative paucity of symptoms. Thus, in contrast to patients with ketoacidosis, whose symptoms usually bring them to medical attention within a short period of time, patients with non-ketotic coma may exhibit a protracted course lasting several days to several weeks."

Non-ketotic coma occurs most frequently in elderly type II patients who have impaired pancreatic beta cell activity and who may be known to have mild diabetes. These patients could also often have an impairment in the ability of the liver to synthesise ketones from free fatty acid substrate, somewhat low

levels of growth hormone and cortisol, and frequently moderate to severe underlying cardiovascular or renal function impairment (this azotemia possibly playing a part in the development of oliguria that often ensues during therapy). In most patients there is a stressful event, such as a major illness. This syndrome also often develops insidiously in patients without previously diagnosed diabetes. Slightly more women than men are affected.

The typical patient is brought to hospital in a confusional (or comatose) state with a history of days or even weeks of polyuria and increasing thirst. Physical examination reveals a striking and profound dehydration, shallow respiration (and hyperventilation), but no odour of acetone in the breath. These patients often present with a variety of neurological signs including seizures, hemiparesis etc. suggesting diffuse cortical and subcortical damage. Not infrequently a cerebrovascular accident is suspected. Most of the localizing, neurological signs are completely reversed with successful treatment (involving mainly the correction of the dehydration and hyperglycaemia). There is a direct relationship between serum osmolality and impairment of consciousness, and comatose patients with hyperglycaemic, hyperosmolar non-ketotic coma most frequently have a serum osmolality above 340mOsm/kg.

(Plasma (serum) osmolality can be calculated from the following formula:

$$\text{mOsm/l} = 2(\text{Na}^+ + \text{K}^+) + \frac{\text{blood glucose}}{18} + \frac{\text{Bld. urea Nitrogen}}{2.8}$$

normal plasma osmolality ranges from 285 to 300 mOsm/l).

### Treatment

Some controversies exist as to the treatment recommended in hyperglycaemic, hyperosmolar non-ketotic coma. Irrespective of the exact amounts and types of insulin and fluids given, the key to recovery lies in the careful monitoring of these patients.

Therapy is directed towards

- (a) correction of the extreme degree of volume depletion.
- (b) correction of the hyperosmolar state.
- (c) detection and correction of any underlying precipitating cause, such as associated illness or drug administration.

### Fluids

Various types of intravenous fluids have been advocated as the appropriate type of initial fluid therapy, but it now seems that 1/2 Normal (0.45%) Saline is the fluid of choice. After confirmation of the diagnosis, circa 2 litres of hypotonic saline should be infused very rapidly i.e. within the first 2 hours. Some authorities however advise using 0.9 (rather than 0.45%) saline for this initial, immediate restoration of intravascular volume.

Thereafter infusion of hypotonic (0.45%) saline is

administered, titrating according to the central venous pressure - on the average an addition 6 to 12 litres of fluid being required during the following 36 hours - (half the estimated water deficit being replaced in the first 12 hours and the remainder in the next 24 hours).

The infusion solution should be charged to 5% dextrose in water (or in half normal saline) when the blood glucose has fallen to 250mg/dl. — potassium supplements are often needed, and should be added if required, once the patient has an adequate urine output. Addition of at least 20 to 40 mEq of potassium chloride to each litre of parenteral fluid should be accomplished early — this is stopped if serum potassium levels rise above 5.0 mEq/l, or doubled if levels fall below 4.0 mEq/l. Since these patients often also have phosphate deficits, potassium phosphate 5 mM/l can be infused instead of potassium chloride.

Determinations of blood glucose, serum electrolytes, blood urea nitrogen and plasma osmolality at frequent (4-6 hrly) intervals will assist careful monitoring of the patient's response to treatment.

If hypotension or tachycardia is present, isotonic saline should be infused until the CVP begins to rise. Blood or plasma is indicated if the systolic blood pressure remains low (i.e. below 80 mm Hg.)

### Insulin

Various regimens for insulin therapy have been recommended, the commoner being regular (short-acting) insulin administered in continuous i.v. infusion or i.m. similar to those used in D.K.A. The insulin needs in HNC are in general usually less than in D.K.A., however on certain occasions large amounts of insulin, similar to D.K.A. are necessary. Close monitoring of the patient and the blood glucose levels is essential.

It is recommended to start with a 'loading' dose of circa 20 units i.v., followed by 5 units i.m. per hour, until blood glucose levels drop to 300 mg/dl, when no additional insulin should be given. If this low dose method is used and the blood glucose does not respond adequately, the amount of insulin should be increased accordingly, (eg. doubling the dose). It cannot be overemphasized that adjusting the therapeutic regimen to the needs of the individual patient, with meticulous clinical care, the vigorous replacement of fluid and potassium and the correction of precipitating factors or associated illnesses are just as important as the details of insulin therapy. Finally, because of the propensity of these patients to develop arterial and venous thromboses, consideration should be given to early use of heparin therapy.

After recovery from the acute episode, the patient is transferred to a daily subcutaneous dose of Lente or NPH insulin, and many of these patients can be then gradually changed over to sulphonylurea therapy at, or after discharge from hospital.

# Risk Factors for Developing Allergy in Children

The factors which seem to influence or *turn on* the allergic response in children can be *prenatal*, *perinatal* and *postnatal*.

In *prenatals* *heredity* takes the first place but *environmental factors* contribute as well as genetic ones. Of *prenatal peristatic (environmental)* factors *highly allergenic food* in allergic mothers and *progesterone therapy* may be important in *turning on* the allergic process in potentially allergic infants. The mother's progesterone therapy during pregnancy was shown to increase significantly the mean IgE levels and the mean percentage of detectable IgE in the cord blood. This hormone has been reported to be immuno-suppressive *in vitro*. As 20-alpha-hydroxysteroid dehydrogenase was discovered in the mouse thymus, the hypothesis has been put forward that this enzyme, engaged in the progesterone metabolism, may have a protective role in reducing progesterone activity in the thymocytes. Thus, the progesterone administered to pregnant women might interact with fetal thymus maturation and because a delayed thymic maturation was involved in the allergy onset, a hypothetical role of progesterone may be explained. According to another hypothesis progesterone may modify the placental biology including a placental transfer of IgE.

Certain *perinatal factors* may significantly affect the likelihood of a child's developing serious atopic disease:

- a) The incidence of *neonatal complications* has been found to be two times greater among asthmatic children compared to non-asthmatics.
- b) Asthma occurs more frequently among the children born in *pollinating seasons*, suggesting that seasonal differences in neonatal antigen contacts are important for development of allergy.

Of *postnatal factors*, probably the most important early influence is the infant's diet. The incidence of atopic dermatitis in potentially allergic infants fed cow's milk, eggs and wheat has been found to be seven times that of the exclusively breast-fed ones. 60-80% of these eczematous children later developed major respiratory allergic diseases, especially asthma, compared to 15% of those in whom cow's milk products were withheld from birth till 9 months of age. Even babies breast-fed for only 6 weeks were found to be considerably less likely to develop asthma or atopic dermatitis.

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Why? Because human breast milk contains a large amount of IgA antibodies and also a factor which stimulates development of intestinal mucosa, the child's own production of secretory IgA being enhanced IgA antibodies prevent the transport of foreign proteins across the gut wall and this is the most probable mechanism whereby maternal IgA antibodies to cow's milk antigen prevent sensitization of the breast-fed baby. However, it is important to remember that while advocating breast feeding in potentially allergic newborns, certain potentially harmful allergens may gain entrance to the infant's relatively leaky gut via the mother's breast milk.

Allergy often begins early in life, in many cases during the first year. The detection of a newborn at high risk of allergy is therefore important. A recent study showed that 71% of the newborns, who subsequently developed clinical allergy, had detectable IgE in their cord blood compared to 21% of the symptom-free infants. Cord blood IgE level was, therefore, shown to be a good predictor of subsequent atopic disease, along with raised level of IgE and presence of specific IgE antibodies in the mother's serum. IgE can be detected in human foetuses by the 11th week of gestation but under normal circumstances is not *turned on* in utero.

In *turning on* this system, prominent role has been attributed to transient lack of IgA and its local protective function in the intestinal mucosa during the first 3 months of life.

- Children with permanent IgA deficiency develop serum precipitating (IgG) antibodies to cow's milk protein much more frequently than normals, suggesting that their gastro-intestinal tracts are unusually *leaky*:
- IgA deficiency was found in a significantly increased proportion of atopic subjects.
- Transient deficiency of secretory IgA in young infants' gastro-intestinal tract is a physiological phenomenon and one should withhold commonly allergenic food in allergic infants until their guts are coated with IgA of their own making. Failure to withhold the potential allergens will *turn on* the IgE system.

In early infancy, *surgery necessitating anaesthesia* (pyloric stenosis, hernia repair etc.) as well as *early hospitalization* for non-surgical reasons seem to *turn on* the allergic diathesis. Early viral low respiratory tract infections can delay maturation and

normal functioning of IgA system, as synthesis of secretory IgA requires complete integrity of the epithelial cells. A clinical continuum of infantile bronchiolitis and childhood asthma has been suggested by some authors. General anaesthesia, associated with early surgery, is supposed to transiently impair the protective layer containing secretory IgA, thus rendering the respiratory mucosa permeable for common airborne allergens.

Another factor influencing the triggering of the onset of asthma in early infancy is the *home exposure* to many *potent allergens*. Important sources of increasing the allergic load in the house are the *presence of pets, stuffings of pillows, mattresses, furniture, and toy stuffing*. *Cigarette smoking* in the house of allergic infants increases both the risk of triggering the onset of the allergic response and of subsequent asthma attacks.

During pollinating season, a child's exposure to pollen can be decreased by keeping the bedroom windows and door closed. To further ensure an interruption of pollen exposure it is important to keep in mind that pollen sticks to human hair and is water soluble. It is thus desirable that pollen-allergic children rinse the pollen out of their hair after coming in from playing out of doors and at bed time.

In the first year of life allergy may involve the *intestinal tract, skin and respiratory tract*. Allergy to food in the first few months of life may be the causative factor of the so-called *coeliac syndrome*. Even a serious form of bloody diarrhoea due to milk allergy has been described. Symptoms subside dramatically when cow's milk is withdrawn from the infant's diet. In the first 2-8 months of life, *nasal stuffiness, brought on by allergy to foods, interferes with a child's sucking, while post nasal dripping may cause coughing*. For this coughing it is important *not to prescribe codeine containing cough mixtures*. Elimination diet and appropriate use of antihistamines usually suffice to solve the problem.

Later, children with allergic rhinitis may develop allergic swelling of the lower end of their Eustachian tubes. This may result in repeated ear infections, ear pain from sterile middle ear effusion, ear popping and hearing difficulties. Children in 3-7 year age group with secretory otitis media may have sufficient conductive hearing impairment to give the impression of being *inattentive, immature, or not bright*.

*Bronchial asthma* in the first year of life may result from food allergy while later it usually results from allergy to inhaled allergens, such as pollens, house dust, animal danders and moulds.

In an effort to put much of the mentioned clinical and experimental evidence to practical use, programmes of prophylaxis of atopic disease in the offspring of atopic parents have been proposed. Their main premises are the following:

1. Simply *planning in advance for the time of birth to coincide with non-pollen season* may lessen the likelihood of those infants going on to develop hay fever or asthma.
2. Avoidance of highly allergenic foods in allergic women during pregnancy and lactation.
3. Breast-feeding for at least 6 months as numerous studies have shown that it significantly lowers the incidence of major allergic diseases.

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# Coronary Artery Bypass Grafting - The State of the Art

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There is now considerable evidence that surgery for coronary artery disease relieves angina very effectively and indeed is more effective in the treatment of angina than medical treatment in matched and randomised series. Furthermore, coronary artery bypass surgery improves life expectancy in those patients who have significant disease of the left main stem or of all three major vessels *three vessel disease*. Some data behind these statements will be mentioned in this article.

It is first important to appreciate the anatomy we are discussing. The left main stem is a small part of the origin of the left coronary artery and clearly disease here is liable to put the whole of the left ventricle at risk. The right coronary artery, the left anterior descending and the left circumflex are the three major vessels. The term three vessel disease implies disease of each of these vessels. Clearly there are sub-branches of these vessels, and these in turn may be diseased. There is some variation between patients in the relative distribution of their coronary arteries and in the number and size of their sub-branches. This variation plays some part in the assessment of the patient for operations and in the technicalities of where and how many grafts are placed. However, it has not been used in the analysis of the results of the trials for angina or survival.

## Angina Relief

Between 1973 and 1976 over 750 patients were randomly and prospectively entered through a multicentre European trial of medical versus surgical treatment of patients with at least 50% stenosis in two major vessels (European trial or ECSS). The surgical group had an 84% improvement of angina by 1 year compared to 45% improvement with medical treatment: at three years, 78% of the surgical group were improved with nearly 50% totally free of angina, whereas in the medical group 50% were improved at three year and just under 20% were free of angina. These differences were highly significant statistically. There have been several other matched studies, particularly in the United States of America, which have shown the benefit of surgery over medicine for angina relief. In individual surgical series, Loop was quoted 87% free of angina at 5 years and Bourassa 50% absence of angina at seven years. There is little doubt that the relief of angina is due to revascularization of the heart and not due to a placebo effect, nor to infarction. There is good correlation between relief of angina and graft patency or completeness of revascularization (by completeness I mean that all the major vessels which were diseased were grafted). Exercise tolerance after bypass grafting is greater after surgery than after medical treatment, (European Trial). Other studies have suggested improvement of left ventricular function after coronary revascularization.

TABLE 1

### EUROPEAN TRIAL (ECSS) ANGINA RELIEF

	1 yr.		2 yr.		3 yr.	
	Free	Improved	Free	Improved	Free	Improved
MED.	17%	45%	17%	48%	20%	50%
SURG.	58%	83%	55%	79%	50%	78%

• • • • • •

• all comparisons M vs S p 0.001

### Life Expectancy

Stenosis of left main coronary artery of 50% or greater provides the patient treated medically with a life expectancy of 60% at five years, but if treated surgically his life expectancy is 94% at five years (European trial). Life expectancy in these figures of course includes any operative or hospital mortality related to surgery or other medical treatment. When the stenosis of the left main coronary artery is much greater than 50%, the heart is very much at risk and it is our practice at present to keep people in hospital for surgery if they have 70% or greater stenosis of the left main coronary artery.

Table 2 shows survival figures for left main disease and three vessel disease as taken from the European randomised prospective trial. These results have been confirmed in the previous Veteran's administration study (VA Study) and the Collaborative coronary artery surgical study in America (CASS).

Patients with 50% or greater stenosis of three vessels (*three vessel disease*) have also been shown to have an improved prognosis after surgical treatment than after medical. The European study showed a 95% survival in the surgical group at five years compared to 85% in the medical group. The CASS study, which looked at 15,000 patients in the United States of America and Canada showed that surgery provided an improved chance of either survival or freedom from a major heart attack in patients who have three or two vessel disease, compared to those treated medically. There has been no evidence to show that patients with one vessel disease have prolonged survival by surgery as against medicine. Probably the aspects which affect survival relate to the ability to develop collaterals from non-involved coronary arteries and relates to the quantity of heart which has not been affected by chronic ischaemia or infarction. (Table 3).

### Risks

The risk of dying at operation has been gradually decreasing over the last 10 years. In 1972 operative mortality was 5.6%, in 1976 3%, in 1978 2% and in 1983 it is probably less than 2%. These figures were taken from the three major randomised studies mentioned above. Improvements have come about through a combination of factors, which include our familiarity and experience in coronary artery surgery, improvements in the understanding in preserving the energy stores of the heart during the operation, by general improvement in understanding of patients undergoing heart surgery and improvement in the overall team experience and possibly by technical improvements with magnification. The major factor which still affects the risk of operation is the condition of the patient's ventricle. Those who have poor left ventricular function as a result of multiple previous myocardial infarction have a higher risk of

operative death and also carry less good long-term prognosis.

To illustrate this, Table 4 shows a five year survival of patients treated medically sub-divided by the degree of dysfunction of the left ventricle. Surgery will improve each group, but the best results are obtained from those with good or moderate left ventricular dysfunction because severe left ventricular dysfunction is not improved much, if at all, following cardiac surgery.

### Patency

Most surgical series show between 80 and 90% graft patency at one month and between 70 and 80% graft patency at five years (Bourassa). The veins used for the coronary grafts do always show changes as a result of being made to work as arteries. There is always intimal hyperplasia and in some cases there will be severe thickening and atheroma occasionally occurs in the vein grafts themselves. There is also some continuing progression of the disease in the native arteries, as the operation itself does nothing to alter the etiology of the condition. There is therefore a continuing incidence of return of angina, due either to increasing disease in the native vessels or of problems with the vein graft, or to a combination of both. Graft patency as expected, is best when the arteries grafted are the largest, and fare the worst with those of less than 1.5 mm diameter.

### Re-Operation

Because of the obvious palliative nature of the disease mentioned above, re-operation is becoming increasingly indicated. The results of re-operation are less good than those of the first operation, but there is still a 50% chance of providing benefit to the patient in terms of release of angina by a second operation.

### Surgery following Myocardial Infarction

Immediate surgery following myocardial infarction has not been shown to be of value. However, there is a series by Rogers, indicating that surgery at 6 weeks following myocardial infarction gave better long-term survival and instance of further infarction, in those patients who had about 25% or more of ventricular muscle at risk from tight stenoses. This study has not yet been translated into surgical practice, except that it is now the basis for another European trial of coronary artery surgery for 3-vessel disease 6 weeks following infarction. The results of this trial will obviously be eagerly awaited in a few years' time.

### Assessment of Vessel Disease

Coronary angiography is the final delineator of the state of the coronary vessels and of the left ventricular function. Exercise ECG's provide the most important screen through which patients who have angina can be assessed as suitable for coronary angiography. Not only can this tell whether there is ischaemia on exercise, but also by using a technique which we have developed at St Mary's of mapping from both front and back chest leads,

**TABLE 2**

**LIFE EXPECTANCY % SURVIVAL**

LEFT MAIN DISEASE	M	S	Significance
ECSS at 5 yr	62	93	< .037
CASS at 3 yr	69	91	< .001
VA at 2 1/2 yr	60	88	< .01
<b>3 VESSEL DISEASE</b>			
ECSS at 5 yr	85	95	< .001
<b>2 VESSEL DISEASE</b> (with 50% LAD involvement)			
ECSS at 5 yr	82	92	

**TABLE 3**

**EVENT-FREE SURVIVAL CASS at 3 yrs**

	M	S
<b>3 VESSEL DISEASE</b>	66	89
<b>2 VESSEL DISEASE</b>	74	95

event = death, myocardial infarct, or re-operation

**TABLE 4**

**% SURVIVAL RELATED TO LEFT VENTRICULAR FUNCTION (LV)**

DUKE SERIES at 5 yrs	MED	SURG
NORMAL LV	90	—
MODERATE LV DYSFUNCTION	68	—
SEVERE LV DISFUNCTION	38	—
<b>SEATTLE HEART WATCH at 5 yrs (mild angina)</b>		
NORMAL LV FUNCTION	92	95
MODERATE LV DYSFUNCTION	70	90
<b>EJECTION FRACTION</b>		
> 50%	"Normal"	
30 - 50%	"Moderate" dysfunction	
< 30%	"Severe" dysfunction	

whether ischaemia is likely to be in the region of 1,2 or 3 coronary arteries.

### Summary

The current indications for coronary artery surgery are:-

1 Stable angina which has continued to produce pain despite medical treatment, or, angina in patients unable to tolerate medical treatment, or, angina for those who medical treatment poses such a limitation of lifestyle or work that they find this unacceptable and prefer surgery.

2 Patients who have *unstable* angina require urgent coronary artery surgery as the pain cannot be settled with intravenous nitrate infusion. Unstable angina is angina which is occurring on minimal or no exertion and at rest.

3 As a result of a coronary angiogram, patients with 50% or more stenosis of the left coronary main coronary artery, or of all three vessels, will be considered for surgery even if asymptomatic, provided they have good or moderate left ventricular function. Those who have a very tight stenosis (95%) of the left anterior descending vessel alone, would also be considered because of the impending likely anterior infarction.

4 Cardiac failure and arrhythmias are not usually indications for surgery, and surgery after myocardial infarction has been discussed above and the results of the European trial are awaited.

### Incidence and Prevention

The current rate of coronary artery bypass

grafting in the United Kingdom is about 100 cases per 1,000,000 per year. It is estimated that we ought to be doing 300 cases per 1,000,000 per year in the United Kingdom to cope with the incidence of the disease in this country. These figures are taken from comparisons and analysis of the work done in Australia and North America.

It is likely that the incidence of coronary disease will continue at the same rate for some years to come, and it is very difficult to define any factors which we can do something about which will reduce this incidence. The first thing, is to stop people smoking, as undoubtedly, smoking has a high correlation with coronary artery disease and indeed those who have coronary artery surgery who are foolish enough to continue smoking have a much higher incidence of return of angina than those who do stop smoking. Control of blood pressure and weight are considered important and in those who have very high cholesterol and triglyceride levels, the reducing of these may be of some value, although we have no data to support this yet. Much emphasis has been put on altering our dietary habits, but there is as yet very little hard evidence to show which part of our diet is directly related to causing coronary artery disease. The most popular is related to the high levels of animal fats that we eat and considerable effort has been related to making us in general reduce our animal fat consumption. Stress has also been suggested as a causative factor and it has been suggested we should reduce the amount of stress in our everyday lives and work. Unfortunately the continuing incidence and the increasing demand for coronary artery surgery is likely to provide little relief in stress for the cardiac surgeon!

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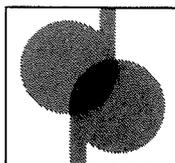
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# Occlusion, Mastication and the Temporomandibular Joint

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**T**he value and importance of mastication and biting forces in helping to promote digestion of food is well known. Being edentulous does for most people lead to restriction of diet with its ill effects and lack of enjoyment of food. The provision of dentures is also a functional necessity in relation to a healthy temporomandibular joint (TMJ). In practice, we find that in many patients, the TMJ adapts itself to a fair amount of varied postures, especially in those who have been without dentures for a period of years. However, changes or deviations from the normal movements of the TMJ introduce risks to its well being.

Some years ago, I carried out practical experiments and observations on a number of middleaged Maltese, with a view to establish a relationship between gape and opening force. Although I did come to some conclusions, these studies are not easy because of TMJ morphology. In contrast to near linear changes in muscle length associated with movements at simple hinge joints, mouth opening in us humans, involves some rotation and translation of the condyle.

Unfortunately, many patients procrastinate to have dentures fitted, without realising the problems they may create for themselves with the passing of time. Although the number is gradually decreasing, we do see patients - who because they did not have dentures fitted at the right time, sometimes for many years, may have very shallow and atrophied gums resulting in poor denture tolerance and angular cheilitis. In cases where there is little bone and gum

support, denture tolerance can be difficult. This is further aggravated in nervous, tense or diabetic patients.

Jaws without supporting teeth or well occluding dentures tend to lose their physiological rest position. The facial muscles and supporting tissues may also be effected. In the physiologic rest position of the muscles, both the depressor and elevator muscles are theoretically in balance, so that the jaw is normally in the same rest position - about 2 to 4 millimetres from tooth contact.

Abnormal occlusion is one of the aetiological factors or a contributing factor in certain TMJ conditions. Patients should be encouraged as indeed they often are, to have partial dentures or some other form of artificial teeth fitted where missing teeth are present - these often stabilize the bite, besides supporting the remaining teeth.

It is relevant to mention that measurements of maximum biting force have been used clinically in scientific studies in a few European Centres, to establish face height in denture construction and in the assessment of dysfunction of the TMJ and jaw muscles.

The articles by Goodfriend and Costen published in 1934 were milestones in the field of TMJ disorders. In the light of present day knowledge, it is easy to pick faults in some of Costen's contentions, but he earns our praise for focusing our attention on this important subject. Subsequent and fairly recent research has shown that Costen's Syndrome, as it was then described occurs less frequently and that

one of the disorders which affect the TMJ is a condition which is described by various research graduates as Pain-Dysfunction Syndrome after Schwartz (1959).

Certain problems concerning this condition are not yet solved, but it is worthwhile to consider in brief the effect of occlusion and mastication as one of the aetiological factors. However, there are cases where an irregular occlusion is not the main cause. In several cases which I have seen, four etiological factors overlap - traumatic occlusion, abnormal mandibular movements, anxiety states and generalised muscle tension. In the articular complex, the occlusion, TMJ, ligaments and muscles combine to brace the mandible against the cranial base in several physiological activities. An inordinate amount of brain tissue is allotted to the functions and sensations of the mouth.

Normally, a person's mandibular movements are characterized by his particular protrusive and lateral condyle paths. With normal occlusion, it is observed that occlusal surfaces maintain contact during lateral movements of the mandible. When several teeth are lost without being replaced, the remaining ones are not effectual enough for mastication. The biting load on the TMJ may become unbalanced and overly severe, with a possibility of resultant damage.

Sometimes we observe traumatic occlusions which are asymptomatic. In these cases, it is possible that the adaptability of the patient offsets to some extent the potential harmful effect. It is also an established fact that pain tolerance varies from patient to patient.

Clenching forces may be measured with intra-oral gnathodynamometers and average values for maximum biting forces between the molar teeth of healthy adults are generally between 50 and 70 kg.

When a single leg is missing from a tripod, it becomes impossible to stabilize the object resting on it. If one were to add another leg to a tripod standing on a given plane, this additional leg must extend exactly as far as the plane, lest it lose its function. During the growing stages of a jaw or during the period of changing dentition from primary to permanent teeth, a single tooth could stick out above the rest, forcing the child to take a bite which may be a deviation from the normal occlusion. Normally, however, other teeth grow out to approximate a new balance for the jaw's position.

The bone of the mandible and maxilla is complex in its variations and reactions in different persons. Some bones can resist a reasonable amount of pressure, whereas other bones can resist very little. It is not always appreciated that a properly constructed appliance will aid in the regeneration of bone around teeth as well as aid in their stabilization.

In a study of several Maltese patients, I observed

that the Pain-Dysfunction Syndrome affects mostly patients between thirty-five and fifty-five years of age. It appears that women are more susceptible than men, this condition being found more often in those with unbalanced bites and highly strung temperaments. The two important symptoms are pain (often nagging) and mandibular dysfunction which may manifest itself as clicking (various degrees) and irregular movements. The centre of occlusion may be deviated slightly. Pain may generally be either (a) related to the underlying muscles of mastication (myalgia) and the muscles in the cervical region, with possible surface tenderness or (b) related to the joint area, probably due to a traumatic inflammatory state affecting the joint capsule, disc and ligaments.

The recognition of degenerative changes follows integration of a careful clinical examination with the radiographic ones. A contour of the TMJ and associated parts can be formulated, special problems and data noted and partial or full dentures planned to help correct the strain or irregular forces acting on the TMJ. Sometimes a special appliance is required.

Although definitely not the only cause, unbalanced or traumatic occlusion may be one of the causes of tension and spasm in the muscles and strain on the disc-joint-ligament relationship. Furthermore, it is worth remembering that cartilage has no recuperative qualities.

This syndrome may be caused by:

- (a) Lack of support or balance between maxilla and mandible due to several missing teeth on one side.
- (b) Loss of all teeth and non wearing of dentures for a long period.
- (c) Angle's Class II occlusion with lack of support posteriorly.
- (d) Overclosure or unbalanced bite in dentures.
- (e) Abnormal intercuspal relation which effect occlusal and grinding movements during mastication.
- (f) Prolonged grinding, clenching and nail biting in nervous patients.
- (g) Abnormally erupting wisdom teeth.
- (h) Fractures of condyles
- (i) Rheumatoid arthritis.

In a good number of cases, the active phase of pain in the TMJ region stops or decreases when the causative factors are eliminated. It is not a good policy to give an unlimited amount of analgesics for a long period as these may mask or alter the symptoms and may put the patient off from undergoing the necessary investigations and treatment. We must do our best to (a) maintain occlusal equilibration (b) assist the physiologic rest position of the jaws and (c) encourage the patient to relax and cooperate.

One final comment. We differentiate between Pain-Dysfunction Syndrome and Trigeminal Neuralgia. In the latter, severe pain generally comes suddenly, but is of relatively short duration, whereas in the former it tends to be less severe but lingers on as a dull continuous ache.

# Malignant Lymphomas

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**M**alignant lymphomas is a generic term given to the tumours of lymphoreticular system that includes lymphocytes of T, B and Null type, histiocytes-monocytes and Reticular cells. This term is reserved for those neoplastic processes that initially present as localized lesions and are characterized by formation of gross tumour nodules. Neoplastic lesions that are systemic and diffuse from their inception are called Leukaemias or Malignant histiocytosis, depending upon their presumed cell of origin: Malignant lymphomas have also been defined as tumours of the Immune System.

The term lymphoma was first proposed by Billroth in 1871. Based upon differences in histology and mode of spread, Dreschfield in 1891 delineated these tumours into two distinct entities namely lymphosarcoma and Hodgkins disease. Roulet in 1930, suggested that in addition to the previously described lymphosarcoma and Hodgkins disease there was a third type of tumour that was cytologically related to the reticular cells and thus different from lymphomas which expressed lymphoid

differentiation. He proposed the term Retothelsarcoma (Reticulum cell sarcoma) for this third type of tumour. The fourth major type of lymphoma was the so called giant follicular lymphoma. This category was originally reported by Ghon & Roman (1916) who reported follicle like structures as part of malignant proliferation. Brill et al and Symmers believed this to be a benign process due to massive hyperplasia of germinal centres. Gall and Mallory in 1942 established detailed criteria by which this neoplastic follicular proliferation could be distinguished from benign follicular hyperplasia. In 1957 Rappaport and Gall proposed the term nodular instead of follicular lymphoma.

Numerous classifications of malignancies of the lympho-reticular system have been proposed. Of these the Rye classification of Hodgkins disease has gained universal acceptance. Difference of opinion still prevails with regards to classification of Non Hodgkins lymphomas. Six different classifications namely: working classification of Non Hodgkins lymphomas, (Dorfman classification), British National

Lymphoma Investigation classification, Keil classification, Lukes and Collins classification, Rappaport classification and W.H.O. classifications, are being widely applied presently. The proponents of each system have advanced arguments for the superiority of their system over others. As a result, clinical studies which utilize one classification cannot be properly evaluated and compared to others which utilize another system. Clinicians, often relatively uninformed about the various systems, have become confused and cannot adequately assess recent publications concerning Non Hodgkins lymphomas. In an attempt to resolve these issues objectively, a unique multi-institutional study was planned and sponsored by the National Cancer Institute and National Institutes of Health, Bethesda, Maryland.

The resultant classification is called *A working formulation for Non Hodgkins Lymphomas for clinical usage*. This working formulation has been welcomed, albeit with reservations, by proponents of all other systems. It is not intended as a new classification but rather as means of *translation* among all other systems. The success of the working formulation as an alternative classification remains to be seen, but it is certainly worth while to familiarise oneself with it.

### Working Formulation of Non Hodgkins Lymphomas for clinical usage:

1. Low Grade
  - a Malignant lymphoma small lymphocytic.
  - b Malignant lymphoma, follicular, predominantly small cleaved cell.
  - c Malignant lymphoma, follicular, mixed small cleaved and large cell.
2. Intermediate Grade
  - a Malignant lymphoma, follicular, predominantly large cell.
  - b Malignant lymphoma, diffuse small cleaved cell.
  - c Malignant lymphoma, diffuse, mixed small and large cell.
  - d Malignant lymphoma, diffuse large cell.
3. High Grade
  - a Malignant lymphoma, large cell, immunoblastic.
  - b Malignant lymphoma, lymphoblastic.
  - c Malignant lymphoma, small non cleaved cell.
4. Miscellaneous
  - a Mycosis fungoides
  - b Composite lymphoma
  - c Plasma cytoma
  - d Unclassified

In Malta ever since it was proposed, W.H.O. classification has been used.

### W.H.O. Classification:

- 1 Hodgkins Lymphoma
- 2 Non Hodgkins Lymphoma.

### Hodgkins Lymphomas

- 1 Lymphocytic predominance type.
- 2 Nodular sclerosing type.
- 3 Lymphocytic depletion type.
- 4 Mixed cellularity type.

### Non-Hodgkins Lymphomas

- 1 Nodular lymphosarcoma. Polymphocytic
- 2 Nodular lymphosarcoma. Polymphocytic -lymphoblastic
- 3 Diffuse lymphosarcoma, lymphocytic
- 4 Diffuse lymphosarcoma, lymphoplasmacytic
- 5 Diffuse lymphosarcoma, polymphocytic
- 6 Diffuse lymphosarcoma, lymphoblastic
- 7 Diffuse lymphosarcoma, immunoblastic
- 8 Burkitt's tumour
- 9 Mycosis fungoides
- 10 Plasmacytoma
- 11 Reticulosarcoma (Histiocytic)
- 12 Malignant lymphoma unclassified
- 13 Composite lymphoma.

### Nodular Lymphomas

These tumours originate from altered B lymphocytes and are characterized by a nodular pattern of growth. In Malta nodular lymphosarcomas comprise 10% of all Non Hodgkins lymphomas whereas in United States Nodular lymphomas comprise about 50% of all the Non Hodgkins lymphomas. Sex incidence in Malta is predominantly Male, Male:Female ratio being 5:1. In United States the incidence is almost equal in both sexes. Histologically the tumour is characterized by a nodular pattern of growth. Neoplastic cells proliferate in nodular aggregates throughout the lymph nodes and compress the intervening parenchyma. Unlike the germinal centres in reactive follicular hyperplasia, these nodules are usually of a more uniform size and lack a well defined lymphoid cuff. The neoplastic cells within the nodules are more monotonous than those in the normal germinal centres and do not exhibit evidence of cellular polarization. Based upon the characteristics of the neoplastic cells the nodular lymphosarcomas may be divided into small cell type, large cell type and mixed cell type. The cells are usually polymphocytes of a mixture of polymphocytes and lymphoblasts. The division of nodular lymphosarcomas into subtypes has prognostic significance. Prognosis is best in the mixed cell type and worst in the large cell type. Involvement of liver and bone marrow is common in small cell type. During the natural history of disease, progression from small cell type to large cell type and progression from nodular pattern to diffuse pattern may occur. A small percentage of cases with nodular lymphosarcoma develop blastic transformation with corresponding leukaemic picture. In such patients survival after development of leukaemic phase is very brief.

### **Diffuse Lymphomas.**

Diffuse lymphomas are a group of heterogenous tumours representing neoplastic proliferations of various cell types.

#### **1. Diffuse lymphocytic lymphosarcoma.**

This is the most common type of Non Hodgkins lymphoma in Malta. It represents 34% of all the Non Hodgkins lymphoma. Median age of patients suffering from diffuse lymphocytic lymphoma in Malta is 54.6 years, Male to Female ratio being 2:1. These patients usually have minimal symptomatology and despite the frequent presence of disseminated disease at the time of diagnosis have an indolent clinical course and prolonged survival. Clinically the patients present with localized or generalized lymphadenopathy. Bone marrow involvement is a late feature in the natural history of disease. Histologically in the lymph node there is diffuse effacement of normal architecture by a monotonous population of small round lymphocytes with clumped chromatin, scanty cytoplasm and inconspicuous nucleoli. A vast majority of these tumours arise from B cells. They bear monoclonal immunoglobulin on their surface, usually IgM. Occasionally the tumour may undergo progression to blastic or histiocytic cell type.

#### **2. Diffuse lymphoplasmacytic lymphosarcoma.**

This is a rare tumour which usually occurs in older people. The tumour is composed of lymphocytes and plasma cells. These cells usually secrete IgM. If the tumour secretes significant amounts of IgM into the serum the disease is usually referred to as Waldenstrom's Macroglobulinaemia:

#### **3. Diffuse Prolymphocytic lymphosarcoma.**

This is a disease of middle aged people, median age of incidence in Malta being 52 years. This is a rather uncommon variant of Non Hodgkins lymphomas. In Malta it represents 5% of all the Non Hodgkins lymphomas. All cases studied in Malta occurred in Male population. The disease follows an indolent course and carries relatively better prognosis than lymphoblastic type. Histologically there is usually diffuse effacement of lymph node architecture. The tumour is composed of a mixture of cells with small rounded nuclei and with cleaved nuclei. The tumour arises from B lymphocytes and the cells usually bear IgM on their surface.

#### **4. Diffuse Lymphoblastic lymphosarcoma.**

This type represents 13% of Non Hodgkins lymphomas. All the cases studied occurred in Male population. Median age of incidence is 40 years in Malta. The tumour has two distinct age related patterns. Majority of cases occurred in older children and young adults. In elderly people the tumour usually occurs after the age of 60 years. The tumour is very commonly associated with a mediastinal mass, especially in the younger age group. Lymphoblastic lymphosarcoma is closely related to acute lymphoblastic leukaemias and when both haematogenous and extra medullary stages of the

disease are present the distinction between the two is impossible and insignificant. The tumour cells, like acute lymphoblastic leukaemia, possess surface markers which show characteristics of either T cells, B cells common type and Null cells. Histologically there is diffuse effacement of the lymph node architecture. The tumour is mainly composed of cells with large round nuclei and convoluted nuclei. Convoluted pattern is more commonly associated with younger age group. The prognosis of diffuse lymphoblastic lymphosarcoma is uniformly grim.

#### **Immunoblastic lymphosarcoma.**

This is a rare variant of lymphomas. Only one case was observed during the five years of study. In larger series (N-HLPC project) it constitutes about 8% of all the Non Hodgkins lymphomas with median age of 51.3 years. The tumour can have T cell or B cell markers. Histologically the tumour is composed of diffusely arranged large lymphoid cells with large vesicular nuclei having prominent nucleoli. The cytoplasm is basophilic and vacuolated plasma cells are also seen. Scarcity of reticulin fibres helps to distinguish the tumour from reticulum cell sarcoma. The tumour carries poor prognosis.

#### **Burkitt's Lymphoma.**

This is a rare tumour in Malta. Only one case was observed during the last 5 years. This tumour occurs most commonly in children but may also be seen in adults. The tumour in children is endemic in Africa where it occurs in younger age. Median age is 7 years. In these regions the maxillo-mandibular region is the commonest site involved. Sporadic occurrence in America and elsewhere has been reported. Median age in sporadic cases was 11 years and abdominal tumours were more common than in the Maxillo-Mandibular region. Ileocaecal region was the most common site. Epstein Barr virus has been isolated from the majority of the tumours in African children. The tumour arises from B lymphocytes. The cells bear monoclonal surface immunoglobulin with IgM being the predominant heavy chain class. Histologically the tumour is composed of lymphoid cells with intensely basophilic cytoplasm and many cytoplasmic inclusions. The nuclei have two to three nucleoli. Macrophages are abundantly interspersed throughout the tumour cells forming so called starry sky pattern. Extensive bone marrow involvement and meningeal infiltration may occur. The tumour carries a poor prognosis.

#### **Reticulum cell Sarcoma (Histiocytic lymphomas).**

This is the second most common Non Hodgkins lymphoma in Malta. (17% of all Non Hodgkins lymphomas). Ironically this relatively common type of lymphoma is a disputed entity. Immunologic studies performed on this group of tumours have shown a remarkable heterogeneity. About 50-60% of histiocytic lymphomas have B cell markers, 5-15% have T cell markers, 25 to 30% have no cell markers at all and only less than 5% have features consistent with true histiocytes. These findings suggest that probably

histiocytic lymphoma is not a specific entity but rather a common denominator for highly anaplastic or blastic lymphomas. However world wide application of the term seems to have justified this misnomer. Median age of incidence in Malta is 53 years (14-71). Sex incidence is almost equal. Histiocytic lymphoma occurs both in children and adults but is more common in the latter. The tumour has great tendency for being localized at the time of presentation and for extra-nodal sites. Involvement of bone marrow and liver are less common. Sometimes the tumour develops during the course of Chronic Lymphocytic Leukaemia (CLL). This is called Richter's syndrome. Histologically the tumour is composed of large cells with abundant cytoplasm, vesicular nuclei and prominent nucleoli. The nuclei may be oval or indented. There is production of intercellular argyrophilic fibres which take-up reticulin stain. The tumour carries a relatively poor prognosis.

### Plasma Cytoma.

This is a localized tumour of neoplastic plasma cells. The tumour is rare. This may be a manifestation of already disseminated multiple myeloma or an initial manifestation of plasma cytic tumour which may become generalized after periods of unpredictable duration of time. A few plasma cytomias however may remain localized. These probably represent the benign counterpart of myeloma.

### Mycosis Fungoides.

This is a relatively rare type of lymphoma representing about 5% of total Non Hodgkins lymphomas in Malta. The lesion usually afflicts elderly people. Median age incidence in Malta is 60 years. It is a T cell lymphoma arising in the skin. Classic mycosis fungoides is clinically characterized by a scaly eruption that progresses through a plaque stage and eventually forms grossly evident tumours in the skin. In about 50-70% of cases visceral and lymph node involvement is observed. Cutaneous biopsy shows a hand like dermal infiltrate of atypical lymphoid cells. These neoplastic cells infiltrate the epidermis to form aggregates known as Darier Pautier abscesses. In about 20% of cases, skin lesions are accompanied by presence of atypical lymphoid cells in the peripheral blood. These cells have been shown to be helper T cells. This entity is known as *Sezary syndrome*. Sezary syndrome is most likely a leukaemic variant of mycosis fungoides.

### Composite Lymphoma.

This is a rare tumour. It is composed of two distinct types of lymphomas within a single lymph node or organ.

### Malignant Lymphoma unclassified.

Some malignant tumours of lymphoid tissue or histiocytoid tissue cannot be classified histologically. Incidence of such lymphomas in Malta is 11% of all the Non Hodgkins lymphomas. Technical imperfections and presence of more than one cell type contribute to

the difficulty in typing. A routine application of immunologic methods to identify the cells should diminish this category.

## HODGKINS LYMPHOMAS.

Unlike Non Hodgkins lymphomas, Hodgkins disease has not been subjected to as many conflicts and controversies. Ever since the original description by Sternberg (1898) and Reed (1902), Hodgkins disease has been recognised as a form of lympho-reticular malignancy with distinctive clinical and pathological features. The first clinically useful classification of Hodgkins disease was provided by Jackson and Parker in 1947. This was improved by Lukes and Butler in 1966, and was further modified at the Rye conference. Rye classification is widely accepted by pathologists and clinicians alike and almost enjoys a universal concensus. According to this classification Hodgkins lymphoma is sub-divided into 4 main categories.

1. Hodgkins disease with lymphocytic predominance.
2. Hodgkins disease nodular sclerosing type.
3. Hodgkins disease with mixed cellularity.
4. Hodgkins disease with lymphocytic depletion.

### Hodgkins disease with lymphocytic predominance .

This is the second most common type of Hodgkins lymphoma in Malta. It represents 28% of all the Hodgkins lymphomas. Median age of incidence in Malta is 35 years (15-65) which is in conformity with the median age of incidence elsewhere. The disease is common in Males (62%). This type of Hodgkins lymphoma carries the best prognosis of all the subtypes of Hodgkins lymphoma. Histologically the lymph node architecture may be completely or partially effaced. The cellular proliferation may be diffuse or vaguely nodular and is composed predominantly of mature lymphocytes. Reed Sternberg cells, eosinophils and plasma cells are few.

### Nodular Sclerosing Type.

This is the commonest type of Hodgkins lymphoma in Malta and elsewhere. It constitutes 36% of all the Hodgkins disease in Malta, median age of incidence in Malta being 44.3 years. This is slightly higher than the median age in the United States. Also unlike other places, Nodular Sclerosing type of Hodgkins lymphoma is commoner in Males in Malta (60% in Males). The disease carries good prognosis and usually presents with enlarged lymph nodes in the neck and/or mediastinum. Histologically the lymph node shows bands of collagen tissue sub-dividing it into nodules composed of lymphocytes, eosinophils, plasma cells, histiocytes, Reed Sternberg cells and Lacunar cells. Lacunar cells with abundant pale and retracted cytoplasm and multiple nuclei are a characteristic finding. For those who are interested in hair-splitting, Nodular Sclerosing type of Hodgkins lymphoma can be further subdivided in three sub-

divisions - namely Nodular Sclerosing with lymphocytic predominance, Nodular Sclerosing with mixed cellularity and Nodular Sclerosing with lymphocytic depletion. It has been reported that increased frequency of lymphocytes correlates with improved prognosis. Remembering this sub-classification of Nodular Sclerosing type is a luxury which an overburdened medical student can ill afford.

**Hodgkins disease with mixed cellularity.**

This entity represents 25% of all the Hodgkins disease in Malta. It mainly occurs in elderly people and is less common in younger age group. No cases were reported in children in Malta. Median age of incidence in Malta is 54 years. The disease is slightly more common in Females than Males. The disease occupies an intermediate position between lymphocytic predominance type and lymphocytic depletion type with respect to prognosis. Abdominal involvement is more common in this type of Hodgkins disease. Histologically, usually, the lymph node is diffusely

involved. Focal involvement is rare. Large numbers of plasma cells, eosinophils, atypical mononuclear cells are admixed with classical Reed-Sternberg cells. Focal necrosis with minimal fibrosis may be present.

**Hodgkins disease with lymphocytic depletion.**

This is the least common type of all the Hodgkins lymphomas in Malta. It constitutes about 11% of all the Hodgkins lymphomas. The disease is more common in Males, Male to Female ratio being 2:1. The disease occurs mainly in adults. Occurrence in children is extremely rare. Average age of incidence in Malta is 40 years. Sometimes the disease may present as fever, hepatosplenomegaly and lymphopenia with sub diaphragmatic involvement. This type of Hodgkins disease carries the worst prognosis. Histologically there is diffuse involvement of lymph node with abundant Reed-Sternberg cells, and atypical reticulum cells. There is paucity of lymphocytes. The lymph node usually shows deposits of non fibrillary eosinophilic material which is negative for amyloid.

**NON HODGKINS LYMPHOMAS**

Incidence 1 in 27,500

Prevalence 1 in 5,500.

Histologic Type	Frequency	Median Age	Male/Female
1. Diffuse lymphocytic lymphosarcoma	34%	54.6 yrs..	2:1
2. Diffuse Reticulum cell lymphosarcoma	17%	53 yrs.	1:1
3. Diffuse lymphoblastic lymphosarcoma	13%	40 yrs.	All Males
4. Unclassified lymphoma	11%	58 yrs.	1:3
5. Nodular lymphomas	10%	48 yrs.	5:1
6. Diffuse Prolymphocytic lymphosarcoma	5%	52 yrs.	All males
7. Mycosis fungoides	5%	60 yrs.	All males
8. Immunoblastic lymphosarcoma	—	51.3 yrs.	—
9. Burkitts tumour	5%	—	—
10. Plasma cytoma	—	—	—

**HODGKINS LYMPHOMA**

Incidence 1 in 55,000

Prevalence 1 in 11,000

Histologic Type	Frequency	Median Age	Male/Female
1. Nodular Sclerosing type	36%	44 yrs.	3:2
2. Lymphocytic predominance type	28%	35 yrs.	3:2
3. Mixed cellularity type	25%	54 yrs.	3:4
4. Lymphocytic depletion type	11%	40 yrs.	2:1

# Oral Polio Immunisation and Breastfeeding

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During the latter part of the Ming Dynasty (1368-1644) a system of inoculation was introduced in China whereby pulverised crusts from smallpox pustules were blown through a silver tube into the nostril, the left in males, and the right in females. Even before the rapid spread of vaccination which started in England in 1799 through the efforts of Jenner, inoculation or "variolation" against smallpox had already been extensively practised in Turkey throughout the previous century.

Due to its dramatic impact on the disease, smallpox vaccination became compulsory in England during the early 19th century; and it was towards the end of the latter era that the immunological basis of infectious disease and their prevention had been established. The early 1900's saw the development of vaccines against diphtheria, tetanus and typhoid, and later cholera. Viruses, being intra-cellular parasites, proved difficult to culture and virus vaccines appeared much later. It was in 1949 that Dr John Enders of Harvard discovered the possibility that poliovirus could be grown in tissues culture; the development of polio and other vaccines rapidly followed.

Initial successes were marred by sporadic disasters. In the Lubeck disaster of 1936, 251 children contracted severe tuberculosis because of contaminated B.C.G. vaccine. Another major disaster in the United States was the Cutter incident of 1955 when live polio virus had been incorporated

with the inactivated vaccine resulting in 298 cases of paralysis and 170 deaths. Henceforth safety precautions and procedures assumed top priority.

Jonas Salk developed the first effective formalin-inactivated poliovirus vaccine which still bears his name; this vaccine was in world-wide use in 1954. It was introduced in the United Kingdom in 1957 after a decade of serious polio outbreaks of up to 8000 cases per year, with a fatality rate of 10%.

The late 1950's saw the mass use of the newer live attenuated Sabin vaccine which did not require parenteral administration; small doses were required and it carried an extra dividend in that it spread to non-immunised contacts conferring herd immunity - at the time it was confirmed that no harmful effects ensued thereby. (Sabin, JAMA 194:872; 1965) In the spring of 1960 the Sabin vaccine was in world-wide use and had superseded the Salk. It was, however, capable of causing paralysis on rare occasions - 1/6 million with Type I, 1/5 million with Type II and 1/2.5 million with Type III. Seven cases of paralytic poliomyelitis were reported in the U.K. in 1978, 5 of which were attributable to Sabin OPV. Small doses of penicillin are also contained in the oral vaccine, and this raised some problems with its use in allergic subjects.

The relative efficacy of the two types of vaccine can be gauged from the following figures relating to annual polio cases in the United States: (Grislain

pre-1954	40,000 cases per year
1960	3,190 (after Salk programme)
1966	44 (after Sabin programme).

In Italy the Salk vaccine produced no marked improvement after its introduction in 1958 (Giovanardi, 1969); there still was an annual incidence of about 3,000. With the introduction of the Sabin vaccine in 1964, however, a marked reduction in cases followed, with a reported incidence of 87 in 1968.

Repeated and continued immunisation of newborn infants is essential if no new epidemics are to take place. In Argentina the annual rate was 6,000 in 1956; it dropped to less than a 1,000 after the introduction of Salk vaccine in 1957, and still further with the Sabin vaccine in 1963. After a 2-year period of non-immunisation an epidemic occurred during 1965/66. (Sujoy, 1969).

Sweden, Finland and the Netherlands, however, have eliminated the disease by utilising Salk vaccine alone. (Barnett Christies, 1981; Fagraens (1980); Sweden reported 18 cases in 1960, and nil in 1967. (Grislain, 1969).

As early as 1950, Sabin himself described an antipoliomyelitic substance in the milk of human being and certain cows. (Am J. Dis. Child, 1950). This finding has been confirmed by a host of other workers. (Vahlquist, 1958; Harfouche 1970; Lepow 1961; Sabin, 1963, Hodes 1962; Michaels 1965; Athreya 1964; Sabin 1962; Pinter 1953; Sabin 1962; Adcock 1971, Hodes 1964; Mata 1971; Kenny 1967; Hodes 1964; Goldman 1973). Antibody activity against poliovirus has been shown to lie in the secretory IgA fraction of human milk. (Hodes 1964). Although colostrum contains 1970; Mouton, 1970). Although colostrum contains between 20-40 mg. of IgA per ml, (Amman & Stiehm, 1966; Hanson, 1971) there is a drastic decrease to about 1mg/ml on the fourth day of life; the large increase in milk production thereafter, however, is sufficient to compensate for this reduced IgA concentration, sufficient amount being present to permit detection in the stools. (Kenny, 1967; Michael 1971; Gindrat, 1972).

Interference with oral poliomyelitis vaccination by breast-feeding was a problem. (Warren, 1964; Holquin 1962; Sabin 1963). These reports by far outweigh the occasional observation that OPV is not influenced at all by breastmilk (Deforest 1973;), Prof. J. Pattison of King's College Medical School, London remarks further that: "the transplacental passive transfer of IgG from the mother to the infant will protect the latter for 6 to 12 months after birth. Because of their protective umbrella, there is no point in administering live vaccines before 6 months of age. (Pattison, 1981.) Before this age antibody response may also be reduced because of the infant's immature antibody forming mechanisms. (Neonatal Medicine 1974) Besides, maternal antibodies depress the response to killed vaccines as well, and these too should not be administered to infants before the age of 6 months (Beale, 1969).

Although the literature dealing with polio vaccination and the breastmilk effect is large and

controversial, there are certain points of agreement. An antipoliomyelitis factor exists in colostrum and breast milk, and this interferes with polio vaccination in the first few weeks of life, on the assumption that the mother herself has antipolio antibodies in her serum. It appears that the human mammary gland is able to concentrate these antibodies and secrete them in the milk. These are resistant to denaturation in the intestine, and to a greater extent than are, say, the anti-E. Coli antibodies. (Kenny, 1967). Polio vaccine is destroyed at a low pH; gastric pH in the neonate is very low indeed. (ibid.).

The main controversy which exists concerns the age at which these antibodies cease to possess an inhibiting effect on OPV and whether breastfeeding should be postponed for a period around the time of vaccination or not. Whilst some workers maintain that this inhibitory effect of human milk lasts only a few weeks, (Adcock, 1971 "Break milk inhibition is *probably* of no clinical significance in older infants receiving routine primary OPV"), several others have shown that it extends to much later in the first year of life, including the period during which infants are normally immunised. (Sabin 1950;): "53% to 73% of the regular milk obtained from one to twelve months after delivery neutralised the virus".

A satisfactory schedule of polio immunisation is required for breastfed infants. The advantages of oral Sabin vaccine include ease of administration, low dosage, gut colonisation and low cost of production. Its spread to non-immunised contacts may not be entirely beneficial, as it rarely causes paralysis; contacts to be avoided include pregnant women, patients with immunological abnormalities, patients on steroids or immunosuppressants or receiving irradiation, and patients with tumours of the reticuloendothelial system especially Hodgkin's disease. Seroconversion is poor in some tropical countries. Although the Salk vaccine is expensive and is unable to displace wild virus from the community, it possesses the advantage of not multiplying in the host and an inability to revert to virulence. Its role in antibody formation is not affected by: social conditions, climate or the presence of other viral infections. It can be administered to the immunodeficient. It will *not* be affected by secretory IgA antibodies in breast milk, so that it would be the ideal choice in breastfed infants over the age of six months. With the oral Sabin vaccine, an alternative schedule which has recently been suggested is an increase in the number of doses, from the usually recommended three to five, that is not including booster doses. (Barnett Christie, 1981; Fulginiti, 1982).

With regard to the necessity of withholding breastfeeding around the time of vaccination, there are some who advocate it and have taken it for granted in their studies (Adcock, 1971), whilst others

recommend that breastfeeding is far more important and should not be interrupted (Barnes, 1977). The American Academy of Paediatrics recommends it. (Redbook, 1982).

In the Maltese Islands, poliomyelitis became notifiable in 1921, but only 61 cases were reported until the first major epidemic of 1942, which incidentally started off in the British adult population here and spread rapidly thereafter, affecting mainly children under the age of four years. Another two outbreaks followed in 1947 and 1950 respectively, but it was not until November 1956 that immunisation with Salk vaccine was started in children between the ages of one and ten years. 41 cases had been notified that year. By July 1959, a total of 34,800 children had been vaccinated against poliomyelitis. (Cassar, 65). The last sporadic case occurred in 1964, two years after immunisation with the Sabin type of vaccine had been introduced in the Maltese Islands. The last small epidemic was in 1962 when 48 cases were notified, and it has been estimated that a total of a thousand cases of poliomyelitis were recorded between 1930 and 1964. (Wyatt)

Immunisation against poliomyelitis, tetanus and diphtheria is obligatory in Malta, and the Department of Health offers the Sabin vaccine which is usually started at age 3 months and is followed by another two doses at six to twelve week intervals during the first year of life; they are usually given at the same time as diphtheria and tetanus, with or without pertussis, by injection. Poliomyelitis vaccine is not given to children in contact with pregnant mothers in the first four months of pregnancy. The Salk vaccine predominates in the private sector, where it is combined with diphtheria, tetanus and pertussis in a single dose injection.

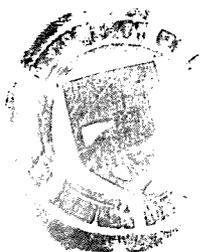
Although remaining subject to individual preference, it is clear that poliomyelitis immunisation cannot be taken lightly particularly in breastfed infants, and at a time when WHO is conducting such a world-wide campaign to promote breastfeeding.

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# The Importance of Speech. Effects of Handicaps in Brain and Language Impairment.

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Impaired language affects all other functioning within the person as well as how other people act towards and relate to him. Impaired language means that the person cannot adequately communicate either his needs or his interests. If the person is a child, he is at an ever-increasing disadvantage with respect to his normal peer who begins to outstrip him at an exponential rate.

The retarded or language impaired person suffers socially. Others do not understand at all or they misunderstand. Often they have neither the patience nor the time to listen to what the handicapped person is trying to say.

We can get some inkling of the difficulties the language impaired encounter by listening to those who were formerly unable to communicate and now, somehow, are able to do so. A Cerebral - palsied man, reminisced that when he was young, he liked to go out -side and play with other children. They would start by asking him why he moved so peculiarly, or what was his name, but as no language followed, they started to laugh and ape him. They would sometimes throw stones at him so the unfortunate boy had to play by himself. The same person also knew why the teachers never tried to teach him any reading or spelling. They would look at his I.Q. tests and say that it would be pointless teaching him anything. This was all because he could not speak their language, and explain that he understood what they were saying.

Even when a mode of communication is available, this is no guarantee that it will be accepted by others. Deaf children prefer sign language to speech but neither parents nor the people of the community actually know the signs. Thus the deaf suffer doubly, firstly because they do not know other people's language, and secondly because others do not understand their particular language. Parental responses to their handicapped children are complex. Often there is a large element of guilt, compounded by the frustration that they cannot understand what their child is trying to say. Yet despite difficulties in understanding, parents do catch on to much of the obscure communication of their handicapped child.

Language defecits often go hand in hand with other defecits. In teaching the language-impaired and the learning-disabled, we must know their present level of receptive and expressive language, as well as their other deficiencies which may have hindered the language development.

If the person is impaired in conceptualising, then he will be linguistically deficient in areas that depend on this ability. If there are problems relating to attention span, sensory motor defecits and learning rate, we will want to know them. We need to know whether a child can respond to pictured objects. If functioning is too slow, he cannot do this and so real objects must be used for initial teaching sessions.

Knowledge will guide us in our search for more

appropriate teaching techniques, and offer clues as to whether one should by-pass or strengthen the child's weaknesses. The autistic have difficulties in perceiving order and meaning in the stimuli which are presented to them; the aphasic show impaired auditory processing and the retarded show short-term memory defects. All have difficulties with ordinary normal language acquisition. By-passing or eliminating areas of impairment could mean successful communication by alternative means, or possibly even stimulate actual language acquisition.

Regardless of their level, the goal in teaching the language-impaired is communication; this communication, must be meaningful and applicable to other situations and useful in other contexts.

**Optimising conditions for learning language.**

- 1 Most of the learning-disabled will benefit by learning under non-distracting and well-structured situations.
- 2 Distractability must be reduced to a minimum to have better concentration.
- 3 The teaching must be consistently applied.
- 4 Cues should be distinct and stand out clearly.
- 5 Always start off by using very simple and familiar words.
- 6 When using coloured pictures, make sure that the picture is not confusing, i.e. if you want to teach the

word "Nurse" first present the subject "Nurse" not a nurse near a patient.

7 Always praise and reward the child for the least effort he does, to stimulate him further.

8 When writing the names of objects, use only nouns and write in *clear capital letters*.

9 Use colourful boards of *Flash Cards* of bright outstanding colours.

10 If the child is deaf use gestures accompanied by words.

11 Try to keep the child as long as possible on his tummy so that he will start crawling; consequently other brain centres will develop to make it clear that a child will be unable to reach, walk, read, and speak unless he has developed the action of crawling.

12 If the child manages to learn a few words, always allow a little time for revision so that you encourage him to memorize them and then go on to the next item.

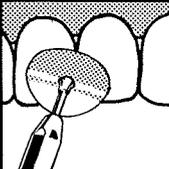
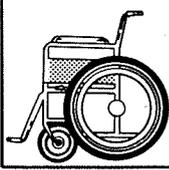
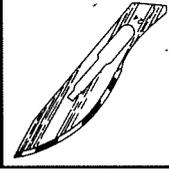
He who possesses language can deal with many abstractions, with concepts and ideas, with things that are not physically present. He can describe past events or predict future events. The man who speaks one language can use it to learn another language.

It is for this reason that we should cherish our God-given gift of language and use it to help others who are in greater need.

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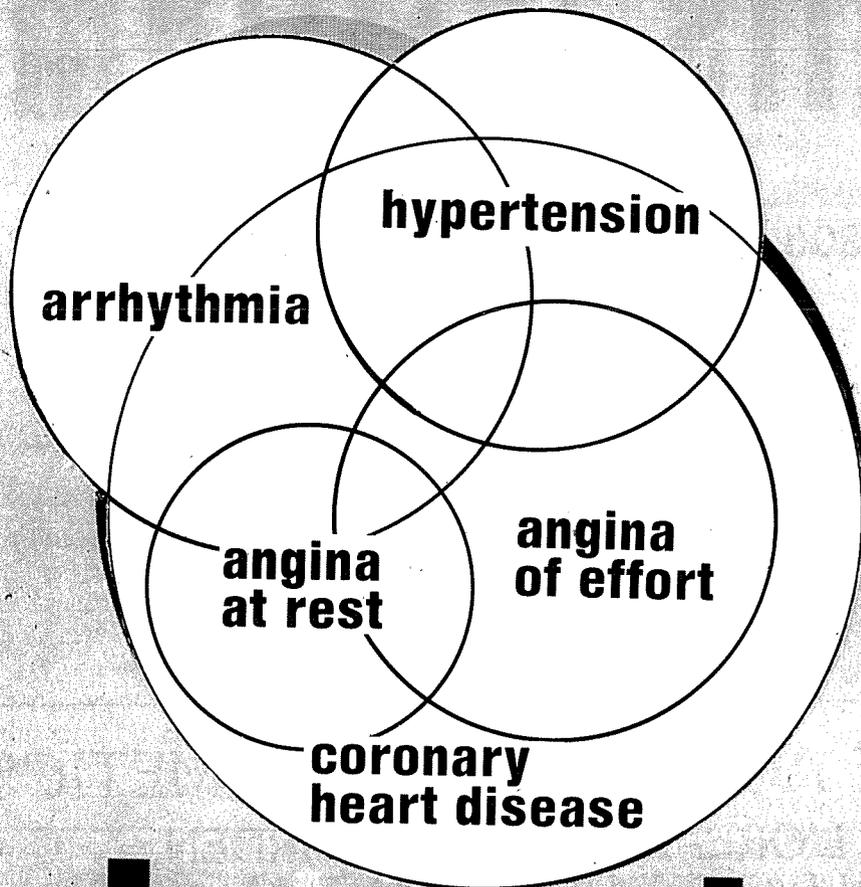
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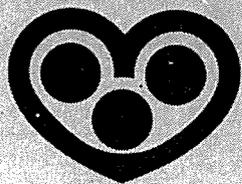
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