14

L LIBRARY
EDICAL SCHOOL
G'MANGIA MALTA

Founded 1983

Medi-Scope

THE MEDICAL JOURNAL FOR STUDENTS OF MEDICINE AND SURGERY IN MALTA

AGEING AND ENDOCRINE FUNCTION

PLACENTA PRAEVIA • SUN AND SKIN • DOPPLER ULTRASOUND • FISH POISONING
'HAGRET IL-GENERAL' • ALCOHOLISM • PREMATURE DELIVERY • MEMORY

UNIVERSITY OF MALTA
LIBRARY

Main Library

Class Mark MZ6

No. of Volumes

Remarks REFERENCE ONLY

438690

PRESCRIBING INFORMATION – INDICATIONS – Osteoarthritis, rheumatoid arthritis and similar conditions requiring anti-inflammatory treatment. DOSAGE AND ADMINISTRATION – **Adults:** The recommended daily dose is two tablets (1g) taken as a single dose at bedtime. For severe or persistent symptoms, or during acute exacerbation, an additional one or two tablets (500mg–1g) may be given as a morning dose. **Use in elderly patients:** In common with many drugs, blood levels may be higher in elderly patients. The recommended daily dose of 1g should not be exceeded in this age group and in some cases 500mg may give satisfactory relief. **Use in children:** There are no clinical data to recommend the use of RELIFEX in children. RELIFEX tablets should be swallowed whole without chewing. **Use in patients with impaired renal function:** See Package Insert Leaflet. PRECAUTIONS – Patients with established aspirin hypersensitivity may react in a similar manner to nabumetone. Patients with a history of peptic ulceration should be regularly reviewed for recurrence of symptoms. Fluctuations in some parameters of liver function, particularly alkaline phosphatase,

There's a powerful new movement in the treatment of arthritis

Relifex is the first of a new breed of antiarthritic agent.[1]

The product of precisely targeted molecular research, it has been specifically designed to deliver well-tolerated power.

Relifex has consistently demonstrated a powerful effect on the pain and stiffness of arthritic conditions.[2,3]

Proving not only powerful in arthritis, but also reassuringly gentle in the patient.

Long term studies have confirmed that the powerful benefits of Relifex continue to give patients the treatment they prefer to stay with.[4]

New Relifex has the power to give your arthritic patients something positive to look forward to.

Surely a solid base on which to start the long term treatment of chronic arthritis.

Relifex
nabumetone

Start as they would like to go on

are frequently observed in patients with chronic inflammatory disorders; there is no evidence that RELIFEX accentuates these changes. CONTRA-INDICATIONS – Active peptic ulceration, severe hepatic impairment (e.g. cirrhosis), nabumetone hypersensitivity. SIDE EFFECTS – Side effects include diarrhoea, dyspepsia, nausea, constipation, abdominal pain, flatulence, headache, dizziness, pruritus, rash and sedation. In clinical trials, increases in dose above 1g did not lead to an increase in the incidence of side effects. AVAILABILITY – RELIFEX tablets: Red, film coated tablets marked RELIFEX on one side and 500 on the other side. Each tablet contains 500mg nabumetone.

REFERENCES: 1. Roth SH, *Am J Med* 1987; **83** (Suppl 4B): 25–30. 2. Appelrouth DJ *et al*, *Am J Med* 1987; **83** (Suppl 4B): 78–81. 3. Carle WK, Rotman H, *R Soc Med Int Congr Symp Ser* 1985; (69): 139–148. 4. Brobyn RD, *Am J Med* 1987; **83** (Suppl 4B): 50–54.

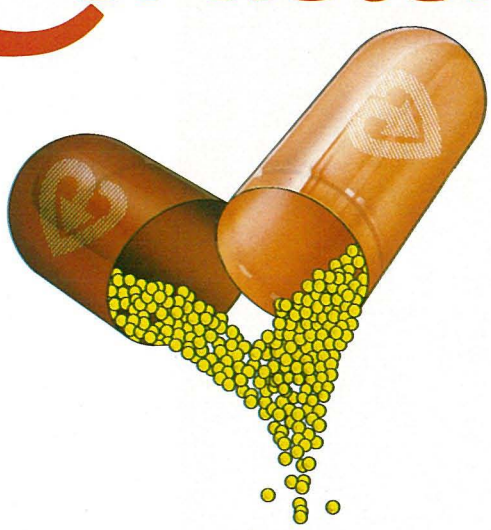
RELIFEX is a product of research from Beecham Pharmaceuticals, Brentford, England. Further information is available from the company on request.

RELIFEX is a trade mark. 001/66/2/6/89

Beecham Pharmaceuticals
BRENTFORD · ENGLAND

Together we'll give arthritis the treatment it deserves.

Coracten



Why choose Coracten in hypertension?

- Coracten is nifedipine – an important Ca^{++} channel blocker, now in a b.i.d. dosage form for sustained control of hypertension.
- Coracten provides smooth and sustained antihypertensive effects. It works rapidly to reduce blood pressure within a few hours.
- Coracten can provide effective control in all grades of hypertension.
- Coracten provides continuing and reliable activity with the exclusive Spansule sustained release system.
- Coracten is suitable for use in both young and old hypertensive patients (see prescribing information).
- Coracten is especially suited to patients with concomitant hypertension and angina.
- Coracten can simplify your prescribing in hypertension.

Coracten clears the way through therapeutic confusion

Prescribing Information

Presentation
Opaque light brown capsules, opaque red capped, cap and body printed containing off-white pellets. Each capsule contains 20mg nifedipine in a sustained release formulation which provides a prolonged therapeutic effect.

Uses: mode of action
Nifedipine is a potent calcium channel blocker whose main action is to produce relaxation of arterial smooth muscle both in the coronary and peripheral circulation. The peripheral action leads to a decrease in cardiac work load through vasodilatation and a resultant reduction in myocardial oxygen demand. Coronary vasodilatation improves myocardial perfusion and reduces coronary artery spasm. Nifedipine has no therapeutic antiarrhythmic effect.

Indications
Nifedipine is indicated in the treatment and prophylaxis of angina pectoris (exercise induced angina, angina at rest including Prinzmetal angina and unstable angina, and angina following myocardial infarction [see contra-indication below]), and in the treatment of hypertension.

Dosage and administration
Adults only: In angina pectoris: Normally one capsule every 12 hours. If necessary, the dosage may be increased to 2 capsules every 12 hours.
In hypertension: Normally one capsule twice a day. If necessary the dosage may be increased to two capsules twice a day.
The capsules should be swallowed whole with a little fluid after meals.

Contra-indications, warnings etc.
Contra-indications: Cardiovascular shock, pregnancy and lactation, myocardial infarction less than 8 days prior to commencing therapy.
Cautions: Use with caution in patients with systolic blood pressure of less than 90mmHg, in patients with poor cardiac reserve: in diabetic patients, as they may require adjustment of their diabetic therapy: and in dialysis patients with malignant hypertension and irreversible renal failure with hypovolaemia, since a significant drop in blood pressure may occur due to the vasodilator effects of nifedipine.
Since nifedipine has no beta-adrenoceptor blocking activity it therefore gives no protection against the dangers of abrupt withdrawal. Withdrawal of any previously prescribed beta-blockers should be gradual, preferably over 8 to 10 days. Nifedipine may be used in combination with beta-blockers and other antihypertensive agents, but the possibility of an additive effect resulting in postural hypotension must be borne in mind.
Ischaemic pain has been reported in a small proportion of patients within 30 minutes of the introduction of nifedipine therapy. Patients experiencing this effect should consult their doctor.
Patients who drive or operate machinery should be warned of the possibility of drowsiness.
Increased plasma levels of nifedipine have been reported during concomitant cimetidine and ranitidine administration, but no clinical effects, to date, have been shown.
Use in pregnancy and lactation: See Contra-indications.
Adverse reactions: Side effects are generally mild and transient and usually occur at the start of treatment. They include: headache, flushing (and usually at higher dosages), nausea, dizziness, lethargy, skin reactions, paraesthesia, hypotension, palpitation, tachycardia and dependent oedema. There have been very rare reports of hepatitis and of reversible gingival hyperplasia.
Overdosage
Signs and symptoms may include bradycardia and hypotension. Treatment consists of the induction of vomiting and/or gastric lavage together with supportive and symptomatic measures including, where appropriate, the use of atropine and noradrenaline. Intravenous calcium gluconate with metaraminol (a potent sympathomimetic agent) may be of benefit.

Pharmaceutical precautions
Store in a cool dry place AND PROTECT FROM LIGHT.

'Coracten' and 'Spansule' are trade marks.

References
1. Murphy MB, Hospital Update, (1983) October, 1119 1126
2. Sorkin EM et al, Drugs, (1985) 30, 182-274
3. Bioavailability study, data on file, SK&F
4. Woods K, MIMS Magazine, (1987) , 1 Feb, 43
5. Dall JLC. Geriatric Med. (1986) 16, 6-7

SK&F
United Kingdom Overseas Group
SMITH KLINE &FRENCH LABORATORIES LIMITED
Welwyn Garden City, Hertfordshire, England AL7 1EY

199 A27

AUTUMN '91

Founders: Mark Bugeja MD
Ronnie Borg MD

Hon. President: Rector of the University of Malta

Editorial Board:

Editor: Jean Karl Soler MD

Secretary: Maria Rose Zammit MD

Article Editor: Valerie Curmi MD

Graphics and Photography Editor: Patrick Zammit MD

Advertising: Aaron Casha MD

The board wishes to thank

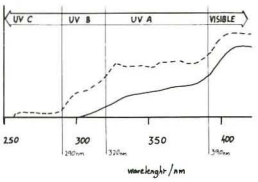
H.S.I.U. staff

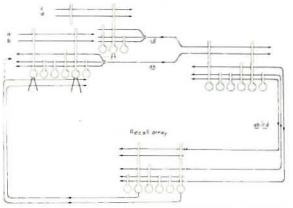
Medical School Secretarial Staff

Cover Photo:
Detail from
"Lengthening Shadows"
(J.D. Nunns ESFIAP)

Set, Designed
and Printed at
Dormax Press Co. Ltd.
Qormi – Malta.

Medi-Scope





Editor's Letter

The editorial board wishes to extend its congratulations to the thirty doctors who have successfully completed the 1990 and 1991 final examinations. As a few of us were amongst that number, we would like to thank the Dean of the Faculty of Medicine and Surgery, and all our tutors in the name of our colleagues.

We welcome our new readers, dentists and veterinary surgeons, to the first issue of Medi-Scope for the 1990's, and invite them to submit material for publication in future issues. Articles of specific interest to dentists or veterinary surgeons as well as those of more general interest are welcome.

I would also like to take this opportunity to invite new members to join the editorial board. Applicants should ideally be clinical year medical students, have a high level of commitment and above all have a professional attitude to the new work. Interested parties may contact any member of the present editorial board, or apply in writing to the editor, stating clearly why they want to be part of the board.

JKSoler.

The Editor
18th September 1991

Contents

Ageing and Endocrine Function 1
Placenta Praevia – Management in the last century 5
Sunbathing – A case of Tan Now Pay Later? 11
Doppler Ultrasound – Clinical applications in the adult and foetus 17
Scombroid Fish Poisoning 19
Hagret il-General – An islet with past medical links 27
Alcoholism – What every doctor should know 31
Delaying an untimely delivery 37
Memory: Part 1: Neurochemistry and Spatial organisation 41

Letter to the Editor: Medical documentalists in Malta 34

Lipo-Merz® –
Lipo-Merz® retard –
Severe primary and secondary hyperlipidemias

Harpagin® –
For the treatment of hyperuricemia and gout

Contractubex® compositum –
For scars of any genesis

Vasotonin® forte –
Vasotonin® forte Serol –
For disorders of venous and locomotive system

Viru-Merz® Ophthalmicum –
Keratitis herpetica

Viru-Merz® Serol –
Local herpes specific

Full details of these and other products are available from:
JOSEPH CASSAR LIMITED
54 Melita Street, Valletta, Malta.

Merz
PHARMA

AGEING AND ENDOCRINE FUNCTION

HERMAN N. FARRUGIA MD Dip. Endoc & Metab. (Paris), Ass. Etr. (Paris)
Senior Registrar Diabetes & Lipid Clinic

Endocrine dysfunction in the elderly is characterised by its presentation in a setting of multiple system disorders and usually manifesting itself in an atypical and even subtle fashion. The consequences are two fold: problems are inevitably easily overlooked and there is rampant direct attribution of symptom complexes and signs to old age itself.

The Hypothalamic-Hypophyseal Axis

As confirmed by a multitude of basal and dynamic function tests and compounded by recent immunocytologic studies of ageing pituitaries, it is clear that the anterior pituitary maintains a practically intact production and secretion rate of its trophic hormones. What in fact varies is the amplitude of response to the hypothalamic releasing factors due to receptor insensitivity or a decrease in their concentration in the pituicyte membrane. There may also be a modification in the portal concentration of local neurotransmitter originating from the hypothalamus. I am emphasising two examples to illustrate this point:

(1) GROWTH HORMONE concentration is basally unmodified with advancing age but the sleep-entrained nocturnal peaks are much flatter as are the post-prandial increments of GH secretion, the response to aminoacid stimulation (e.g. arginine) and to the recently isolated and synthetic growth hormone releasing hormone (GRH).

(2) Similarly, PROLACTIN secretion is reduced post-menopausally but this is due to the fall in oestradiol with its prolactin stimulating as well as priming properties. It is no surprise to note that with Hormone Replacement Therapy, prolactin levels are normalised.

Superimposed on these examples, the centrally acting neurotransmitters are equally implicated: dopamine and the endogenous opiates exert an inhibitory tone on luteinising hormone releasing hormone and luteinising hormone secretion but in old age have reduced bioactivity and this explains the refractoriness of the gonadotrope to respond appropriately to negative feedback input by the circulating gonadal steroids.

Ageing is also characterised at this level by the preservation of anterior pituitary function and even more selectively, the corticotrophic axis which is the one most easily spared or more rapidly restored after hypothalamic-hypophyseal insult (including surgery) and this vis-a-vis the more fragile gonadotrope and thyrotrope lines. In fact, circulating levels of cortisol and adrenocorticotrophic hormone remain within the normal range in the elderly as do dynamic (stimulation and suppression) tests of the corticotrophic axis. The observed reduction in urinary 17-hydroxy corticosteroid levels is only an indication of diminished hepatic clearance of cortisol with subsequently prolonged half-life.

The modification of the gonadotrope axis is well known in women at the menopause which entails near complete absence of ovarian secretion of oestradiol as well as progesterone whereas circulating levels of testosterone and oestrone are preserved as a result of aromatisation in peripheral adipose tissue of $\Delta 4$ androstenedione whose origin is bifocal: ovarian and adrenal cortex.

The evolution of androgen secretion in old age is quite interesting albeit still widely disputed. Some authors describe a modification parallel to that of tri-iodothyronine (T3) whereby circulating testosterone levels are lowered only in chronically ill, debilitated, malnourished or alcoholic septuagenarians. However it is now thought that there is a progressive decline in total and free testosterone as well as dampening of their circadian fluctuations.

Hydro-electrolyte homeostasis is generally unaltered in normal elderly individuals such that plasma anti diuretic hormone (ADH) levels are generally normal. They and their precursor neurophysins may be occasionally above basal normal concentrations due to insensitivity of the distal nephron to anti diuretic hormone (ADH) and due to acquired increased responsiveness of the "osmostat" in the hypothalamus.

On the other hand, orthostatic hypotension is frequently encountered in old people due to diminished baroreceptor input to the supraoptic nucleus evidenced by an inadequate ADH response to volume depletion on assumption of the erect posture. The syndrome of inappropriate ADH secretion may be easily overlooked in the geriatric patient and the hyponatremia of water intoxication must be distinguished from that caused by a progressively decreasing glomerular filtration rate of an aging kidney with its inability to excrete a given water load and from the hyponatremia caused by

prolonged diuretic administration. The water intoxication of ectopic or excess ADH secretion is predominant in the elderly who develop pulmonary (e.g. oat-cell carcinoma) or central nervous system (infections/ infiltrations) disorders.

As to the renin-angiotensin-aldosterone cascade, one observes a progressive drop in plasma renin activity after fifty years of age and this applies for basal situations and also during stimulation by orthostatism or salt restriction. Concurrently, plasma aldosterone and urinary tetrahydroaldosterone concentrations drop but generally to a lesser degree. Therefore hypertension with low renin activity has no physio-pathologic significance in the elderly and although diuretics are mandatory in this group, there is a constant risk of perpetrated hyponatremia.

The Thyroid

The chapter on thyroid dysfunction merits special focus when one comes to discuss elderly populations. There is an undeniable if not inevitable drop in thyroid hormone production rate with age. However the metabolic clearance rate of most hormones is concurrently decreased to a pro-portionate degree (hence the necessity to reduce replacement doses) so that thyroxine levels are maintained in the normal adult range in healthy old people with preserved normocaloric food intake. Tri-iodothyronine levels may be lowered but still within the low normal range. Thyroid stimu-lating hormone (TSH) levels remain therefore normal. It is the TSH response to thyrotropin releasing hormone (TRH) that is decreased in elderly males. The TRH test (used to assess pituitary reserve of TSH and prolactin) is thus rendered uninter-pretable in this category of patients as it cannot discriminate between normal individuals and men suffering of hypopituitarism or hyperthyroidism. In a number of hospitalised or sedentary people who are particularly undernourished and/or systemtically ill, one observes an isolated fall in circulating T3 (the low T3 syndrome) which implies a deficit in desio-dination of thyroxine. (See table 1)

SICK EUTHYROID SYNDROME

Findings:
- T4 & Free T4 Index are low
- T3 is Low or Undetectable
- *TSH is usually normal*
- Reverse T3 is either Normal or Elevated)

Mecanisms:
(a) Preferential production of reverse T3 in response to illness & fasting.
(b) Reduced desiodination of reverse T3 to its metabolites.
(c) Reduced desiodination of T4 to T3 peripherally.
(d) Reduced levels of binding proteins including TBG.
(e) Presence of circulating thyroid hormone binding inhibitors.

TABLE 1

Hyperthyroidism

Only 75% of patients have classic signs and symptoms since oph-thalmopathy is very infrequently encountered and goitre is rarer than in younger individuals. There is an increased incidence of multi-heteronodular toxic goitre, toxic adenoma and iatrogenic causes characterised by intake of iodine containing medications, 30% of these incidents being amiodarone induced in this age group.

The real danger is to overlook forms of hyperthyroidism which are paucisymptomatic or even frankly atypical in presentation: unexplained heart failure or tachyarrhythmia, recent onset of hallucinatory or manic-depressive psychoses, profound myopathy bordering on to akinesia should all raise questions about masked/apathetic hyperthyroidism.

Hypothyroidism

The symptoms and signs of hypothyroidism are usually over-looked when such complaints as fatigue, memory loss and hypoacuesis are ascribed to ageing without having a Free T4 and TSH measurement. Goitre is rarely seen with hypo-thyroidism in the elderly except when it is iodide induced through a mechanism described by Wolff and Chaikoff. Thyroxine levels may be depressed in seriously ill and chronically debilitated patients and this is why hypothyroidism should not be diagnosed on the basis of low T4 levels alone. The T3 level may be in the normal range in hypothyroidism but conversely, the low T3 level with normal or elevated Reverse T3 is consistent with the SICK EUTHY-ROID SYNDROME mani-fested by a host of acute and chronic systemic illnesses (See table 2). Both these ten-dencies contribute to the unreliability of testing T3 levels in hypothyroidism. Free T3 is always preferable.

THYROID FUNCTION CHANGES IN AGEING

	Healthy	Thyrotoxic.	1°Hypothy.	Sick Euthy.	Amiodarone
TOTAL T4	N	↑	↓	↓	↑↓
FREE T4	N	↑	↓	N	
TOTAL T3	N	↑	↓/N	↓↓	↓
TSH	N	↓	↑	N	↓↑
FREE T4 INDEX	N	↑	↓	↓	↑↓
REVERSE T3	N			↑	
TSH response to TRH	↓ (males)	↓	↑	N/↑	↓↑
Thyroid hormone product rate	↓	↑	↓	N/↓	
Metabolic clearance rate of thyroid hormone	↓	↑	↓	↓	

TABLE 2

The anaemia of hypothyroidism may be multifactorial when associated with pernicious anaemia or iron deficiency anaemia. Finally, autoimmune polyendocrinopathies (such as that described by Schmidt) may associate hypothyroidism with concomittant adrenal cortex insufficiency and diabetes mellitus so that one should exercise great care in thyroid hormone substitution in myxoedematous elderly subjects and all the more so if coronary insufficiency coexists.

Carbohydrate Metabolism

Disordered carbohydrate metabolism is the most frequently encountered problem to such an extent that nearly 50% of elderly people have some degree of glucose intolerance due to diminished peripheral glucose utilisation associated with insulin resistance rather than insufficient insulin pancreatic reserve and secretion. The mechanism involves an intrareceptor defect of phosphorylation of the B chain component of the insulin receptor resulting in secondary down-regulation of the concentration of receptors in the cell membranes of adipocytes, skeletal muscle etc.

Although, theoretically speaking, the therapeutic goal for diabetes mellitus in the aged is the same as that in younger patients, one must learn to tolerate moderate elevations of fasting plasma glucose rather than to persist in over-enthusiastic control, thereby bordering onto hypoglycaemia. Hypoglycaemia is particularly subtle in the elderly due to impairment of cathecolamine responsiveness resulting in diminished compensatory counter-regulatory gluconeogenesis, and absence of the classic autonomic symptoms such that only belated neuroglycopoenic manifestations tend to prevail. This is why chlorpropamide is generally contraindicated in the elderly with its prolonged time of action and hazardous risk of inappropriate antidiuresis.

An increased incidence of hyperosmolar non-ketotic coma is observed in aged diabetic populations typically developing over days to weeks. This constitutes an emergency possibly presenting with focal or generalised seizures associated with the hyperosmolarity induced by the high serum sodium and blood urea nitrogen.

Bone Metabolism

One must make out clearly the distinction between TRABECULAR osteoporosis (Type I) and CORTICAL osteoporosis (Type II). Type I occurs predominantly in women relatively early in the post menopause and generally presents with vertebral collapse in the sixties. Cortical bone is usually preserved. Trans iliac bone biopsy should enable one to appreciate osteoclastic resorption with induced osteoblastic hyperactivity. Osteocalcine is a bone protein used as a biological marker of bone remodelling and turnover. Hormone replacement therapy with topical oestrogen preparations prescribed as from early menopause has proved to go a long way in preventing or retarding this osteoporosis. Type II (senile) osteoporosis occurs later on (70-80 years) and is typically associated with spontaneous or stress fractures principally of the femoral neck. Here trabecular bone is usually conserved and this renders the therapeutic use of sodium fluoride useless in this form of osteoporosis as this acts solely by increasing trabecular bone formation. Here calcium salts and vitamin D3 are indicated prophylactically.

Other Endocrinopathies

Primary hyperparathyroidism is one of the conditions easily overlooked in the elderly because although the symptomatology is similar to that in younger individuals, bone demineralisation, weakness and osteoarticular complaints are preponderant features of senescence. One must strive to differentiate the hypercalcemia from that induced by malignancy and the presence of a circulating Osteoclast Activating Factor.

Ectopic parathyroid hormone secretion and its entrained hypercalcemia has been described with renal cell carcinoma and hepatomas probably attributed to expression of the Human Parathyroid Related Peptide gene by these tumours.

Other rarer ectopic hormone syndromes affecting the elderly suffering of malignancy are the ectopic 'adenocorticotrophic hormone (ACTH)' production of oat-cell carcinoma of the bronchus which usually is heralded by clinical features of hypokalaemia and of hyperglucocorticism.

References on page 14

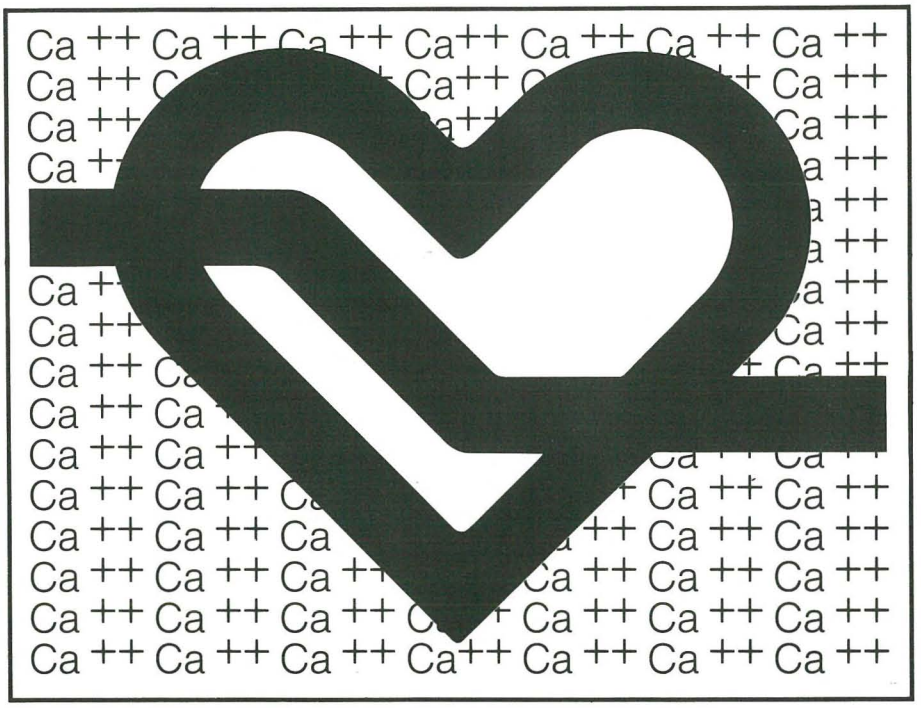
LABORATORY FINDINGS IN METABOLIC BONE DISEASE

	Calcium	Phosphate	Alkaline Phosphatase	Parathyroid Hormone.	Osteo Calcine
1° Hyperparathy – roidism	↑↓	↓/N	↑/N	↑↑	↑
2° Hyperparathy – roidism	↑	↑	↑	↑	↑↑↑
Osteomalacia	↓/N	↓	↑/N	↑	N/↓
Osteoporosis	N	N	N	N/↑	N/↓
Hyperthyroidism	↑	↑	↑/N	↓	↑
Cushing's Syndrome	N/↓	↓	N/↑	↓/↑	↓/↑
Paget Disease	N/↑	N/↑	↑	N	↑

TABLE 3

KNOLL

the pioneers of Calcium Antagonism



What could be more normal
than treating hypertension and angina
with

ISOPTIN®

knoll

Knoll AG · D-6700 Ludwigshafen · F.R. Germany

Agent: Joseph Cassar Ltd., 54, Melita Street, Valletta, Malta

PLACENTA PRAEVIA MANAGEMENT IN THE LAST CENTURY

MEDICAL LIBRARY
MEDICAL SCHOO
G'MANGIA MALT

C. SAVONA VENTURA MD MRCOG SPEC OBS GYNAE (LEUVEN)

Placenta praevia is nowadays managed by Caesarean section in most cases, and only in the marginal or lateral placenta praevia is vaginal delivery considered. The situation was very much different in the past, when the mortality associated with the operation prohibited the use of Caesarean section in the management of placentae praevia. The maternal mortality following section in 1888 was reported (18) at 54-62%, while that following complications of placenta praevia was lower at 30% (17). The parental mortality following vaginal delivery in cases of placenta praevia was 50-74% (17). Caesarean section for placenta praevia was recommended in 1898 by Lawson Tait (19) but acceptance only gained ground slowly. In 1923, it was noted (5) that "the performance of Caesarean section for cases of placenta praevia .... is being overdone." As late as 1951 (1) Caesarean section was noted to be contra-indicated if the patient had been examined vaginally in her home, or after a pack had been inserted in to the vagina, or if the child was too premature. It was considered the method of choice in elderly primigravida, total placenta praevia and in those cases of partial placenta praevia in which the cervix was long and closed. The reduction in foetal mortality was only brought about after Macafee (11,12) introduced the conservative antenatal management of placenta praevia with the aim of allowing the pregnancy to continue until the fetus has a chance of survival ex utero.

Progress in Midwifery on the Maltese Islands followed closely that on the continent. The first recorded Caesarean section was performed by Professor G.B. Schembri on the 28th May 1891 (15) on a woman who had cephalopelvic disproportion resulting from a rachitic pelvis, though other Maltese obstetricians as early as 1804 had recommended abdominal delivery to save the mother and child (3). The management of placenta praevia did not include abdominal delivery. In 1883 Prof. S. L. Pisani in his lectures to student midwives told his class that whenever the placenta delivers first, this must be inserted in tepid water until the arrival of the medical practitioner (14). In 1896 Prof. G. B. Schembri in his textbook for midwives (16), advises his students to manage the condition by bed rest and immediate recourse to medical help. A vaginal plug could be used until the arrival of the medical practitioner. The vaginal plug was made from several pieces of medicated cotton wool separately tied with a thread. The lumps of cotton wool are used to plug the vaginal canal completely, the threads being left hanging outside the vulva. To avoid turning an external haemorrhage into an external one, an abdominal binder made of crumpled napkins was bandaged over by a tight bandage.

In 1938 (7), Prof. Jos. Ellul described the management of placenta praevia in use at the time. "The routine treatment is to perform the classical tamponage when the cervix is closed; Caesarean section is preferred in certain primipara with a closed cervix and severe haemorrhage when there is an interest in saving the baby's life. In lateral and marginal cases, rupture of the membrane is performed and a pressure bandage applied over the abdomen. These cases are often delivered spontaneously. In other cases when bleeding continues the pulling down of a leg with a 2 lb weight (after internal or Braxton-Hicks version) or the use of Willet's forceps on the caput have been found very satisfactory." That year there had been twelve cases of placenta praevia delivered in the hospital. Five of these were more or less central, two marginal and five lateral. None of the cases were delivered by Caesarean section. Four of the central placenta praevia were complicated by puerperal sepsis and are described. Three of these cases were delivered by internal version and breech extraction, while one case was managed by Braxton-Hicks version and the application of a weight to the foot. Two of the cases of lateral and one of the marginal placenta praevia were similarly associated with puerperal sepsis. There were no maternal deaths from placenta praevia in the hospital, but many infants were sacrificed. Five babies were stillborn and two died a short time after birth. The Caesarean section rate at the Central Hospital at Floriana in 1937-38 (6,7) stood at 4.4% of all deliveries, the abdominal deliveries being performed for cephalopelvic disproportion (24 cases), ruptured uterus (7), and postmortem (1). The classical Caesarean section was the most frequent operation performed (18 cases: 56.3%). The lower segment approach was performed in 3 cases (9.4%). Porro's Caesarean hysterectomy was performed in 9 cases (28.1%), while Portes operation was used in 2 cases (6.3%). Portes operation, involving exteriorisation of the uterus, was limited to those cases where sepsis was advanced, or when the uterine rupture was small and it was desirable to preserve the

uterus. The mortality rate associated with surgery stood at 31.3%. During the same two-year period, four deaths attributed to complications of placenta praevia were reported from the Maltese Islands accounting for 4.9% of all registered maternal deaths with a specific mortality rate of 21.95 per 100,000 births.

Fifteen years later in 1951-52, 9 cases of placenta praevia were delivered by Caesarean section accounting for 12.0% of all sections performed at St. Luke's Hospital at Gwardamangia (8,9). Caesarean section in the hospital was undertaken in 6.8% of all deliveries and was associated with a mortality of 2.7%. The lower segment Caesarean section was the commoner approach (48: 61.0%) with the classical approach being performed in 15 cases (20.0%) and Porro's hysterectomy in 12 cases (16.0%). During the same period, 3 cases of placenta praevia were delivered after the application of Willett's forceps to the scalp, while the application of weights to the leg after internal version was reportedly used four times (Babies Labour Ward Register 1951-52). Two maternal deaths followed haemorrhagic complications from severe placenta praevia accounting for 16.7% of maternal deaths occurring in the hospital. There were thirteen fresh stillbirths and two neonatal deaths following complications of placenta praevia accounting for 6.7% of perinatal deaths occurring in the hospital (8,9).

A number of methods, other than Caesarean section, were thus available to the obstetrician to control haemorrhage and accelerate delivery. These methods remained in use long after Caesarean section became a reasonably safe alternative in the management of placenta praevia.

Classical Tamponage

Classical tamponage was first mentioned in Maltese medical literature in 1896 as a temporary measure to control blood loss by the attending midwife until the arrival of the medical practitioner (16). By 1938 the use of this method appeared to have become routine whenever the cervix was closed (7). By 1951, standard obstetric textbooks (1) justified this method only in infected cases which have too little cervical dilatation to permit the employment of one of the other vaginal methods, and as a temporary expedient to check dangerous haemorrhage pending the institution of alternative management. For efficient application, an anaesthetic is required and a firm abdominal binder is first applied. A large Sim's speculum should be used. At least fifteen yards of twelve-inch moist sterile roll gauze are required and the upper part of the vagina must be tightly packed if the plug is to be effective. The gauze should be soaked in a suitable antiseptic (acroflavine or chlorhexedine solution), and prophylactic antibiotics should be prescribed. The firm tampon in the vagina controls the haemorrhage and favours dilatation of the cervix. It is never safe for the pack to remain in situ for more than 8 hours, and if labour does not ensure within a few hours, the risks of sepsis are enormous (1,2,10). When this method was in general use at the Central Hospital in Malta, the choice of antiseptics was limited. Acriflavin and Dettol were the only local antiseptics available in 1938 (7), these being used routinely to prevent and treat puerperal sepsis. Sulphanilimide was first tried in Malta in 1935 with encouraging results, but only came in general use in 1937. Sulphapyridine appeared in 1938-39, while penicillin was first administered to civilians in 1945 (4).

Continuous Traction on the Foetal Head

Willett in 1925 (20) designed a special pair of forceps with which to grasp a fold of the scalp tissues and draw the head down onto the placental site, the membranes having already been ruptured. Continuous traction by attaching the forceps to a small weight of 1-2 lbs could be applied. Considerable trauma to the scalp may result. After the description of the vacuum extractor by Malmstrom in 1957 (13), an alternative method of grasping the foetal scalp was through the use of the smallest cup of the ventouse (2). Willett's forceps appear to have quickly gained favour in Malta, so that by 1938 their application

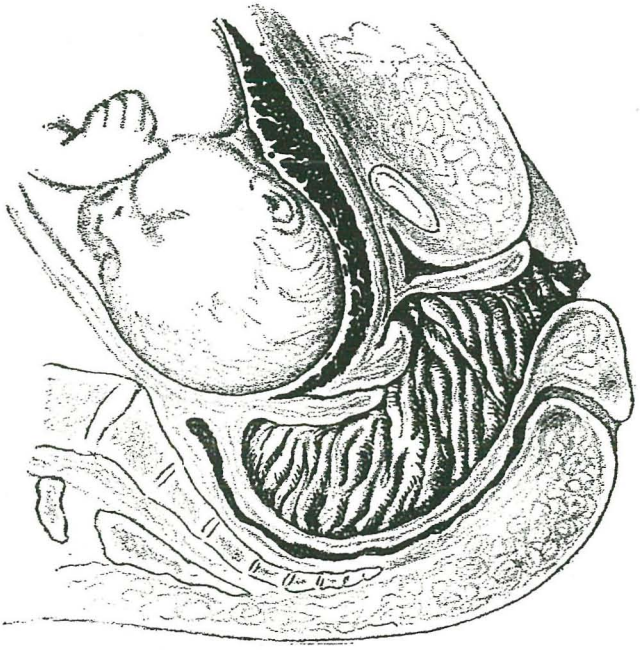
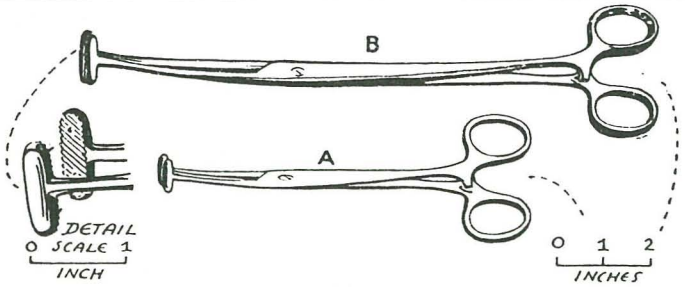


Figure 1. Haemorrhage controlled by the use of a gauze tampon in the vagina.



Willet's scalp forceps. **A.** Short pattern. **B.** Long pattern.

to the caput was one of the standard methods of managing placenta praevia (7). Their use continued until the 1950's (8,9) and were only slowly replaced when Caesarean delivery became a much safer alternative.

Pulling Down a Leg

The procedure of podalic version and breech delivery was the save-all for many obstetric problems and was the method of choice described for the management of placenta praevia in 1888 (17). The use of the fillet for applying traction in cases of breech presentation was described by Dr. Butigieg in his lecture notes to medical students dated 1804 (3), though he does not apparently specify their use in placenta praevia. Podalic version continued to play an important part in the management of placenta praevia until Caesarean section became a safer alternative. The procedure can only be performed if the patient is in labour. It is an effective method of controlling bleeding by compressing the placental site with the half breech and will after an interval excite labour pains. If the cervix is sufficiently dilated internal version is performed, otherwise external version or bipolar podalic version (Braxton-Hicks version) will be necessary. Having pulled down a leg, the pressure of the half breech is usually sufficient to arrest further bleeding, but if not, a weight of 2-3 lbs may be applied by means of a clove-hitch formed in a length of a strong roll gauze to the child's ankle (1,2,10). The foetal mortality of this procedure was prohibitively high and infants were routinely conditionally baptised on the foot as soon as this was brought out of the vulva (Babies Labour Ward Register 1956-57, Victoria Hospital, Gozo).

Hydrostatic Bag

On the same principle of controlling bleeding as the pulling down of a leg in cases of placenta praevia, a large hydrostatic bag, such as that of Champetier de Ribes was introduced into the uterus. A small weight could be attached to produce the desired pressure (1). This method does not appear to have gained ground in Malta.

In general the methods in force to control haemorrhage and facilitate early delivery required the application of traction either to the Willett's forceps applied to the scalp, or to the infant's leg brought down into the vagina. The application of this traction was continuous and may last for a few hours. Ian Donald in 1959 (10) suggested that the weight should be suspended over the foot of the bed, while Alfred C. Beck in 1951 (1) advised that care must be taken to allow for free play of the attaching cord when the patient moves, otherwise the tension may be sufficient to cause rupture of the uterus through the friable placental site. Alan Brews in 1963 (2) advised continuous traction by a cord passing over a pulley. A simple pulley system was in use in Victoria Hospital, Gozo. This

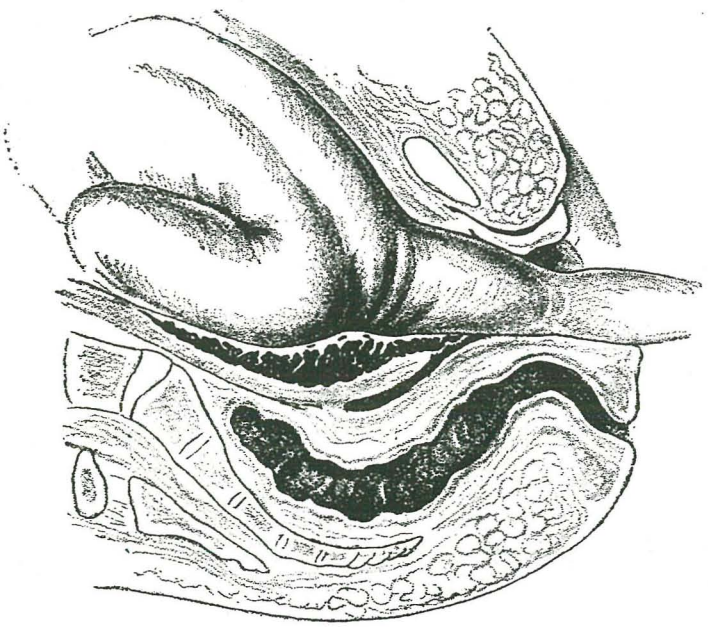


Figure 2. Haemorrhage controlled by Braxton Hicks version.

Figure 3. Haemorrhage controlled by the use of an intraovular bag.

involved the adaptation of a normal chair with re-enforcement of the back with an attached wooden bar.

Perpendicular to this, was attached an iron bar at the end of which was a pulley. The chair was placed at the foot of the patient's bed and the cord attached to the infant was passed over the pulley to a sterile bag into which a 2lb weight was placed. The weight allowed for continuous traction while the infant's presenting part was kept warm by the application of heated towels until delivery. Cases which underwent this management in 1938 have been described (7). Version followed by the application of weights was used for a variety of indications other than placenta praevia. The procedure had a very high foetal and maternal morbidity.

Photo of the chair used in Gozo for applying continuous traction to presenting part – the specially reinforced back can be seen *(Photo: Author).*

The recorded uses for version followed by the application of weights in 1938 (7) included:

Placenta praevia - "Central placenta praevia. Modest haemorrhage. Braxton-Hicks version, weight applied to foot. Temperature 100.5F by the evening. Streptocide was started but temperature kept rising during the next 48 hours to 101.5F. On the third morning the temperature was normal, only to rise again to 101F. Hobbs treatment was given with some success. It was repeated on four other occasions. On the fourteenth day the temperature dropped to normal but went up again to 101F by the evening. Hobbs was repeated with good result. Patient was discharged well 4 weeks after delivery."

Accidental haemorrhage – "One case deserves special mention. Internal version was performed and a light weight was attached to the leg which was covered with a warm towel. The haemorrhage was stopped and birth took place spontaneously after four hours. The baby was alive and well."

Unengaged head – "C.S. Aged 39 years. Multipara (8). Admitted on 2.5.38 for pregnancy and myocarditis. Pendulous abdomen and albuminuria. Cardiotonics, diet, rest in bed, abdominal binder.

31.7.38 Labour pains started in the morning – membranes ruptured at 3 p.m. Head not engaged – internal version performed under general anaesthetic. Weight applied.

1.8.38 Morning. Signs of rupture of uterus. Pain in right iliac region, pulse 130, respiration 40, labour pains stopped. Manual delivery of a macrosomic (13 lbs) macerated fetus. Patient died from haemorrhagic shock after rupture 1.8.38."

The use of traction continued well into the 1950's. The use of Caesarean section for cases of placenta praevia gained ground slowly so that while in 1937-38 no abdominal deliveries were performed for placenta praevia, in 1961-62, seventeen sections were performed for abnormal placentation (Table 1).

Caesarean section is generally a safe procedure, but the increased bleeding in cases of anterior placenta praevia and the higher incidence of placenta accreta in cases of placenta praevia increases the risks of surgery. Management of cases of placenta praevia should not be left to inexperienced junior staff and section should be performed or directly supervised by an experienced obstetrician.

References on page 43

	1937-38	1951-52	1961-62	1971-72	1981-82
Number of Caeserean Sections for placenta praevia	Nil	9	17	18*	24
Total number of Caesarean Sections performed	32	75	212	421	912
Hospital maternal mortality from placenta praevia	Nil	2	Nil	Nil	Nil
Hospital perinatal mortality from placenta praevia	7	15	Nil	1+	Nil

Note: **Number of Caesarian Sections for placenta praevia for period 5/7/71 - 31/12/72*
+Hospital perinatal mortality from placenta praevia for period 1/1/71 - 31/7/72

TABLE 1

Endo-flexibility!

HOPPE, KRÄMER & PARTNER

Everything Endodontic – The Kerr System

Kerr offers an integrated system
of products –
from files and gutta percha points to
state-of-the-art root canal
sealers – with the proven consistency
you can rely on.
Insist on the Kerr Endo Difference.

KERR®

Bart Enterprises Ltd. · 172, Strait Street · VALETTA
Telephone: 23 54 03, 22 23 19 · Fax: 62 05 04

PAUL BINHOLD GMBH

3B

MANUFACTURERS OF EDUCATIONAL MODELS FOR ANATOMY AND BIOLOGY

VARIOUS MODELS AVAILABLE IN STOCK

More than 30 Years in 70 Countries of the World

LOCAL AGENTS

Technoline

Technoline Ltd., "Regional House " Edgar Bernard Str., Gzira – Malta. Tel: 337975, 311642, 310567, 342366

SUN BATHING: A CASE OF – TAN NOW ... PAY LATER ?

ANTOINE VELLA MD AND MARK A. VASSALLO MD

The sun, the largest and brightest of the stars visible to the naked eye has always been regarded by man, from the earliest days, as a source of energy, good health and happiness. The Plains Indians of the 19th Century used to worship the sun by a most important and spectacular religious ceremony - the Sun Dance. This was held in early summer by each tribe and used to continue for many days and nights, the participants mutilating themselves and getting exhausted to the point of death (1). In an effort to curb such practices, the U.S. government outlawed the Sun Dance in 1904. Nowadays, the Sun Dance is largely over and done with, however, we still 'worship' the sun on our beaches with just as much fervour as the Plains Indians and with just as many mutilating results. It is perhaps high time that we curb such practices rather than tan now and have to pay later at a costly price.

Sunlight consists of a spectrum of wave bands. The part of the spectrum which is responsible for the harmful effects of sunlight is largely in the ultra violet region.

The Ultra Violet spectrum is further subdivided according to the wavelengths into UVA, UVB and UVC as shown in fig 1 above. The wave lengths of ultra violet radiation which are most likely to produce acute and chronic effects are within the short wave UVB range 290 - 320nm. Wavelengths less than 290nm are absorbed in the atmosphere and are therefore not transmitted to the earth's surface. Wavelengths ranging from 320-400nm are relatively inefficient in producing erythema but enhance UVB induced carcinogenesis in animal models and may enhance UVB induced skin aging. The intensity of ultra violet light reaching the earth's surface varies with altitude, latitude, time of day, time of year, cloud cover and shade; so variations are very large. Cloud cover and moderate shade do not greatly attenuate ultra violet but ultra violet scatter from blue sky and ultra violet reflection from rippling water or sand may greatly increase ultra violet intensity. Sunlight is the only natural source of UVB. Artificial sources of ultra violet radiation include UVA and UVB sources used diagnostically and therapeutically in dermatology departments, sun beds, some lasers and some fluorescent and other lighting sources.

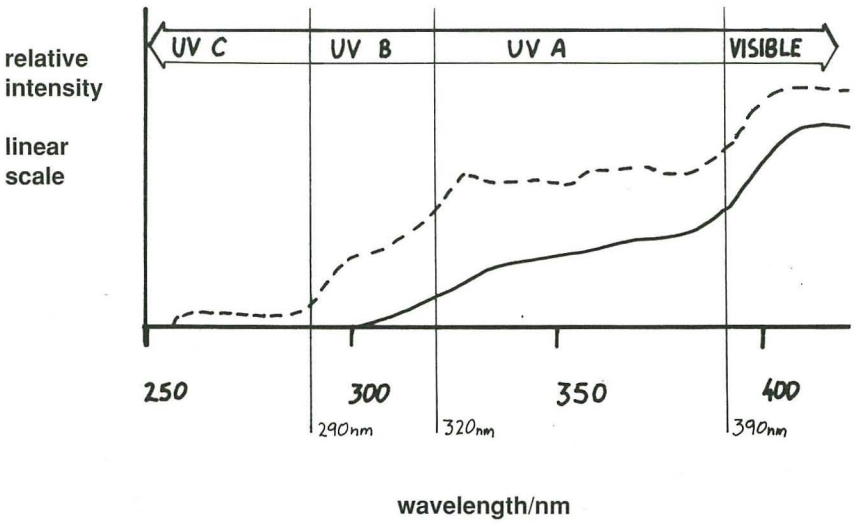


Figure 1. Relative intensity of Solar radiation in the UV spectrum showing atmospheric absorption
Key: — — — — Emitted solar radiation
———— Radiation transmitted by atmosphere.

Acute and chronic effects of sunlight on human skin result from excessive exposure to sunlight. Excessive in this context means significant exposure to strong midday sun and any sun exposure that results in prolonged redness of the skin and discomfort, scaling or peeling. The acute effects of excessive exposure to natural sunlight include sunburn, with erythema, sometimes swelling, blistering and subsequent peeling of the skin commencing within hours of exposure and taking several days to resolve. The severity of the acute reaction depends on both the individual's skin type and on the intensity of radiation. With regard to reaction to sun exposure, there are 6 types of skin (Melski J.W. et al 1979). See Table 1 below.

TYPE	REACTION TO EXPOSURE TO SUNLIGHT
1	Never tans, always burns
2	Tans with difficulty, burns frequently
3	Tans easily, burns rarely
4	Always tans, never burns
5	Genetically brown skin (Asian and Mongolian)
6	Genetically black skin (Negroid)

TABLE 1

The more chronic effects of ultra violet exposure basically consist of two major categories – skin cancer and premature ageing. One only needs to walk through the streets of one of the rural Maltese villages, where farmers spend most of the time in the scorching sunlight, to be aware of premature skin ageing, which is one of the most evident of the harmful effects of sunlight. This premature ageing includes dryness, wrinkles, laxity and patchy variation in skin pigmentation. All these have been traditionally associated with ageing but more recent studies comparing habitually exposed facial skin to habitually unexposed buttock skin in an elderly person, have shown that exposure to the elements is more important than age per se in causing these changes. Premature skin aging results largely from damage to the epidermis causing epidermal keratosis and to the connective tissue of the dermis. The latter has three components; cells – mast cells, histiocytes, fibroblasts; ground substance – mucopolysaccharides, lipids, glycoproteins and non-fibrous proteins: and lastly fibrous elements consisting of elastin, collagen and reticulin fibres. Sunlight mainly effects the ground substance and the fibrous elements of the connective tissue to result in premature skin aging also referred to as actinic elastosis. A study by Graham Smith et al (1968) showed that normally both hyaluronic acid and chondroitin sulphate decrease with age, the decrease in hyaluronic acid being greater than the decrease in chondroitin sulphate. However, in chronically sun damaged human skin there is an increase in hyaluronic acid with a slight increase in chondroitin sulphate.

As mentioned above besides the mucopolysaccharide component of the connective tissue, its fibrous element is also effected. Studies by several investigators have demonstrated that there is a decrease in soluble collagen and an increase in insoluble collagen as a function of age (Sobel et al 1959, Clausen 1962). On the other hand the elastin content of the dermal connective tissue increases with age (McGavack and Kao 1960).

An increase in the number of interstrand and intermolecular cross-links renders the collagen molecule less and less soluble. This effect was found to be enhanced by sunlight which acts as the hydroxyproline cross-linkages to result in an increase in insoluble collagen. The effect of sunlight on elastin results in a decrease in glutamine and lysine (Thomas et al 1963) and an increase in desmosine and isodesmosine and it has been postulated that desmosine may partly behave as the cross-linking unit of elastin.

The current increasing awareness by the general public and the media in the hazards of exposing the skin to sunlight are mainly founded on the association between excessive sun exposure and skin cancer. Studies in Australia (McLeod G.R. et al 1985), Scotland (Doherty, MacKie 1986) and certain parts of USA (Rieget et al 1986) have shown the clear association between excessive sun exposure and skin cancer and have given information on the early recognition of skin cancer.

There are basically three types of skin cancer; basal cell carcinoma, squamous cell carcinoma and malignant melanoma. Carcinoma of the skin is most prevalent in countries such as Australia, South Africa and the Southern part of the United States of America where fair-complexioned people are exposed to the sun. In these countries, which are only a few examples, there is a dry sunny climate and since the atmospheric filtration of UVB is increased as the angle of incidence of the solar rays decreases, there is an increased prevalence in these countries with decreasing latitude. In fact in the USA the incidence rate for white people of the same age group increases as their place of living becomes closer to the equator (Auerbach et al 1961). Caucasians are affected 15 times more than Negroes for the same degree of exposure. The relative immunity of dark-skinned people is found in all countries and is due to skin colour rather than any other racial characteristic, as is shown by the high incidence of skin cancer in the albino Bantu (Cohen et al 1952). The most susceptible of the fair skinned people are those with blue eyes, red hair and freckles. As an index of susceptibility a light colour of the iris is more significant than fair hair. In sunny climates susceptible subjects develop their keratosis and skin cancer a decade or more before those who tan easily and have been exposed to similar conditions. However it would be a mistake to assume that skin cancer occurs mainly in people with skin which does not tan easily on sun exposure. In areas like Australia, the majority of the white population tan readily and tumours occur in such people although at a somewhat later age than those who do not tan. Earlier studies showed an increased association in incidence of skin cancer with changing age structure of the population, habits of dress and recreation (MacDonald 1959, 1964). In a way, this finding can be used positively since reversion to healthier habits especially recreational ones and the use of preventive measures can result in a significant decrease of skin cancer.

Genetic factors have an important role to play since it is the genetic code which determines the type of skin a person acquires. Patients suffering from Xeroderma Pigmentosa, a rare and significant genetically recessive condition are unable to break down pyrimidine dimers formed by ultra violet radiation. This results in a higher incidence of actinic carcinogenesis in such patients. A study by Hueper et al 1946 showed an association of long-term cumulative exposure to natural sunlight in outdoor workers, such as farmers, fishermen with the incidence of basal cell and squamous cell carcinoma. Also the commonest sites to be involved are those that are habitually exposed, that is, the face, the dorsum of the hand and the forearm.

Malignant melanoma, the most lethal of the skin cancers, has some features which are different from those of basal cell and squamous cell carcinoma. It tends to affect a younger age group, around 50 years of age,

rather than the 70 year age group for non-melanoma skin cancer. Also melanoma is more common in professional and managerial groups, whilst basal cell and squamous cell carcinoma is commoner in those with unskilled occupations (Lee and Strickland 1980). In fact a study by Looke, Stregy and Fraser 1984, showed that the melanoma type of cancer is more common in indoor than in outdoor workers in contrast to other types of skin cancer. A study in Australia where there is the highest incidence of melanoma showed that possible childhood sun exposure is of critical importance since European immigrants arriving before the age of ten years have risks similar to those of the natives while arrival at any age after fifteen constitutes a lesser risk (Holman and Armstrong 1984). A Canadian study by Edward, Gallagher and Davidson et al 1985 has shown that the risk of melanoma is increased in individuals who have high levels of intermittent exposure to the sun from holiday or recreational activities, while there is no parallel increase in individuals whose excessive exposure has been the constant, everyday, occupation type of sun exposure. This has been further confirmed by Scottish and American studies (MacKie, Hitchison 1982). All these studies suggest that the increasing incidence of melanoma may be related significantly to intermittent exposure to excessive sunlight, often with a history of sever sunburn, but who otherwise have a low level of exposure throughout the year. This factor has a special relevance in countries like Malta where holiday makers especially from countries like the UK, grill themselves to a lobster red and then flock to the pharmacist for something to relieve their burning agony only when it is too late and when the actinic damage has already occurred. Persons who have large numbers of pigmented naevi, usually large, having an irregular edge, looking inflamed – the dysplastic naevus syndrome – are at an increased risk of developing melanoma. These persons even more than others, must be wary of excessive sunlight exposure as shown in a study by MacKie 1982, where out of 12 patients who had both malignant melanoma and dysplastic naevi, 9 had a history of excessive sun exposure.

There is also an association between immuno-suppresssed patients and cutaneous malignancy. Renal transplant patients, leukaemia patients on treatment and other immuno-suppressed patients have an increased incidence of cutaneous malignancies and this was found to be especially high in areas with high natural sunlight intensity.

The prognosis for skin cancer ranges widely with the type of neoplasia. Basal cell carcinoma has an excellent prognosis after local excision or radiotherapy. Squamous cell carcinoma has a very good prognosis if it is recognised and treated early. However if not, the prognosis deteriorates due to spread to lymph nodes later on in its course. Malignant melanoma has a much more sinister prognosis which depends very much on the thickness of the primary tumour. This can be measured by the Breslow technique, see Table 2.

If caught early, malignant melanoma can be treated with a good cure rate. In order for this to be possible public awareness to malignant melanoma must be increased. To the effect, in Scotland, a public awareness campaign included a 7-point check list with features commonly seen in malignant melanoma. See Table 3 below.

From the above one can easily come to the conclusion that the price we might have to pay for sun bathing unorthodoxly might be surprisingly high. Public awareness of this fact is still lacking and a campaign should be set rolling to this effect equally in Malta, where sun bathing is so popular amongst both locals and tourists. However sun bathing can be made much safer if the necessary precautions are taken. The most commonly used protection consists of topical sunscreens known as sunblocks. These topical agents have a variable Sun Protection Factor (SPF). Currently available preparations range from SPF 2 to 20. It is only agents in the range of SPF 8 to 10 which have significant protection against the acute and more importantly against chronic sun damage.

Thickness (mm)	5 Yr. Survival Rate (%)
1.5	91
1.5 - 3.5	67
3.5	38

TABLE 2

A revolutionary device in the field, which has been launched recently in the local market, is an umbrella of variable size which has complex light-absorbing chemicals bonded into its fabric. These chemicals block only the undesirable wave length of natural sunlight, see Table 4 below, while at the same time allowing the wave lengths necessary for sun tanning to pass through. In addition as shown in Table 4 it also blocks those wave

Points	*Score*
1. Presence of itch or altered sensation.	One point per feature
2. Diameter of 1 cm or greater	<3 pts. – 90% non-melanomatous pigmented lesion
3. Increasing size	
4. Variation in density of black or brown pigment within the lesion	>3 pts. – refer to specialist
5. Presence of an irregular or geographic lateral border	>5 pts. – 95% a melanoma
6. Inflammation	
7. Bleeding or crusting	

TABLE 3

lengths which produce heat and glare. Hence this fabric (SUN SELECT[R]) creates a cool comfortable shade in which to tan. The fabric offers protection equivalent to traditional sun care products with SPF 8-10. Due to the ability of this special material to selectively absorb only those wave lengths which cause burning, the sun's natural ability to tan will not be affected by the device.

Characteristics of SUN SELECT[R]

- BLOCKS 99% of UVB (290-320nm) which causes sunburn
- ALLOWS up to 80% of UVA (320-400nm) which allows tanning
- REDUCES heat and glare by 50% (over 440nm)

TABLE 4

In conclusion whilst the sun really does wonders for our 'soul' – a fact that makes Malta such a popular tourist resort – it does nothing but damage to our skin. Taking a glance at the animal world, one notices that all creatures living in conditions that resemble those of our beaches, have through the process of evolution acquired some kind of protection either anatomical or behavioural. Perhaps it is about time that we follow the example of these creatures of lesser intelligence but surely with a greater survival instinct than ours.

References

1. L. Spies 'The Sun Dance of the Plains Indians' Americas Museum of Natural History Anthropological Papers Volume 16.
2. J. Graham Smith, Eugene A. Davidson, Ralph W. Taylor in Advances in Biology of Skin Volume VI 'Aging'.
3. W. Mitchell Sames, J. Graham Smith.
4. Nicholas J. Lowe - Medicine International (49).
5. Doherty, V.R. and MacKie, Rona M. (1986) - British Medical Journal.
6. Cox, N.H., Jones, S.K., MacKie, R.M. et al (1986) - British Journal of Dermatology.
7. Lee, J.A.H. and Strickland, D (1980) - Cancer.
8. Breslow, A (1970) - Annals of Surgery.

Continued from page 3

References

1. FRANCHIMONT P. (Liege) Etudes hormonales et immunocytologiques sur l'antehypophyse a un age avance. (Bordeaux Symposium 1984 on: Hormonal and metabolic alterations in the elderly).
2. EPELBAUM J, DROUVA SV, TAPIA L: Interactions entre neuromediateurs et neuropeptides impliques dans le controle de la secretion hypothalamique in vitro. Ann. Endocrinol. (Paris) 1980, 41:478-486.
3. KNOBIL E: The role of signal pattern in the hypothalamic control of gonadotropic secretion. In R Ortavant, A Reinverg: Rythmes et Reproduction. Masson. Paris. 1980 pp 73-79.
4. KORDON C, ENJALBERT A: Opiates and neuroendocrine regulation. In JD Vincent, J Nunez: Hormones and Cell Regulation, Elsevier, North Holland, Amsterdam 1980, pp 151-159.
5. WEINER RI, GANONG W: Role of brain monamines and histamine in regulation of anterior pituitary. Physiol Rev., 1978, 58:905-976.
6. BREMNER WJ, PRINZ PW: The diurnal variation in testosterone levels is lost in aging normal men. Abstr. Endocrine Soc. Meeting Abstr. 480:1981.
7. HARMAN SM: Clinical aspects of aging of the male reproductive system. In El Schneider: The aging reproductive system. Raven Press, New York, 1978 pp 29-58.
8. SPARROW D, BONE R, ROWE JW: The influence of age, alcohol consumption and body fluid on gonadal function in men. J. Clin. Endocrinol and Metab., 1980, 51: 508-512.
9. VERMEULEN A, DESLYPERE JP, SCHELFHOUT W, VERDONCK L, RUBENS R: Adrenocortical function in old age: Response to acute adrenocorticotropin stimulation. J. Clin. Endocrinol Metab., 1982, 54: 187-191.
10. BECKETT GJ et al: Thyroid status in patients with chronic renal failure. Clin Nephrology, 19: 172, 1983.
11. HERRMANN J et al: Thyroid Function and thyroid hormone metabolism in elderly people. Low T3-Syndrome in old age, Klin Wochenschr. 59: 315, 1981.
12. CAHILL GF, Jr: Hyperflycemic Hyper-osmolar coma: A syndrome almost unique to the elderly. J. Am Geriatric Soc. 31: 103, 1983.
13. RIGGS BL et al: Effect of the Fluoride/ Calcium regimen on vertebral fracture occurrence in post-menopausal osteo-porosis. Comparison with con-ventional therapy. NEJM 306: 466, 1982.

Did Queen Elizabeth I write Shakespeare?

Who wrote Shakespeare? As with the authorship of many books of the Bible, the answer is not necessarily the obvious one. Ever since the mid-19th century, alternative authors have been proposed for many of the works attributed to the Bard of Avon.

Now, thanks to a computer programme developed by Robert Valenza of Claremont McKenna College in California, there's an even more unlikely runner in the Shakespeare stakes – Queen Elizabeth I.

What Valenza did was to use a technique called modal analysis to compare poems attributed to Shakespeare with those known to have been written by twelve contemporary authors, including Elizabeth.

Aided by a grant from the Sloan Foundation, Valenza and his co-worker Professor Ward Elliott spent three years establishing what they call 'structural relationships' between a selected set of 50 keywords.

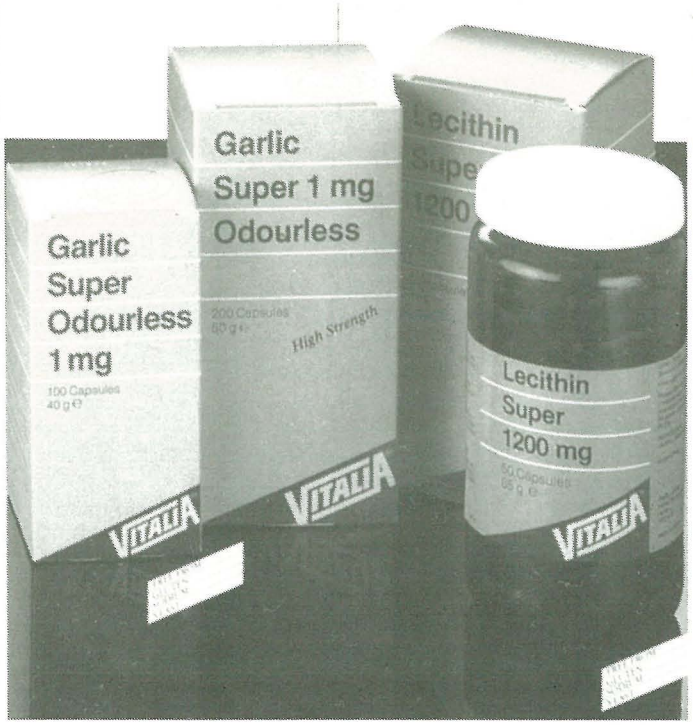
Initially the computer selected the 50 most common words found in Shakespeare, an approach which produced no clear-cut results. When it was realised that this group of 50 included unavoidable words such as "and" and "the", a second attempt was made using Shakespeare's 50 next most favoured words. This time the computer produced startling results.

Of all the pretenders to the Shakespearean throne, Edward de Vere emerged "badly wounded". Out also went Marlowe, Bacon and many others. Those who survived this structural relationship test included Elizabeth I (whose modest known output consists mainly of translations of the Psalms), Sir Walter Raleigh and Faulk Greville, author of an obscure set of sonnets.

Unfortunately (at least for the pretenders), all those who at this stage were still in the running fell down when the computer examined their verbal styles. Shakespeare used far more compound words and only half as many relative clauses as any of his challengers. Exit the Virgin Queen.

Of the poems that are merely attributed to Shakespeare, most also seem to fail these tests. Conversely, at least one collection of unattributed poems comes out as being more Shakespearean than Shakespeare! Ward Elliott says that the former conclusion is perhaps the more reliable.

One thing is sure: as with the authenticity of the Turin Shroud, no classical Shakespearean scholar is likely to let the arguments rest there.



Garlic Super 1mg Odourless

For centuries now garlic has long been considered a health food. This ancient idea is now supported by modern research and an increasing number of people are deriving general benefits from this plant used since ancient times.
With Vitalia Garlic Capsules you can enjoy many of the benefits without having to pay the high price of socially unacceptable breath odour.

CAPSULE CONTENTS

Garlic Oil	1 mg

Lecithin 1200mg Super

Lecithin has a vital role to play in maintaining a healthy, balanced life-style. It helps in the safe transport of fats, lowering cholesterol levels, a factor considered essential for a healthy heart.
Our popular lecithin supplement has been specially formulated for your convenience as a high strength one a day capsule.

CAPSULE CONTENTS

Lecithin	1,200mg

VITALIA®

GALEA & GALEA ENTERPRISES LTD.
William Savona Str. San Gwann.
Tel: 337928 - 472120

Hair Formula

Healthy hair is dependent upon blood circulation which in turn is dependent on nutrition. Partial lack of any nutrient can cause hair problems.
The Vitalia Hair Formula will greatly assist in providing all the nutrients in minute quantities and in addition contains Valerian extract, well known for its properties to reduce anxiety – another factor that contributes to hair loss.
Vitalia Hair Formula has been specially prepared to help maintain healthy hair, and regular use is recommended for optimum results.

This product has been specially formulated for those people who want their hair to look at its best.

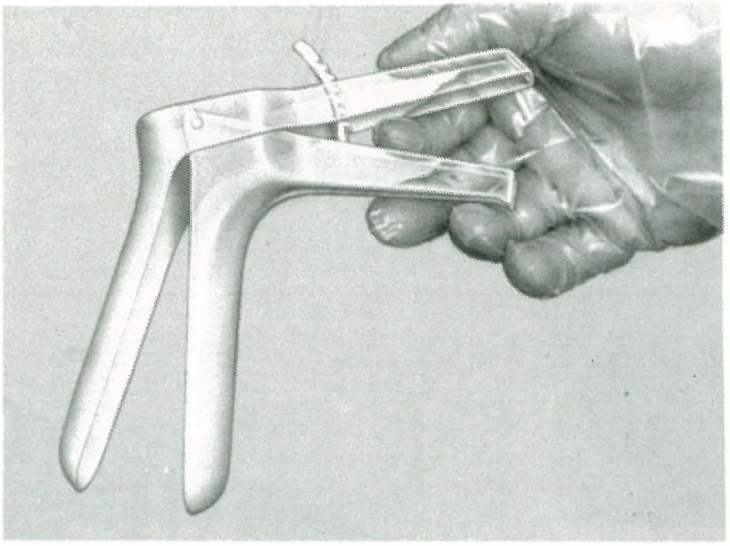
TABLET CONTENTS:

Brewers Yeast	Para Amino Benzoic Acid (PABA)
Sea Kelp Powder	L-methionine
Valerian Extract	L-cysteine
Pantothenic Acid	L-lysine
Zinc	Choline
Iron	Inositol
Biotin	

VITALIA®

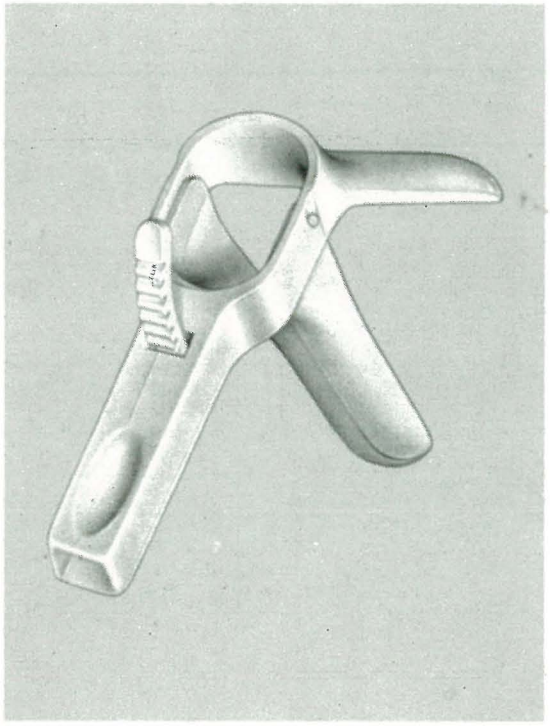
GALEA & GALEA ENTERPRISES LTD.
William Savona Str. San Gwann.
Tel: 337928 - 472120

EXPORT - SPEC



Speculum vaginale monouso mod. EXPORT. Dimensioni: mm. 90 x 28
Materiale atossico, atattico (che non attira la polvere), trasparente.
Imballo: ogni 20 pezzi in sacchetto plastica. Ogni cartone contiene 120 speculum.

Disposable vaginal speculum mod. EXPORT. Sizes: mm. 90 x 28
Atoxic, transparent material, not attracting dust.
Packing: every 20 pcs. in a plastic bag. Each carton contains 120 speculum.



Speculum vaginal à usage unique mod. EXPORT.
Dimensions: mm. 90 x 28
Matériel non toxique, transparent, non attirant la poussière.
Emballage: 20 pièces en sachet plastique. Contenu de chaque carton: 120 spéculum.

Espéculo vaginal monouso mod. EXPORT.
Dimensiones: mm. 90 x 28
Material atòxico, transparente antipolvo.
Embalaje: cada 20 piezas en bolsa de plàstico. Contenido de cada cartòn: 120 espéculos.

Vaginal Spiegel zum einmaligen Gebrach mod. EXPORT.
Dimensionen mm. 90 x 28
Ungiftigen, transparenten unstaub Kunstoff.
Verpackung: Jedes 20 stûck im plastische Tasche. Packungen zu 120 Spiegel

DOPPLER ULTRASOUND

Clinical applications in the adult and the foetus

J. MAMO M.B., CH.B, D.OBST., M.R.C.O.G.
Senior Registrar in Obstetrics and Gynaecology

Y. MUSCAT BARON M.D.
Senior House Officer in Obstetrics and Gynaecology

The application of Doppler signals in medicine has been available for the past 25 years. The Doppler effect is the change in frequency of waves when there is a relative movement between source and observer. The technology used in medical Doppler is capable of profiling the pattern of flow within specifically identifiable vessels (Jaffe 1984). This therefore should have several applications in different branches of medicine.

The use of Doppler Studies in the examination of patients with peripheral vascular disease was first reported by Satomura in 1959. Doppler technology has provided the clinician with a means for the quantitative assessment of the severity of arterial occlusive disease. This non-invasive technique provides objective and repeated assessments relating to the long term prognosis following reconstructive surgery.

Doppler ultrasound has provided a versatile technique for use in the diagnosis of disorders of the venous system. Screening of the deep venous system of the lower extremity using this portable method needs considerable attention to detail but is quick and simple to learn.

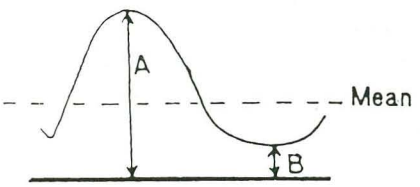
The use of Doppler ultrasound is a good adjunct to echocardiography in the evaluation of patients with cardiac disease. These techniques reduce the need for invasive investigations and aid in the proper timing of surgical procedures.

Transient and permanent cerebrovascular ischaemic events may be associated with either haemodynamically significant carotid artery stenoses or nonstenotic carotid plaques that serve as sources of microemboli. Duplex scanners, that is real time B-scan imaging coupled with pulsed range-gated Dopplers, are noninvasive devices which have helped in the grading of stenotic lesions (Dreisbach). The development of an accurate computerised method for the interpretation of the carotid artery waveform has reduced the subjective evaluation, and therefore increased the sensitivity of this technique. This may help in screening which segment of the population is at greater risk of developing a stroke. Duplex scanning is a cost effective noninvasive neurovascular test for evaluating carotid bifurcation disease.

There is a wide spectrum of applications of Doppler ultrasound in the abdomen. There is good evidence that the use of small, hand-held Doppler units in the operating room is of value in detecting regional blood flow in the kidney and the gastrointestintestinal tract. Doppler ultrasound has been applied in the investigation of renal arteries. This is especially important in the early post-operative assessment of renal transplant function. Renal transplant main vessel vascular occlusion must be diagnosed early in order for remedial surgery to be successful. Doppler ultrasound may become the examination of choice for distinguishing between acute tubular stenosis and transplant rejection.

Apart from other applications in medicine the Doppler effect has been a useful noninvasive repeatable technique to assess foetal and uteroplacental circulations. This is clinically useful in the investigation and management of complicated pregnancies, in particular intrauterine growth retardation (I.U.G.R.) and pregnancy induced hypertension (P.I.H.).

The blood flow in the umbilical vessels gives rise to a characteristic waveform. Using continuous wave Doppler equipment directed at the umbilical vessels, both the sound and the waveform shape are recognised. The flow velocity waveforms can be analysed by comparing the systolic or peak (A) and the diastolic or trough (B) of the frequency shift. There are three commonly used ratios:



$$\frac{A}{B} = \text{A/B ratio}$$
(Stuart et al 1980)

$$\frac{A - B}{A} = \text{Resistance index}$$
(Porcelot 1974)

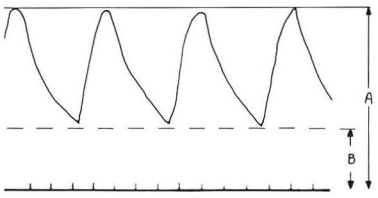
$$\frac{A - B}{\text{Mean}} = \text{Pulsatility index}$$
(Gosling and King 1975)

The normal A/B ratios vary with gestation, at 28 weeks the A/B ratio is 5 or less, decreasing to a value of 4 at 34 weeks and 3.5 or less between 34 weeks to term. The Resistance Index should be less than 0.5 in normal pregnancy. Although the Pulsatility Index seems to be the most accurate, it requires a computer programme whilst the first two ratios can be calculated simply. The Pulsatility Index is 2.41 + 0.3. in high risk pregnancy while it is 1.99 = 0.2 in pregnancies which are low risk.

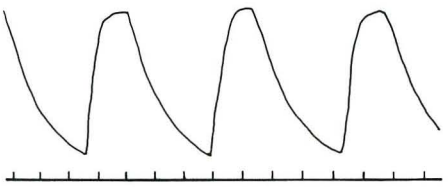
The most important characteristic of the waveform is the trough which represents the end-diastolic flow. As normal pregnancy progresses, an increase in the end-diastolic volume occurs due to a decrease in the foeto-placental resistance. Developmentally, the appearance of the end-diastolic flow coincides with the invasion of the myometrium by the cytotrophoblast. In I.U.G.R. and P.I.H. there is an increase in the resistance which in turn results in a reduction in the end-diastolic flow. When the disease is severe, the trough may reach the zero mark or even become negative (see waveform diagrams). It is also noted that a diastolic notch that is normally only present until the 26th week, tends to persist in I.U.G.R. and P.I.H. indicating reduced vessel compliance.

Umbilical flow was noted to be high in patients with Rhesus iso-immunisation and in ante-partum haemorrhage. In patients with a low end diastolic flow there is an increased risk of neonatal morbidity (Pearce 1989).

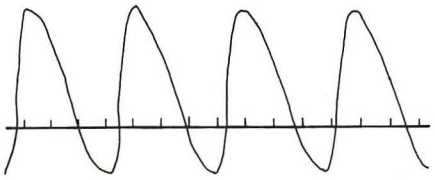
Uterine and arcuate artery blood flow may also be reduced in patients with P.I.H. and I.U.G.R. in whom there is placental insufficiency due to impaired utero-placental circulation (Rightmire 1988). The blood flow in the uterine artery has been found to be reliable in the diagnosis of I.U.G.R. while arcuate artery blood flow may forecast foetal distress during labour. Blood flow in the foetal aorta and carotid arteries may be quantified. In asymmetrical growth retardation, there is a brain sparing effect in which the blood is shunted to the brain thus reducing the pressure ratios in the descending aorta. The abnormal flow velocity waveforms in the descending aorta seem to precede the changes in the umbilical vessels. Moreover, the reduction in the end-diastolic flow in the descending aorta suggests chronic ischaemia of the splanchnic and renal circulations. This would predispose to necrotising enterocolitis in the newborn. The concomitant reduction in the renal circulation results in less urine production and hence oligohydramnios.



A: Normal tracing



B: Abnormal tracing A/B > 6



C: Abnormal tracing A/B > 6 with reverse flow

Sketch of umbilical artery flow velocity-time waveforms in which the vertical dimension represents the Doppler-shifted sound frequencies (Hz) and the horizontal dimension represents time. Waveforms presented below the broad horizontal line represent flow in the direction opposite to that above the line: **A**, normal umbilical artery flow velocities over umbilical vein flow velocities at 34 weeks gestation; **B**, waveform characterized by a high A/B ratio indicative of high impedance with low end diastolic velocities that approach the limits of the high-pass filter; **C**, very abnormal waveform with reversal of the direction of flow in diastole as indicated by the segment of the arterial waveform in each cardiac cycle which appears below the broad horizontal line.

Absent end-diastolic velocity in the umbilical artery indicates poor foetal prognosis in general but it does not indicate imminent foetal death, and may improve. Low end-diastolic flow values occur approximately one week before the first abnormal trace. It is encouraging to note that absent end-diastolic velocity does not occur within a week of having a normal umbilical waveform. Therefore Doppler waveform studies may be repeated weekly. This may be a good predictor of foetal risk, allowing for timely intervention.

The study of Doppler velocity waveform is a relatively noninvasive investigation of the foeto-placental circulation which may help in the reduction of perinatal morbidity. Doppler waveform studies may become a new tool in the screening of high risk groups in early pregnancy, since changes in the waveform predate conventional tests of foetal wellbeing.

References

1. Dreisbach, J.N. (1984) Duplex Ultrasound Evaluation of Carotid Disease; Clinics in Diagnostic Ultrasound; 13,69-103.
2. Jaffe, D.C. (1984) Doppler Applications and limits of the method in Vascular and Doppler Ultrasound (Churchill Livingstone).
3. Pearce J.M. (1989) Doppler Ultrasound Blood Velocity Waveforms in Foetal Monitoring: Spencer J.A.D.
4. Rightmire D.A. (1988) Clinical Doppler Ultrasonography: Clinical Obstetrics and Gynaecology (1988) 31,1,27-43.

SCOMBROID FISH POISONING AFTER INGESTION OF DOLPHIN FISH (LAMPUKI)

M. BALZAN MD M.R.C.P. (U.K.)

Senior Registrar, Department of Medicine, St. Luke's Hospital, Malta.

A. PORTELLI MD

Senior house officer, Admitting and Emergency Department, St. Luke's Hospital, Malta.

Scombroid fish poisoning affecting all five members of a family from Zejtun is documented. The clinical features and the management of this condition are reviewed.

Introduction

Scombroid fish poisoning results from the ingestion of toxic substances that accumulate in improperly handled fish.(1) In October 1990 local general practitioners, health centre medical officers and emergency room staff noted a number of 'allergic' reactions related to the ingestion of Lampuki (Dolphin fish) particularly in the Zejtun area.

Case report

All 5 members of one particular family from Zejtun had fried lampuki for supper. Within 30 minutes they all developed a histamine-like reaction. The clinical features of each case are shown on Table 1.

Only one out of the five patients seen in the emergency room had respiratory distress due to bronchospasm. This responded immediately to the administration of nebulized salbutamol. All five received 25mg of promethazine intramuscularly. They all felt much better after 2 hours and in fact none of them was hospitalized. Twelve hours later they were all symptom free.

Discussion – Pathophysiology BNI

Scombroid fish poisoning is caused by the ingestion of fish with a high histamine content. Scombrotoxin is formed when bacteria on the hide of the fish (Proteus and Klebsiella) proliferate on fish protein because of improper refrigeration.(2) Free histidine is degraded to histamine by the enzyme histidine decarboxylase produced by bacteria.(3) Fig 1.

As the ingestion of free histamine even in large doses is not associated with clinical effects(4), the presence of accompanying synergistic substances that permit the absorbtion of histamine from the intestine to the bloodstream has been suggested. There are two possible mechanisms. The first is the facilitation of histamine absorbtion by short chain aliphatic amines such as Putrescine and Cadaverine which act as 'carriers' in the intestine.(5) Fig. 2a,b. The other possibility is that other diamines in the degraded fish flesh compete for the enzyme diamine oxidase (i.e. the enzyme which metabolizes histamine).(6) Fig. 2c.

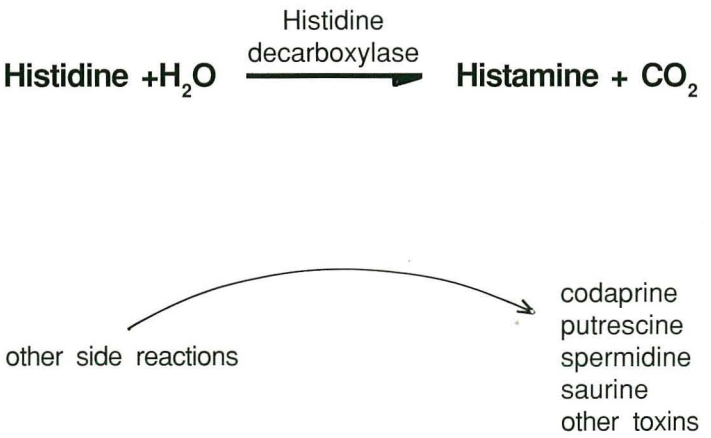


Fig. 1.

Epidemiology

This form of poisoning was originally described in Scombroid fish, but numerous other fish all over the world have been associated with this condition.(7) Dolphin fish have also been implicated.(8)

In the U.S.A. the yearly number of reported cases between 1978 and 1981 was between 30-153 involving a total of 73 outbreaks. These accounted for 5% of all reported cases of food poisoning.(7) In 1974 a large outbreak, involving 232 people was caused by canned tuna fish.(9)

Clincial features

Scombroid fish poisoning typically presents as a histamine reaction. It usually occurs in a group of people after the ingestion of the fish.

Symptoms may occur within minutes to hours of ingestion, thirty minutes on average in 27 reported outbreaks. Common symptoms are headache (44%) and flushing of the head and neck usually with a burning sensation of the mouth and throat (63%). Gastro-intestinal symptoms such as nausea (86%), abdominal cramps (71%) and diarrhoea (55%) are prominent. A bright red rash with itching or sometimes urticaria can be seen in a third of cases. In more severe cases bronchospasm and respiratory distress can occur. Tachycardia is frequently present and is sometimes accompanied by cardiac arrythmias or hypotension.

In 27 reported outbreaks, the mean duration of symptoms was 4 hours. Most cases resolved within 24 hours. There are a few sporadic reports where symptoms persisted for 3 days. No deaths have ever been recorded.(1,9,10)

Diagnosis

Diagnosis is essentially clinical. The only laboratory test is the determination of the histamine content of the affected fish. Histamine levels above 100mg/100g of fish are considered toxic.(11) As concentrations may vary from one part of the fish to another, multiple areas must be sampled.(12) Normally fish contains less than 1mg histamine per 100g of fish.(5) The Food and Drugs Administration of the United States has established that more than 50mg/100g of canned tuna is unacceptable for human consumption.(8) One must note though that histamine levels as low as 20mg/100g of fish have been associated with illness.(2)

Treatment

If no gastrointestinal symptoms are present emetics should be prescribed.

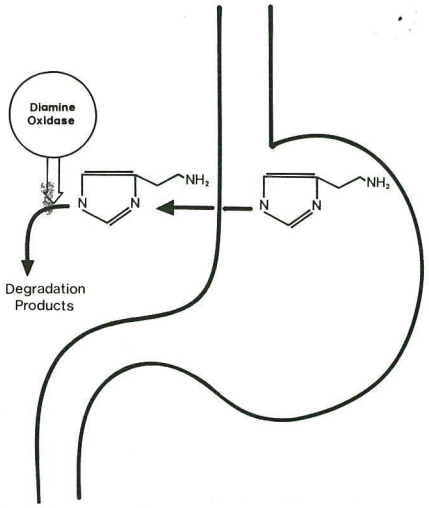


Fig 2: Normal transport and degradation of histamine by diamine oxidase

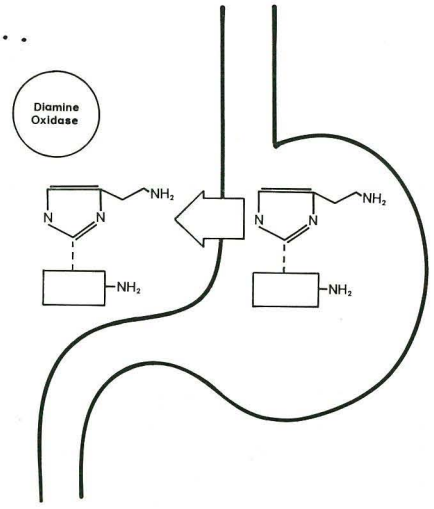


Fig. 2a: Facilitation of histamine transport by short chain aliphatic amines e.g. putresceine.

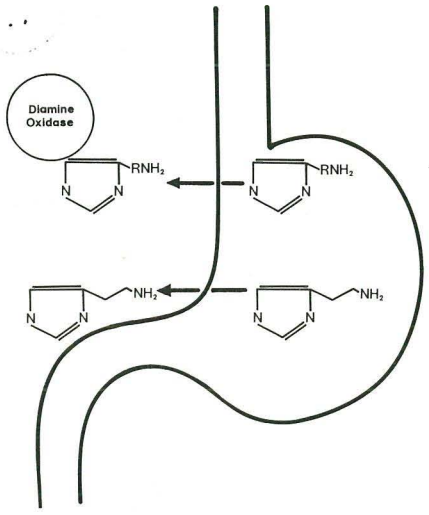


Fig. 2b: Competitive inhibition of diamine oxidase by other diamines.

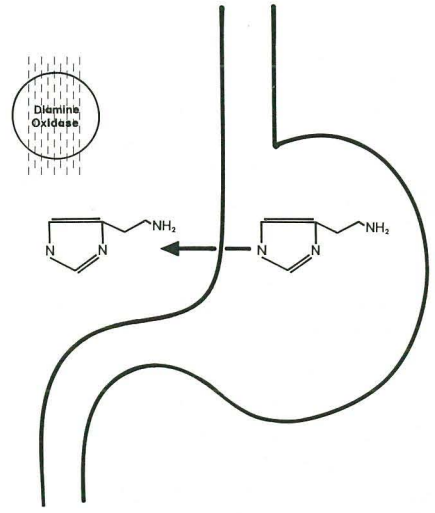


Fig. 2c: Inactivation of diamine oxidase by other inhibitors e.g. isoniazid.

The Original Power

Amoxil

amoxycillin

Prescribing Information

AMOXIL is a broad spectrum antibiotic suitable for a wide range of infections caused by susceptible organisms.

Indications
Respiratory, ear, nose and throat, genito-urinary and skin and soft tissue infections.

Dosage
Children: Oral and injectable – up to 2 years: 62.5mg–125mg every 8 hours. 2–10 years: 125mg–250mg every 8 hours. Based on bodyweight (including neonates) 35–100mg/kg/day.
Adults: Oral – 250–500mg every 8 hours. Injectable – I.M. 250–500mg every 8 hours or more frequently if necessary. I.V. 500mg–2g every 4–6 hours. (Doses in excess of 1g should be given by infusion over 30 minutes.)

Presentations
Capsules: maroon and gold capsules, each containing 250mg or 500mg amoxycillin*.
Syrup: 125mg amoxycillin* per 5ml.
Syrup Forte: 250mg amoxycillin* per 5ml.
Paediatric drops: 125mg amoxycillin* per 1.25ml in bottles with calibrated dropper.
Injection: Vials containing 250mg or 500mg amoxycillin as the sodium salt. *as the trihydrate.

Precautions
Reduced dosage is required in patients with impaired renal function.

Contra-indications Penicillin hypersensitivity.

Side-effects
Side-effects, as with other penicillins, are usually of a mild and transitory nature; they may include diarrhoea, indigestion or an occasional rash, which may be either urticarial or erythematous: in either case it is advisable to discontinue treatment.

Further information is available from

Beecham Pharmaceuticals
BRENTFORD · ENGLAND

Amoxil is a trademark.

01/2139/10/88

FIRST OF A NEW GENERATION OF MACROLIDES

RULID® 150 mg bd

roxithromycin

A TURNING POINT IN THE TREATMENT OF R.T.I.

Form and presentation: Film-coated tablets: 150 mg. Box of 10 tablets. • Pharmacological properties: Roxithromycin is a semi-synthetic macrolide. • Indications: The indications are limited in the adult patients: to infections from sensitive organisms, particularly: U.R.T.I.-L.R.T.I. - Uro-genital infections and sexually transmitted diseases, with the exception of gonococcal infections - Skin and skin structure infections. To prophylaxis of meningococcal meningitis in contact subjects. • Contra-indications: Known allergy to macrolides. Association with ergot derivatives. • Adverse reactions: Digestive: nausea, vomiting, gastralgia, diarrhoea. Allergic skin rash. Possible transient rise in ASAT/ALAT transaminases and/or alkaline phosphatases. • Precautions: In patients with hepatic insufficiency, the prescription of Rulid should be avoided. If considered necessary, hepatic function must be monitored and dosage adjusted accordingly. • Pregnancy: The safety of roxithromycin in pregnant women has not been demonstrated. However, studies in various animal species did not show any teratogenicity or foetotoxicity. • Lactation: Minute quantities of roxithromycin have been found in human breast milk. • Drug interaction: Associations contra-indicated with ergotamine-type compounds and vaso-constrictive derivatives of ergot. • Dosage: Adults: 150 mg twice daily before the morning and evening meals.

For further therapeutic information, please see data sheet or request to:
Laboratoires ROUSSEL - Interphar - 1, terrasse Bellini - Puteaux Cedex 3 - 92080 Paris La Défense - France

01-90

SURGAM®

tiaprofenic acid

Antirheumatic potency "on site"

INDICATIONS

Rheumatoid arthritis, osteo-arthritis, low back pain, musculo-skeletal disorders such as fibrositis and other soft-tissue inflammatory conditions.

DOSAGE

Adults only: 600mg daily in divided doses. Current research suggests that it is not necessary to modify the dosage of Surgam in the elderly or in cases of mild to moderate renal impairment. In severe renal impairment, it is suggested that the dosage should be reduced to 200mg twice daily.

CONTRA-INDICATIONS

Active peptic ulceration, hypersensitivity.

PRECAUTIONS

Use with care in patients with a history of peptic ulceration, severe renal or hepatic insufficiency, asthma, sensitivity to aspirin or other non-steroidal anti-inflammatory agents (NSAIs), incipient or actual congestive heart failure. Modification of dosage may be necessary in concurrent therapy with highly proteinbound drugs, e.g. anticoagulants, sulphonamides and hypoglycaemic agents. Safety in pregnancy and lactation has not been established and, in common with other NSAIs, administration during the first trimester should be avoided.

SIDE EFFECTS

Gastro-intestinal upset, headache, drowsiness and skin rash have occasionally been reported.

OVERDOSAGE

Supportive and symptomatic therapy.

COMPOSITION

Tiaprofenic acid.

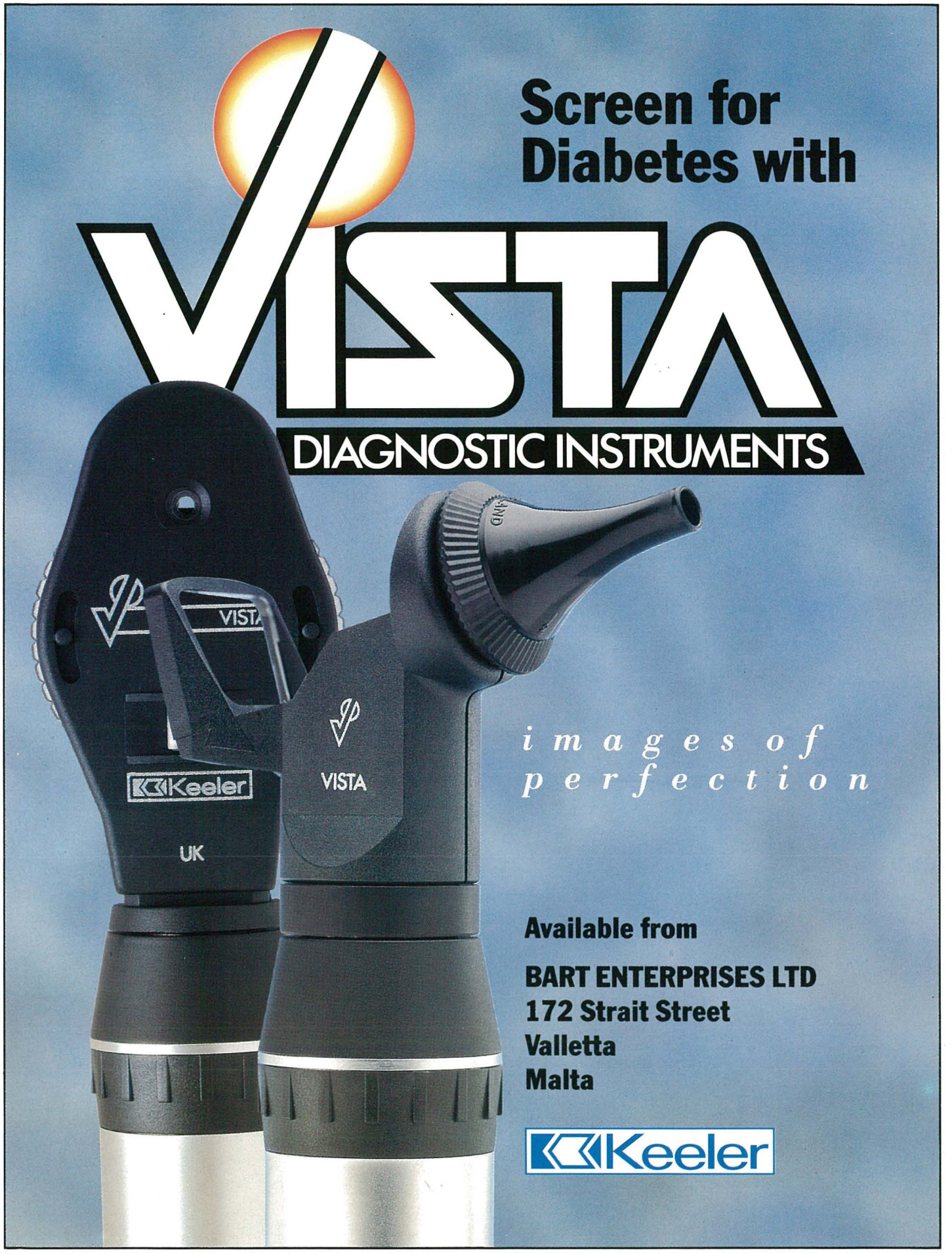
PRESENTATION

Surgam 300mg tablets.
Surgam 200mg tablets.

Further therapeutic information available on request from :

ROUSSEL

Charles de GIORGIO LTD
39-40 South Street - VALLETTA
P.O.Box 374 - MALTA
Tel.: 226346/222862


Screen for
Diabetes with
VISTA
DIAGNOSTIC INSTRUMENTS
VISTA
Keeler
UK
VISTA
images of
perfection
Available from
BART ENTERPRISES LTD
172 Strait Street
Valletta
Malta
Keeler

SCOMBROID POISONING

SYMPTOM or SIGN	40yr M	38yr F	16yr F	20yr M	18yrs F
Headache	*	*	–	–	*
Dizziness	*	*	–	–	*
Bright red rash	–	*	–	–	*
Urticaria & itching	–	*	–	–	*
Facial flushing	*	*	*	*	*
Conjunctival injection	*	*	*	–	*
Blurred vision	–	–	–	–	–
Burning sens. mouth	*	–	–	–	–
Mouth blistering	–	–	–	–	–
Tongue swelling	–	–	*	–	–
Nausea	*	–	–	*	–
Abdominal cramps	*	*	–	*	*
Diarrhoea	–	–	–	*	–
Tachycardia	*	*	–	–	*
Bronchospasm	*	–	–	–	–
Nasal obstruction	*	*	*	–	*

* *Present*

– *Absent*

Table 1. Scombroid Poisoning. Signs and symptoms in 5 patients.

Intramascular anti-histamines have been shown to reduce the duration of symptoms.(13) A recent report has claimed prompt resolution of symptoms with the intra-venous administration of the H2 histamine blocker cimetidine.(14) Respiratory symptoms due to bronchospasm may need sympathomimetics such as salbutamol by nebulizer or intra venous aminophilline.(2) Subcutaneous adrenaline and parenteral coricosteroids have also been used successfully but they should be reserved for the rare severe case.(14) All cases should be notified to the health authorities to enable the identifidation of the source so as to prevent further cases.(2) The patient should be reassured he is not allergic to fish.(2)

Public health measures

Enzymatic decarboxylation of histidine can occur readily at typical summer temperatures of around 30° Celsius.(4) Time and temperature must allow the production and accumulation of histamine for the fish to become toxic.

The general public should be advised to avoid fish showing evidence of putrefaction. Early features are skin wrinkling and 'honeycombing' of the fish flesh.(9) Affected fish sometimes have a characteristic sharp and peppery taste, but unfortunately they are usually of normal taste.

The toxin is heat stable and is not destroyed by cooking, freezing, canning or smoking.(4)

The disease is totally preventable by proper refrigeration of fish at all levels of handling.(2)

References

1. Hughes J.M., Merson MH: Fish and Shellfish Poisoning. N. Eng. J. Med. 1976; 298: 1117-1120.
2. Eastaugh J., Shepherd, S.: Infectious and toxic syndromes from fish and shellfish consumption. Arch. Int. Med. 1989; 149: 1735-1740.
3. Murray C., Hobbs, G.: Scombrotoxin and Scombrotoxin-like poisoning from canned fish. J. Hyg. 1982; 88: 215-219.
4. Arnold S.H., Brown W.D.,: Histamine toxicity from fish products. Adv. Food Res. 1978; 24: 113-154.
5. Etkind P., Wilson M.E., Gallagher K., Cournoyer, J.: Blue-fish associated Scombroid poisoning. JAMA 1987; 258: 3409-3410.
6. Parrot J.L., Nicot G.: Absorbtion de l'histamine par l'appareil digestif, in Eichler O, Farah A(eds): Handbook of experimental pharmacology. New York, Springer-Verlag NY inc, 1966, vol. 18, pp. 148-161.
7. Centres for disease control. Food-Borne Disease outbreaks: Annual summary 1982. Atlanta, Ga: Centers for disease Control; 1985.
8. Kim R.: Flushing syndrome due to Mahi-mahi (Scombroid) poisoning. Arch Dermatol. 1979; 115: 963-965.
9. Merson M.H., Baine B.W., Gangarosa E.J., Swanson R.C.: Scombroid Fish Poisoning; Outbread Traced to Commercially Canned Tuna Fish. JAMA. 1974; 228: 1268-1269.
10. Fish Poisoning. Lancet. 1979; 2: 1059-1060.
11. Simdu W., Hibiki S.: Studies on putrifaction of Acquatic products: XXIII. On the critical concentrations of poisoning for histamine, in Halstead BW, Courville DA(eds): Poisonous and Venomous Marine animals of the world. US government printing office, 1967, pp. 649-668.
12. Lerke P., Werner S., Taylor S., Gutherz I.: Scombroid poisoning: report of an outbreak. West J. Med. 1978; 129: 381-386.
13. Russell F., Maretic Z.: Scombroid poisoning mini-review tih case histories. Toxicon. 1986; 24: 967-973.
14. Dickenson G.: Scombroid fish poisoning syndrome. Ann Emerg. Med. 1982; 11: 487-489.

Eye-opening prospects for anesthetists: the advantages of

midazolam

‹Dormicum›

(Also marketed as HYPNOVEL)**

ampoules

The first 'ready-for-injection' benzodiazepine in a stable, aqueous solution:

- *for more reliable i.m. premedication*
- *for better i.v. basal sedation and anxiolysis*
- *for smooth induction and controlled duration of 'atar-analgesia'*

Components: Midazolam. *Indications and standard dosage:* Short-acting sleep-inducing agent for premedication, and induction and maintenance of anesthesia. *Intramuscular administration – Premedication before an operation:* 20–30 minutes before induction of anesthesia. Adults: 0.07–0.1 mg/kg i.m., according to age and general condition. Usual dose about 5 mg. Children 0.15–0.20 mg per kg bodyweight. *Intravenous administration – Conscious sedation:* 2.5–5 mg 5–10 minutes before the start of the operation. Further doses of 1 mg may be given as necessary. Special dosage recommendations for the induction and the maintenance of anesthesia are available on request. *Contraindications:* Hypersensitivity to benzodiazepines. *Precautions:* Elderly patients and patients with impaired cardiac and respiratory function. Early pregnancy, unless absolutely necessary. Myasthenia gravis. *Packs:* Ampoules 5 mg in 1 ml, 10's. Ampoules 15 mg in 3 ml, 5's, 25's. Full details are available on request.

ROCHE

‹Dormicum› is a Trade Mark

agents & distributors: **Cherubino Ltd.**

F. Hoffmann-La Roche Ltd, Basel, Switzerland

1989/30138 pi

HAGRET IL-GENERAL – AN ISLET WITH PAST MEDICAL LINKS

C.J. BOFFA, BCHD, BPharm, FICD, PHD

Consultant Dental Surgeon and Part-Time Lecturer
Department of Health

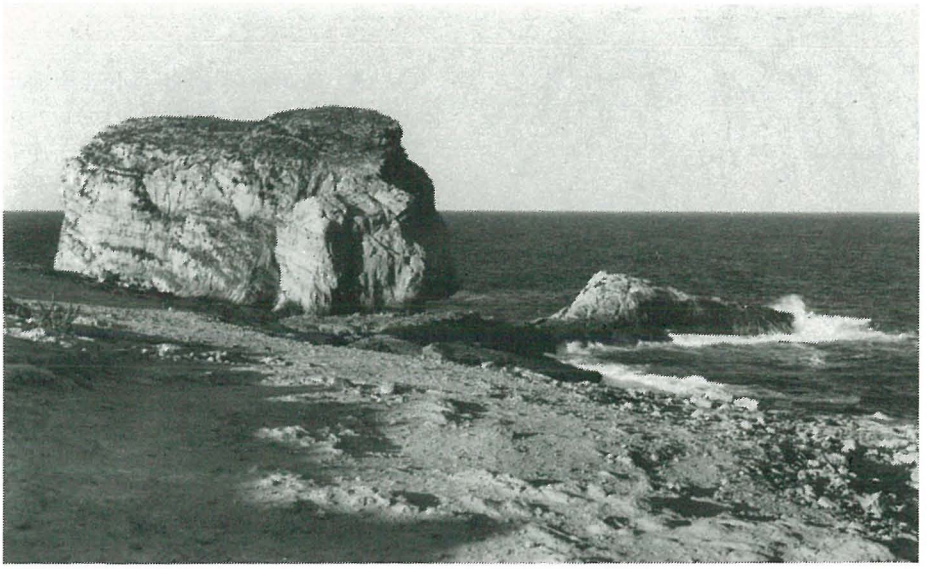
From the high ground in the locality marked on maps of Gozo as Ghajn Abdul, Ghar Ilma and Ta' Dbiegi, permeated so strongly with the ghosts of the past, one's eyes can roam over a lovely panorama. One of the topographical features that catches the eye is the massive rock known as 'Hagret il-General' or 'Hagra tal-General' subtitled 'Fungus Rock', situated at the entrance of lagoon like Dwejra. The huge rock stands out, stark and barren as it did in the days of Neolithic man so many centuries back. This locality presents a fine vista in colour and time. In the past this rock had a certain importance as it was (and still is) the habitat of a plant which was used extensively for medicinal purposes.

How wonderful is the solitude and silence in the midst of which it stands like the remains of some forgotten monument carved by nature. The rock lies off the steep western coast and at the entrance to the picturesque horseshoe-shaped bay. This is one of Gozo's major attractions and yours to enjoy. About five hundred and ninety five metres to the north of Dwejra one can admire the unique feature known as Qawra or Inland pool, connected with the open sea through a natural rocky tunnel. The effects of sea erosion can also be seen in the opening in the cliffs – one of which is shaped like a large window. Those interested in geology can study the peculiar formation of the seashore.

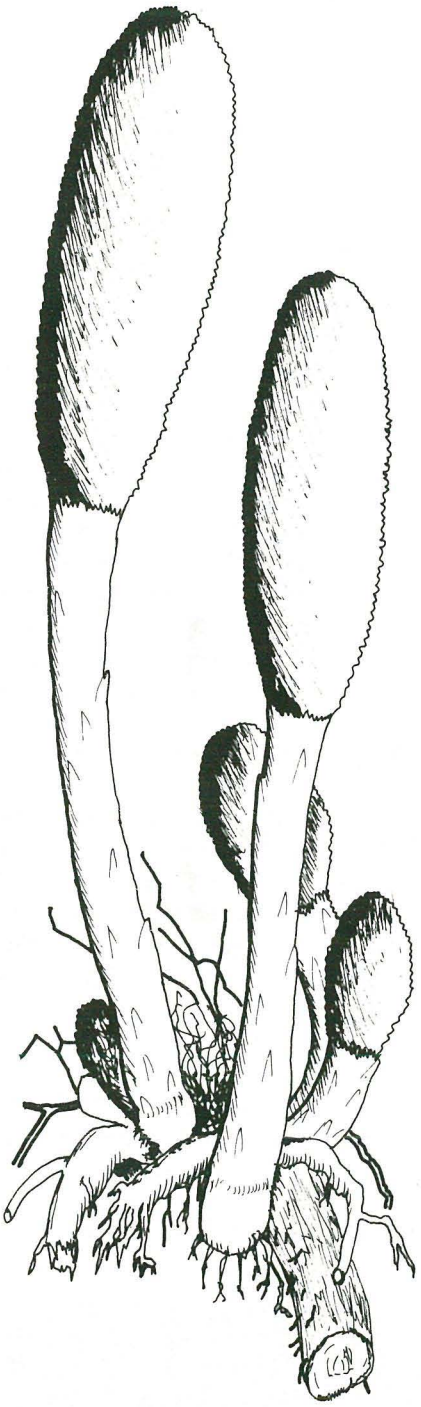
Hagret il-General has survived storms, winds and rains. Its size is deceptive. I vividly remember how surprised I was with its size. Seen from close quarters, the coastline of Hagret il-General blends with the stratification of its grey cliffs. The rock which is about one hundred and eighty metres in length and about sixty metres in height, looms high above you as you approach it on a boat. It rises gaunt and impressive from the blue Mediterranean. At sunrise and sunset, its reflection shimmers on the surface of the sea.

In 1953, I spent a few days in Gozo with other University students namely Joe Mejlaq, Salvino Scicluna, Joe Galea, John Spiteri, Tony Wood and Tommy V. Zarb. Scaling its precipitous cliffs is difficult and dangerous. Grappling irons, hooks, ropes and boots have to be used for this purpose. Our first attempt to climb up to the top was not successful. However we managed it with difficult the second time and proceeded to collect specimens of the uncommon plant *'Cynomorium Coccineum Linn'* which grows on the summit. Besides the *'Cynomorium Coccineum Linn'* we had also found twenty species of plants growing on the rock.

Subsequently I took the specimens of the plant to the University and the late Prof. H. Micallef and I analysed them. The plant resembles Eqisetum but it is variegated. It is rather succulent, slightly bitter, astringent and mucilaginous. Its rhizome is thick,



Ħaġret il-Ġeneral today. *(Photo P. Zammit)*



Gynomorium Coccineum Linn. The General's Root Artist's impression showing the halophyte (Inula) root from which the "Fungus" derives it nourishment. *(Approx. lifesize)*

tuberous and dark. On dissection its tissue and juice turns vermilion – a rather brilliant red colour. It also has a small flower which comes to seed. However it is propagated by tubers.

From June to September, the plant dries up and the rhizome remains underground. Normally it sprouts in November, flowers in March-April and is at its best by April and early May. There is nothing remarkable about its appearance and is not attractive. It generally grows to a height of about seven inches, contains mucilage and during the spring months has a rather bitter taste. On drying it resembles a garnet in colour and has a limited astringent property.

There is little wild life on the rock except a small number of sparrows, bats, lizards, worms and some plant bugs. Some birds, mainly of the aquatic type such as herring gulls and the Manx and Cory's Sherwaters live on the rock and sometimes nest on ledges and in cracks in the cliff face. During the spring and autumn migrations, more varied types such as petrels, quails, herons and warblers visit or rest here. During spring, swallows and martins are a common sight, flying gracefully or gliding low. Coral and two common species of sponges are found in deep water just off Dwejra.

On the elevated surface which looks like a sloping platform – between Dwejra and Qawra – one can find fossilised sea-shells embedded in the sedimentary rock strata and eroded limestone. These include sea urchins; small fish-like creatures and sharks' teeth (becoming rarer as many have been collected by people). How did they get there? These shells must have been deposited millions of years ago at the time when the strata were being formed and obviously this locale must have been underwater. What is also interesting is the fact that at least some of these fossils are remains of creatures now extinct. This area has also a scientific interest no less for some uncommon birds which used to be seen occasionally here earlier this century.

The history of Hagret il-General goes back a long way. Its story may be a forgotten page in the history of our Islands, but is nevertheless interesting. Hagret il-General owes its name to the fact that the *Cynomorium Coccineum Linn* was discovered by the Commander of a squadron of galleys belonging to the Order of St. John. This plant which still grows on the summit and is a living reminder of the past, has its own unusual story.

This plant which is a parasite on a species of Inula, was first spoken of as a remedy against dysentery and haemorrhages of all sorts by the celebrated Maltese physician Bonamico and named *Fucus Coccineus Melitensis* by the botanist Boccone (1874). The mode of use was as follows: the Root was dried and pulverised and of the powder 30 to 40- grains were suspended in wine syrup of Quince jelly. Sometimes the dry powder was sprinkled on bleeding wounds after suturing.

It is difficult for us today to understand the strong beliefs by rulers and people alike in bygone days, regarding the supposed potency of this herb. It was considered of great value and was regarded as a remedy against haemorrhage, dysentery and certain stomach complaints. It is surmised that during the Great Siege, Grandmaster La Valette had a wound in his leg staunched (possibly with a view to decrease haemorrhage as it does have a limited astringent property) by means of this plant. According to tradition, it was also used sometimes by surgeons with a view to decrease bleeding following certain injuries, amputations and extraction of carious teeth. How much this helped, we cannot say. It was also claimed to be beneficial in the treatment of ulcers and gingivitis.

In the interesting book 'Malta Illustrata' (1772), G.F. Abela and G. Ciantar mention that it was given to patients (possibly tuberculous) who spat blood. Strangely enough it was also considered useful in the treatment of syphilitic diseases.

The more colloquial title 'Fungus Rock' comes from the plant that still grows there and was the reason why the Knights treasured it so highly. Furthermore it was believed that this plant flourished only on the rock. Earlier this century it was also found to exist in a few spots on the inaccessible cliffs at Dingli and Ta' Cenc. The name 'Maltese fungus' is a misnomer for it is not a fungus and it is not, as it was firmly believed in the past, peculiar to our Islands. It has also been found in Lampedusa, Sicily and North Africa.

Throughout the centuries, the plant has been referred to in Maltese as 'Gherq il-General', 'Gherq is-Sinjur', 'Fungu Ghawdxi', etc. Its importance today lies in its historical associations and not in its therapeutic properties, which in the light of modern science are non-existent.

One of the first writers to mention it was Comm. G.F. Abela. He referred to it as *"un herba che tira al vermiglio non dissimile nel di fuori, ed quanto alla forma, ha i finocchi marini"*. He recorded that the plant was dried, powdered and drunk to relieve dysentery.

The Knights of St John had a high opinion of its efficacy. It is recorded in the archives of the Order that various Grandmasters used to send it as a gift to Kings, nobles, relatives and other personalities in Europe.

Hagret il-General has seen few human beings on its summit, since the expulsion of the Knights form our Islands, when the guards were withdrawn.The Grandmasters had done their best to guard the rock and the plant. In 1744, Grandmaster Pinto ordered that the sides of the Rock were to be smoothed to render access to it more difficult. Anybody caught collecting the plant was liable to be condemned to the galleys – a harsh penalty indeed.

An old painting at the Museum depicts an unusual means of transit which has long disappeared - a sort of basket suspended on ropes stretched between the rock and the mainland. The holes where the ropes, about sixtyseven metres long, were tied to the rock face, still exist. A small chamber which was excavated on the rock probably served as a shelter or a storage room for the men who were employed in 1746 to guard the rock. Its wall niches are still blackened by the lamps or candles used at some time in the past. Some steps in the rock surface can also be seen.

DeSoldanis, while mentioning Qala Dwejra, records the existence of a cave which was excavated on the initiative of Grandmaster Pinto to house the guards. However, one cannot be sure whether he was referring to this small chamber or to the other small rock cave facing Hagret il-General and not far from Dwejra Tower.

The following proclamation by Captain A. Ball, R.N., the first Civil Commissioner in 1800, clearly shows the value in which this plant was still held in those days and obviously was still being used to some extent in medicine and surgery:-

"Si priobisce a tutti di raccogliere il Fungus Melitensis. Avendo a caro Sua Eccellenza, che i luoghi produttivi le radici comunemente dette Fungus Melitensis, ossia Ghirch Signur (Gherq Sinjur) si erano mantenuti, ed illesi, come si mantenevano nell'antico governo, ha percio' proibito a qualunque persona di qualunque stato, condizione di non ardire di raccogliere dette radici senza li permesso di Sua Eccellenza, o del suo Segretario" Barone F. Gauci, Capitano di Verga.

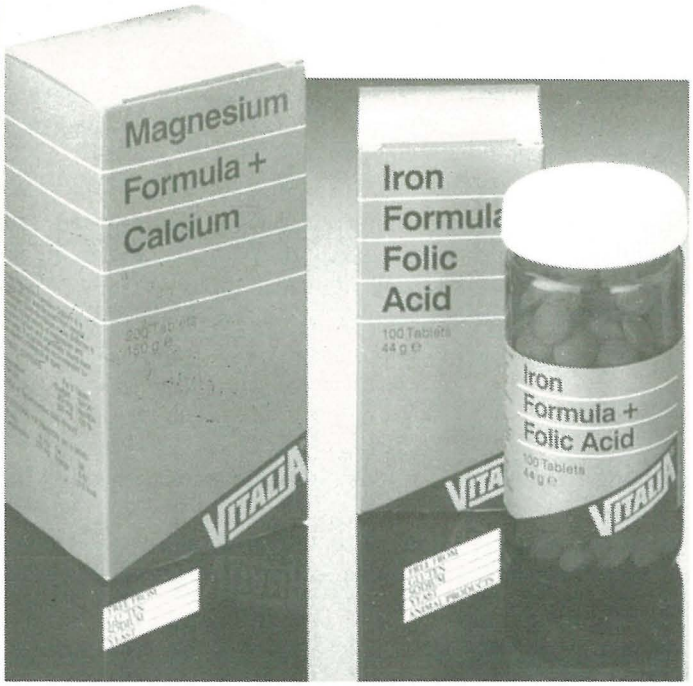
Hagret il-General is quiet and remote. The peace reigning here is well nigh incredible and one finds a solitude for reflection beyond all time and change. Only the throb of an occasional boat's engine may disturb the silence. In the heat of midday during spring and summer, the human intruder may feel lulled into drowsiness by bursts of song from the blue rock-thrush and by the gentle lapping of wavelets against time pitted rocks.

Sometimes the froth from the dark blue sea, froth that would do credit to any soap powder, breaks in excited dashes against the rocks, adding more colour to this beautiful locality.

In the hour before sunset, this area is transformed by the rose light into unreality. For a while the arid landscape with its ancient watch tower and chapel, the crisscross of the remains of old stone walls, the huddled flat-roofed rooms adjoining Qawra and the whole unbleached nearly shadeless landscape take on a pink radiance. Then the colour deepens and the violet shadows give outline and form while the light lasts. Like many others, I find the locality of Dwejra and Hagret il-General one of Gozo's major attractions.

References

1. Abela, G.F. and Ciantar G.: Malta Illustrata, 1772.
2. De Boisgelin, L.: Ancient and Modern Malta, Vol. I, 1805, p 73.
3. Lacroix, P.: Malta and Gozo, 1806-1884, p.62.
4. Caruana Gatto, A.: The Fungus Melitensis, 1892.



Magnesium Formula + Calcium (Dolomite)

Every body cell needs Magnesium for growth and good health and it is thought that many of life's functions depend on a sufficiency of this vital trace element.
Calcium is necessary for maintaining healthy bones in people of all ages. Vitalia's tablets are produced using extracts from special Norwegian Dolomite rock. It is one of nature's richest sources of Magnesium and also contains Calcium.

TABLET CONTENTS PER 6 TABLETS

Magnesium	362 mg
Calcium	600 mg

Iron Formula+Folic Acid

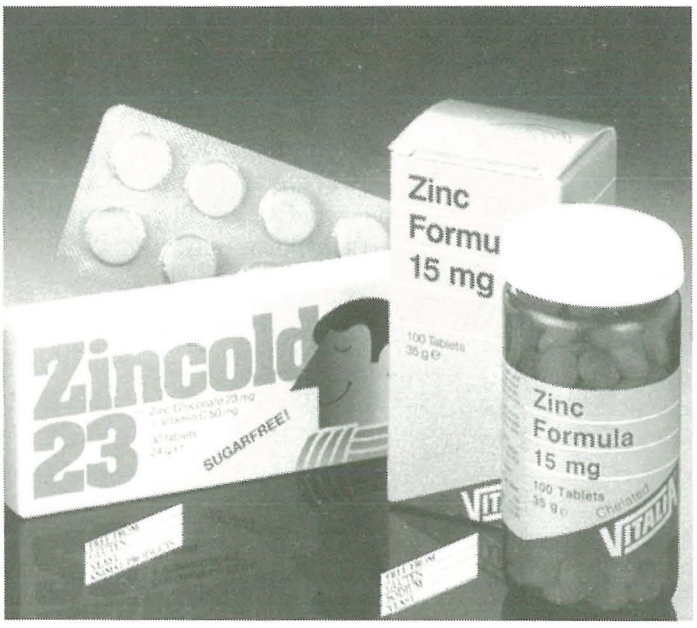
Iron is essential to help the body build and repair vital tissues and plays a vital role in maintaining a healthy bloodstream.
The added Folic Acid is essential for the formulation of Iron containing proteins including haemoglobin, which is necessary for the formation of red blood cells.

TABLET CONTENTS

Iron	66 mg
Folic Acid	100 mcg

VITALIA®

GALEA & GALEA ENTERPRISES LTD.
William Savona Str. San Ġwann.
Tel: 337928 - 472120



Zincold 23

Zincold 23, which combines Zinc and Vitamin C, is a remarkable product, and a valuable food supplement, especially in the cold winter months.
Government-funded trials have shown that it can help reduce some of the symptoms of colds.
The tablets contain Zinc Gluconate, which coats the membranes of the mouth and throat with Zinc ions before being swallowed.
Both Vitamin C and Zinc are essential for growth and good health.
The tablets have a refreshing peppermint taste, but are sugar free, and both the Zinc and Vitamin C are supplied in such a way as to be gentle on the stomach.
One tablet should be sucked every two hours for optimum protection.

TABLET CONTENTS

Vitamin C	50 mg
Zinc	3 mg
Zinc 3 mg (derived from 23 mg of Zinc Gluconate)	

Zinc Formula 15mg (Chelated)

Zinc is an essential trace element necessary for growth and health and normal sexual functioning, and our bodies need small but regular amounts every day. Over-processing of food, intensive farming of land and convenience foods reduce the amount of natural Zinc available in our diet.
Besides people who want to ensure an adequate intake, many women on the contraceptive pill, pregnant women (on doctor's advice) and nursing mothers, like to take a Zinc supplement. The formula contains Zinc which has been chelated for efficient absorption.

TABLET CONTENTS

Zinc	15 mg
Zinc 15 mg (derived from 150 mg of the Chelate)	

VITALIA®

GALEA & GALEA ENTERPRISES LTD.
William Savona Str. San Ġwann.
Tel: 337928 - 472120

ALCOHOLISM – What every doctor should know

PROF. A. GALEA M.D. F.R.C.P. (Ed.), D.P.M., F.R.C. Psych.

Head of Dept. of Psychiatry Physician Superintendant
Mount Carmel Hospital

MEDICAL LIBRARY
MEDICAL SCHOOL
G'MANGIA MALTA

The general practitioner (or the doctor at the Casualty Department) has assumed the single most important role in our fight against one of the most devastating diseases of our time – alcoholism. It has now been accepted that the most useful role for doctors at present are, first to detect the many heavy drinkers passing through our hands at an early a stage as possible, and then to provide brief interventions designed to persuade them to drink less, and second to do what we can to help change the drinking habits of the population as a whole, a task which may involve changes in our own behaviour (Kendall R.E. (3)).

Alcoholism means so many things to different people – weakness in character to the man in the street, a vice to the moralist, a personality deficit to a psychologist, a social problem to a sociologist and a sin to a clergyman (Glatt, M. (2)). In the end however it becomes a medico-social problem and the province of the doctor. One may add that our attitude changes from one circumstance to the other – a girl who gets drunk at a party elicits our disgust, a father who spends too much on drink our condemnation, a man who drives under the influence our censure, a drunkard who beats his wife our blame, an intoxicated guest who tells dirty jokes our attention but when the excessive drinker becomes an alcoholic we all agree that he requires medical treatment.

Who is an Alcoholic?

Like the proverbial elephant it seems no one can define an alcoholic but everybody recognises one when he sees him. This is the greatest block to diagnosis. The *"faccia di pulcinello"*, the spider naevi, the palmar flush and the bloated belly are rarities confined to the 'skidrow' stereotype. An alcoholic may in fact be working with you, sitting next to you in a stadium, talking to you in a party, a member of your family. Alcoholism is not an "either-or" entity like pregnancy (you either have it or you don't) but it is a matter of "more or less" like heart disease which starts insidiously but progresses relentlessly. A young doctor must keep in mind the presence of alcoholism in many varieties of patients – an alcoholic may present at the Casualty Department demanding something for his nerves or his stomach, a certificate for sick leave, a minor accident – or the greatest surprise of all - the alcoholic may be a woman.

The greatest lesson of all : don't rely on how the patient looks, nor listen to what the patient says but enquire what the patient does!

What Alcoholics Do

An alcoholic drinks excessively but it is not the excess that forms the hallmark of the disease (the alcoholic starts getting drunk on less and less drinks as tolerance wanes) but the pattern. He drinks not just for pleasure but because he must. He drinks every day, every morning and perhaps alone to avoid withdrawal (sweating and shaking). He is obsessed with drink so that he sneaks drinks and adopts strategies to get more drink and in the end he feels guilty about it. At this stage (prodromal stage), intervention by the family doctor would save the patient from eventual destruction.

The start of the "road of no return" begins with the patient getting "black outs" (forgetting complicated tasks he did the night before, surprised when told about them but recalls them on further drink). The alcoholic has characteristically lost his control on drinking so that "the person with alcoholism cannot consistently predict on any drinking occasion the duration of the episode or the quantity that will be consumed" (W.H.O.). He loses interest in his family, absents himself from his job and becomes a menace on the road. He feels guilty about the condition he finds himself in but he drinks further to drown his sorrows.

The chronic stage is reached when there are physical and mental complications. He loses his job, beats his wife, becomes impotent and blames his partner and soon he is in delirium tremens if he stops drinking (e.g. admitted to hospital for a medical or surgical condition) or dementing

in various ways (Wernicke-Korsakov).

His liver shows various stages of the cirrhotic process and his heart, pancreas and nervous system produce the classical clinical picture of alcoholism.

Catching the Alcoholic in Time

The doctor in his clinic or at the Casualty Department (the trenchline of our profession) should remember "the forgotten illness" and must know how to ask relevant questions.

GUIDELINES FOR SELECTION

(a) *"HIGH RISK GROUPS"*

Certain walks of life (*occupational hazards*):
- catering trades,
- travelling salesmen,
- entertainers,
- seamen,
- hard pressed executives,
- businessmen.

(b) *PHYSICAL CLUES*

Gastro-Intestinal: Vomiting, nausea, dysphagia, vague abdominal pains, diarrhoea.

Neurological: headache, in-somnia, 'black out'.

Cardiovascular System: palpitations.

Traumatic: frequent accidents, falls or injuries, cigarette burns.

(c) *PSYCHOLOGICAL CLUES*

Behavioural: frequent financial difficulties, excessive absenteeism from work, poor performance, marital difficulties, immoderate use of coffee, tobacco, tea.

Emotional: Anxiety, panic attacks, hallucinations, depression, suicidal attempts

TABLE 1

He must be aware of the "high risk group" and how they present themselves. (Table One). Doctors easily associate dementias and liver disease with alcoholism but its relationship with pancreatitis, hypertension, cancer, heart disease, infertility, infections, accidental and self inflicted injury and the foetal-alcohol syndrome are less well known.

Alcoholism is a disease and behaves like any other physical disease with its own aetiology, signs and symptoms, prognosis and treatment and must therefore get the medical response it deserves.

Alcoholism has a genetic component (risk factor) and the family of the alcoholic (especially the children) should not escape the terms of reference of the caring physician.

Alcoholism is not the monopoly of the lower social strata (the milk of the poor) but the signpost of affluence because as wages rise higher and higher, alcohol becomes relatively cheaper and with more and more availability the problem drinkers multiply. Alcoholism is not only a medical disease but it is also a social disease and as social problems create a craving for alcohol, alcohol in turn compounds social problems so that alcoholism must not be tackled on the medical model alone but rather on the medico-social model. The alcoholic must be saved from himself and the company he keeps but must also be helped in his confrontation with the employer, the creditors and sometimes the police. No challenge greater than this has ever faced a doctor devoted to the physical, psychological and social well being of his patient.

The practitioner should know how to ask questions relating to alcohol and for this purpose many questionnaires exist which are all highly suitable. I would recommend the CAGE questionnaire. (Table Two).

The *CAGE* Questionnaire

(1) Have you ever tried to *C*ut down on drinking?
Was it difficult?
How was it done?
Why did you start drinking again?

(2) Have you ever been *A*nnoyed about criticism?
Who criticised you?
Why was your drinking criticised?
Was the criticism justified?

(3) Have you ever felt *G*uilty about your drinking?
What caused the guilt?
Does your behaviour change when you are drinking?
Have your ever resolved not to drink as a consequence of your behaviour?

(4) Have you ever had a morning *E*ye-opener?
Do you drink in the morning in order to make it through the day?

Since 18: any fracture or dislocation? injuries in road accidents? injuries from fights? head injuries?

TABLE 2

Management of the Patient

Once the suspicion and the confirmation of "excessive drinking" have been sustained, the doctor should assess whether this is simply "excessive" drinking becoming too frequent or the patient is already an "alcoholic". It must be remembered that excessive drinking at any time is a dangerous proposition in this age of the motor car. If the patient is in the first category then the doctor must determine whether there are any precipitating factors like psychological or social difficulties (which must be tackled) or whether the "habit is turning into a vice". The simple advice is a warning and simple directives: The patient must stick to a routine of no more than 21 units a

week (1 unit = 1 whisky, 1 beer, 1 glass of wine or equivalent) with two alcohol free days a week in between. For women the allowance is 14 units. If the patient is a "prodromal" alcoholic (i.e. there are no signs of damage to the liver or the central nervous system which must be looked after by a physician) then one proceeds on different lines.

First he must be challenged to assure him that he has lost control over his drinking (in spite of his resolutions) and that he cannot give up his drinking alone. You challenge him that for the next three to four weeks he must continue to attend the bars, meet the same friends and keep the same hours as he is doing at the moment. Nothing is to change but he must restrict his drinking to not more than three drinks each time. An alcoholic will not stand it, he may give up drinking altogether for weeks (on the wagon) but relapse is inevitable.

The next time around, shameful in defeat or grinning with Dutch courage you react by assuring him that you accept him and will do your best for him. Do not give him any Valium or refer him to a psychiatrist or to the Alcoholics Anonymous (A.A.). These agencies are no better than you are and in so doing you lose the patient.

You explain and emphasise all the possible consequences of heavy drinking – not only dementia and cirrhosis but also impotence and injuries. This is part of the educational process so that the patient may in fact start assuming responsibility for his actions. As a sign of good faith he must start getting off alcohol ALTOGETHER – this is simpler than cutting down – and to report immediately any withdrawal symptoms; like confusional state or hallucinations. He must also avoid attending bars, eating out or going to parties. His wife may not like such seclusion from social life but probably she has already been cut off for a long time; either because he prefers other venues where he can do anything without censure or because she has refused to be made a laughing stock or a fool in public (or scared of driving with him). Furthermore she must be implicated in treatment - praising him when he does not "fall", supporting him when he does.

Then he must be put on the road to recovery which entails four milestones - the first is that he must have a constant reminder that he must not drink. A nagging wife or a peptic ulcer are not prerequisites but the patient must tell everybody around that he is dry and say "no thank you, I don't drink". The second milestone is to tolerate a "vice-vice substitution" which means he is allowed to drink frequent coffees or teas or simply water (better than cigarettes or fatty foods). The third milestone is the enhancement of self esteem by being encouraged and praised (and accepted by the wife!) and the final and most difficult is the improvement of social fabric which means new friends, new activities and new commitments. The wife must be warned that she must now share decisions and tolerate him around.

An alcoholic who is dry should never be allowed to revert to a "social drinker" but only to a total ban on alcohol. The chances of success are not high but in any case worth the time the doctor can afford. What he is actually doing is investing in a change of life style for his patient which is much more than is expected from him.

LEVELS OF PREVENTION

PRIMARY PREVENTION

(a) Policies regulating terms of commercial availability:
Taxation, Licensing hours,
Age limit on alcohol sales,
Limits of alcohol sold, reduction in outlets (bars, restaurants)

(b) Policies that seek to influence drinking practices:
Law and education

(c) Policies designed to render the external environment less hostile:
sale structure, safe machinery, traffic control, road signs, emergency services

SECONDARY PREVENTION

The medical and paramedical staff should be aware of the problems of alcoholism and be equipped for early detection.

TERTIARY PREVENTION

Hospitals, Outpatient Departments, Rehabilitation Units
Day Units, Alcoholics Anonymous

TABLE 3

On the same lines the medical doctor should support any measures or policies listed in Table Three in the Primary prevention of alcoholism and should be in the forefront in Secondary prevention. The doctor is being invited not only to "cure diseases" (which he rarely does) but to participate in changing life styles for his co-citizens. In the case of alcoholism, brief counselling sessions by General Practitioners often succeed in preventing "heavy drinkers" drifting into "problem drinkers" which is highly satisfying and cost effective.

There is no statistical evidence of any significant difference between inpatient or outpatient care and simple advice (Valliant G. (5))

References

1. Deblanco, T.L. Salzburg Seminar "The CAGE Questioner in Abuse of Alcohol: Strategies towards control" Session 248 Feb 1986.
2. Glatt M. "Alcoholism - A Social Disease" Teach Yourself Books 1975.
3. Kendall R.E. 1989 Proceedings of the Royal College of Physicians of Edinburgh 19.3, 283-284.
4. Kessell N. and Halton H. Alcoholism Pelican Books.
5. Valliant G. Salzburg Seminar (ibid).

LETTER TO THE EDITOR:
MEDICAL DOCUMENTALISTS IN MALTA

What are German Medical Documentation students doing in Malta?

We are three students, spending eleven weeks of practical training at the Health Services Information Unit (HSIU). An article in the last issue of this journal gave an overview of the tasks and the objectives of the unit.

In order to give you an idea of what we are doing here, we would like to provide some information about our profession in Germany.

Due to social developments and progress in medical research, the public health system has been faced with completely new tasks. Chronic diseases, geriatric diseases, multimorbidity and non-specific diseases have markedly increased. In addition, specialisation and the improved accuracy of diagnostic methods generate a greater amount of data than in former times. Nowadays, a patient is usually treated by more than one physician. Thus, the importance of information exchange amongst the attending doctors is growing. Moreover, the early detection and prevention of non-communicable as well as infectious illnesses raise new problems in the field of medical documentation, because a lot of data has to be stored and evaluated, mostly by computer. Today it has become impossible for a physician to fulfil the tasks of documentation and information processing in addition to his/her medical work.

Therefore a new profession has been created: Medical Documentalists.

Medical Documentalists are mediators between doctors and computers, and help the medical practitioners in the collection and processing of information.

Further important tasks are:

- making the medical experience stored in medical records accessible
- the implementation of electronic data processing (EDP) in medicine
- documentary and statistical supervision of therapeutic studies and their evaluation, testing of new drugs
- the retrieval and indexing of literature.

To fulfil these tasks our curriculum includes topics like medicine, documentation and occupational information. We learn programming in two languages, PASCAL and FORTRAN. The statistical field is also very important for us and we are taught descriptive and vital statistics.

As a result of the wide range of topics covered by our training, medical documentalists are employed by hospitals, pharmaceutical industries, university and research facilities for medical documentation, computer science and statistics, medical libraries, literature services and other institutions that could be compared with HSIU.

Thus, what are medical documentalists doing here?

Firstly we were given an overview of the hospital, its facilities and the special situation of Malta as a small island in the field of medical documentation.

After becoming acquainted with the different running projects of the unit, we took part mainly in statistical applications. We helped in the analysis of data regarding a smoking survey that had been carried out among doctors. Another task was to assist the local workers with quality assessment as well as in the analysis of the eye disease survey. Besides, we were involved in the planning for the mid-point survey of the MONICA-Project by selecting a random sample of the Maltese population for a pilot-study.

Some smaller tasks included writing a Mumps programme for a reliability-calculation, aiding with coding of underlying cause of death (ICD-9), data checking and so forth.

To conclude, the practical experience was helpful to our training and we are glad that we could have an insight into the problems and challenges a small country is faced with in this very important field of medical science.

Elisabeth Kellner
Ulrike Bay
Elke Kosler

Potential new contraceptive?

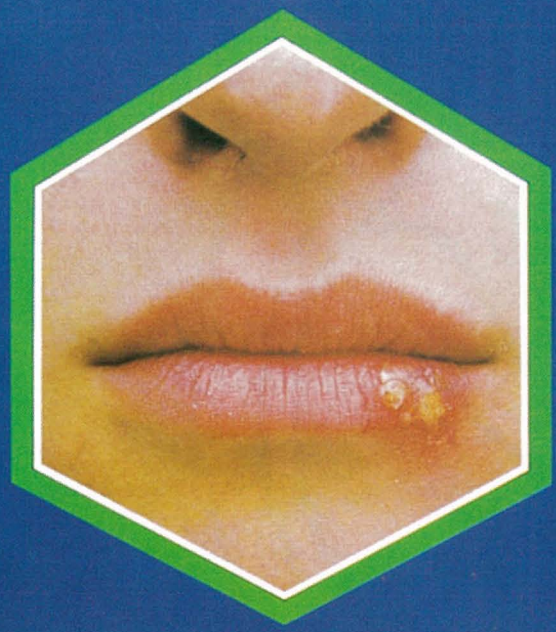
Novel ways of keeping us out of the family way know no bounds, according to a conference report published in the *General Practitioner.*

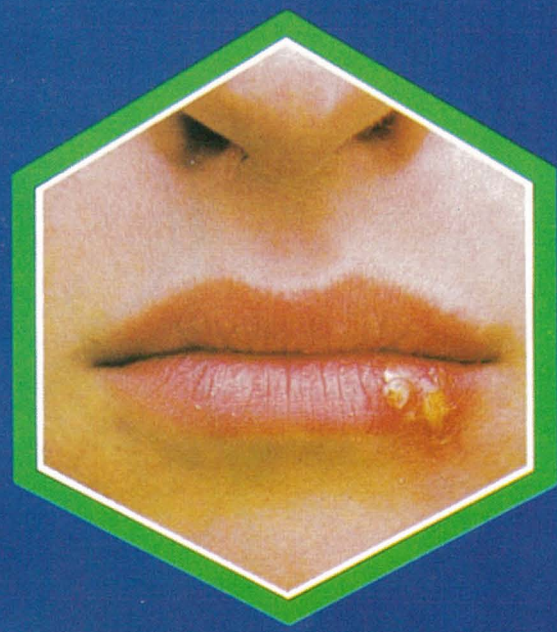
Tests on baboons in the USA have apparently shown that sperms can be immobilised and even electrocuted by means of a 'battery device' surgically inserted in the female cervix. The report, I hasten to add, emphasises that satisfactory results, i.e. no little baboons, were achieved by means of a low current that caused no discomfort to the animals (male, I hope, as well as female).

Dr Stephen Kaali, director of the Women's Medical Pavilion in Dobbs Ferry, NY, who developed the idea, reckons, however, that it will be many years before women can switch themselves on or off to order. A major problem, for example, is that of ensuring bio-compatibility, i.e. preventing rejection or some nasty interaction with body fluids.

Also, how could you ever face the prospect of telling your family that they owed their existence to a dud PP3?

FOR RECURRENT HERPES LABIALIS





"THE FIRST TRULY SPECIFIC ANTI-HERPES AGENT, ..."[1]

FOR ALL YOUR PATIENTS WHO SUFFER FROM COLD SORES

A SIMPLE REGIMEN

Zovirax Cream should be applied to the affected area five times daily. Start as early as possible in an attack.

Local Agents: GEORGE BORG LIMITED

Address: 26/2 Merchants Street, Valletta, P.O. Box 334, Valletta, Telephone 225441/2.

Wellcome

Helping you and baby to better health

Uses: For the prevention and treatment of ***iron*** and ***folic acid*** deficiencies and to improve overall nutritional health throughout pregnancy and during breast feeding period.

Advantages: PREGNATAL contains ***vitamin C*** and ***copper*** for optimal iron uptake and utilisation. It provides all essential and appropriate nutrients incl. adequate levels of ***zinc***, a nutrient now considered particularly important in pregnancy.

Dosage: ***Adults only: Prophylactic during pregnancy:*** Usually 1 tablet daily, during or after meals. Not to be given to children. Some pregnant women may need a higher prophylactic dose, especially during the last four months of pregnancy, when so prescribed by a doctor.

Scanpharm A/S
Healthcare Products
Copenhagen, Denmark.

Composition:	Each tablet contains:	High dose (2 tablets daily) provides:**
Nicotinamide BP	10 mg	100 %
Calcium pantothenate BP	2.5 mg	50 %
Vitamin C BP	45 mg	150 %
Vitamin E BP	15 i.u.	100 %
Copper	1 mg	100 %
Magnesium	50 mg	22 %
Magnesium	0.25 mg	-*
Potassium	0.75 mg	-*
Iodine	75 mcg	100 %
Zinc	7.5 mg	100 %
Iron (Fe) (present as 200 mg Ferrous fumarate BP)	65 mg	722 %
Folic acid BP	0.5 mg	125 %
Calcium (present as 325 mg Calcium carbonate BP)	130 mg	20 %
Vitamin A BP	3,000 i.u.	75 %
Vitamin D BP	200 i.u.	100 %
Vitamin B 1 BP	1.5 mg	176 %
Vitamin B 2 BP	1.5 mg	150 %
Vitamin B 6 BP	2.5 mg	200 %
Vitamin B 12 BP	4 mcg	100 %

** % of U.S. Recommended Daily Allowance (U.S. RDA) for Pregnant or Lactating Women.
* No U.S. RDA has been established for this nutrient.

PHARMASUD LIMITED 'ZERNIQ' TRIQ IS-SEQER, ST. JULIANS TEL: 316882

DELAYING AN UNTIMELY DELIVERY

MARK FORMOSA MD MRCOG

Registrar Department of Obstetrics and Gynaecology, St Luke's Hospital, Malta.

Preterm labour is defined as the onset of labour before 259 days of gestation or 37 completed weeks.

When diagnosing a case of preterm labour, problems arise because of the difficulty in defining established labour. Labour is usually heralded by the onset of regular uterine contractions which produce effective cervical dilatation. Premature births account for a large fraction of perinatal mortality and morbidity. Despite major advances in neonatal care, retention of the foetus in utero is preferred in most instances.

It is often difficult to determine if premature birth is imminent, and 50% or more of patients who present with regular contractions will respond to simple bed rest. If this fails, a tocolytic may be administered. The desire to prolong intrauterine development must be balanced against the risks of continuing the pregnancy, for both the mother and the foetus. One must also consider the risks of pharmacological intervention in the particular patient.

In general, the use of tocolytic agents is reserved for those pregnancies where the gestational age is greater than 20 and less than 34 weeks. At more advanced gestational ages definite evidence of foetal immaturity should be sought. When the decision to use a tocolytic agent is taken, therapeutic success is most likely if cervical dilatation is less than 4 cm and cervical effacement less than 80%. Opinion varies as to whether tocolysis should be attempted in the presence of ruptured membranes. In cases of P.R.O.M. (premature rupture of membrances) however, the greatest risk to the neonate is the prematurity rather than infection.

Definite contra-indications include eclampsia or sever pre-eclampsia, premature detachment of the placenta, foetal distress and overt chorio-amnionitis.

Various drugs have been used in order to suppress uterine contractions including intravenous ethanol. However, since it was shown that uterine relaxation is a sympathetic β_2 receptor function, pharmacological manipulation of the synaptic junction has been successfully attempted.

β_2 Adrenergic Agonists

These agents are preferred for the treatment of premature labour. Currently, only ritodrine is approved for this purpose in the USA. Ritodrine hydrochloide is available in a solution (10mg/ml) for I.V. administration and in 10mg tablet preparations. Treatment is initiated by the intravenous infusion of a solution of ritodrine (0.3mg/ml) at the rate of 0.1mg per minute. If tolerated, the dose is gradually increased (0.05mg per min. every 10 mins.) to a maximum of 0.35mg per min. or until labour is controlled. Once contractions cease, the infusion is usually continued for 12 hours at the rate attained. Oral therapy is begun 30 minutes before termination of the infusion by the administration of 10mg every 2 hours for the first 24 hours, followed by 10mg to 20mg every 4 to 6 hours. The total daily dose should not exceed 120mg. A number of other selective β_2 adrenergic agonists have been used in preterm labour, and include salbutamol, terbutaline, fenoterol and orciprenaline.

No tissue in the body is either strictly β_1 to β_2, but the relative receptor concentrations vary in the various organs. Selective beta-agonist therapy is therefore associated with both β_1 and β_2 side-effects, of which probably the most important are the cardiac side-effects. The pulse rate of the patient is the usual dose-limiting side-effect of treatment.

With β_2-agonist use in preterm labour there is a consistent rise in cardiac output, which reaches its highest value at 40 minutes from the initiation of therapy (56% over the control). To this, one must remember that the cardiac output naturally rises in normal pregnancies, reaching the highest value by the first trimester. This rise is mostly due to a rise in the stroke volume as opposed to the increase in pulse rate mediated by β-agonists.

The systolic blood pressure rises by about 12% during treatment with β-agonists while the diastolic pressure is decreased by about 10%. The result is a raised pulse pressure while the mean arterial blood pressure remains stable.

There are a number of situations where it is **considered unwise** to use β-agonists in the management of preterm labour:

1. Hyperthyroidism is considered to be a hyper-beta-adrenergic activity state. Theoretically a patient with this disease could be pushed into thyroid storm.
2. The patient with insulin-dependent diabetes mellitus; the risks to the patient with non-insulin dependent diabetes mellitus are far less.

3. The asthmatic who is already on β-agonists; because their beneficial bronchodilating effects they may be at risk of a paradoxical response from excess adrenergic stimulation.
4. The patient who has congenital or chronic heart disease.
5. The hypertensive patient.
6. Monoamine oxidase inhibitors will modify the dosage of β-agonists used for uterine relaxation.
7. Chronic medical disease may result in placental insufficiency thereby contra-indicating prolongation of the pregnancy.

Maternal Side Effects

Many patients experience nausea and vomiting which may be central or secondary to an effect on the gastrointestinal tract (decreased motility). Other phenomena reported are allergic dermatits, effects on the bladder detrusor reflex, and thrombocytopoenia secondary to the effect on platelet adenylate cyclase activity. With use, β-agonists cause a decrease in the number of β-adrenergic receptor sites leading to tachaphylaxis.

The most dramatic **complications** of β-agonist therapy in the suppression of preterm labour which have been reported are pulmonary oedema (even fatal and especially associated with the use of fenoterol) and hyperglycemia which may lead to diabetic ketoacidosis.

Pulmonary oedema has been reported from single case reports and were associated with sudden stopping of the drug postpartum without the appropriate weaning the with concurrent use of corticosteroids. At least two maternal deaths have been reported. One had an underlying viral myocarditis and the other congenital Dardiomyopathy. Patients with pulmonary hypertension or obstruction to the left ventricular outflow, such as with hypertrophic subaortic stenosis, could be at particular risk as the cardiac output increases. The use of electrocardiograms in pregnant women about to be embarked on β-agonist therapy is strongly recommended in an effort to identify those at risk. Furthermore, total fluid intake should be restricted to less than 2 litres over 24 hours as overhydration will increase the chances of pulmonary oedema.

β-agonists cause hypergycaemia by phosphorylation of liver glycogenolytic enzymes and cause hyperinsulinaemia by a direct stimulation on the pancreatic islet cell. This can be enough to cause diabetic ketoacidosis in an insulin-dependent diabetic. The concurrent use of coricosteroids will exagerate the hyperglycaemia in the diabetic. However, with careful blood glucose monitoring during I.V. ritodrine therapy and appropriate exogenous insulin, euglycaemia can be maintained.

Hypokalaemia has also been shown to occur due to a concomitant influx of potassium into the cell because of insulin-dependent glucose movement and as a direct effect on the Na^+-K^+ pump. Correction of the hypokalemia occurs rapidly on stopping the transfusion.

As a result of β_1-stimulated lipolysis there is a mobilisation of free fatty acids in the blood and glycerol as well. These are metabolised to acetoacetic CoA, which in turn is converted to aceto-acetic acid, β-hydroxybutyric acid and acetone. The presence of these ketone bodies in the blood stream will lead to acidosis.

Foetal Side-effects

Foetal tachycardia, acidosis and hyperglycaemia also occur as a result of β-agonists. Changes in foetal heart rate are inconsistent, occur later and return sooner to baseline than those of the mother. Foetal pH may decrease as a result of transplacental passage of fixed organic acids. Foetal hyperglycaemia results from maternal hyperglycaemia and as a result of a direct effect on the foetal liver. β-agonists also have a positive effect on lung maturation producing a synergistic action with corticosteroids, if these are employed.

In concludions, it is important to remember that although B-agonists can delay delivery for at least 24 hours and slightly reduce the proportion of preterm deliveries, they do not reduce the incidence of low birthweight or perinatal mortality.

Other Tocolytic Agents

Magnesium sulphate in doses higher than those used to treat pre-eclampsia, and **ethanol** (a 10% solution at a rate of 7.5mg/hr for 25 hours and 1.5mg/hr for a maximum of another eight hours) are effective alternatives. Most of the expertise in the use of magnesium sulphate, as for its use in pre-eclampsia, is in North America. The side-effects of ethanol have made it obsolete with the availability of better drugs.

Calcium channel antagonists are known to relax the myometrium in vitro and to inhibit markedly the amplitude (but not the frequency) of oxytocin-induced contractions. One such agent, nifedipine, appears to be effective in delaying parturition by 4 to 27 days. However, the available date are limited and the potential usefulness of nifedipine or related agents cannot be estimated at this time.

Inhibitors of prostaglandin synthesis, such as indomethacin, can prolong gestation in both term and preterm pregnancies, but their use in the management of premature labour has been curtailed because of concern in their potential to cause adverse effects in the foetus. Of particular importance is the possibility of premature closure of the ductus arteriosus and the development of pulmonary hypertention. This class of drugs may be much less hazardous if employed for brief periods at earlier gestational ages when there is less possibility of premature closure of the ductus.

The latest innovative approach is an **oxytocin inhibitor** introduced by Dr Akerlund in a pilot study in November 1987. The preparation is an analogue of oxytocin which acts as a competitive inhibitor of the action of oxytocin on the uterus. The greatest advantage of this approach is the absence of side-effects and if proven to be equally effective as beta-agonists, would obviously make it the drug of choice.

References

1. Rall, T.W., Schleifer, L.S. (1985). Drugs affecting uterine motility, in The Pharmacological Basis of Therapeutics. (Goodman & Gillman Eds). Macmillan Publishing Company pp. 926-945.
2. King, J.F., Grant, A., Keirse, M.J.N.C., Chalmers, I. (1988); Beta mimetics in Preterm Labour: an overview of the randomised controlled trials. Br. J. Obstet Gynaecol 95, 211-222.
3. King, J.F., Keirse, M.J.N.C., Grant, A.m Chalmers, I. (1985). Tocolysis – the case for and against; in Preterm Labour and its Consequences (Beard R.W. and SHarp F. Eds). Proceedings of the 13th Study Group of the RCOG, Royal College of Obstetricians and Gynaecologist, London (pp. 199-208).
4. Page, I.J. et al. (1986), Fatal Pulmonary Oedema associated with the use of ritodrine in pregnancy (letter). Br. J. Obstet Gynaecol 93(2), 197.
5. Read, M.D., Wellby, P.E. (1986). The use of a calcium antagonist (nifedipine) to suppress preterm labour. Br. J. Obstet Gynaecol 93, 933-937.
6. Akerlun, M. et al. (1987). Inhibition of Uterine Contractions of Premature Labour with an oxytocin analogue. Results from a pilot study. Br. J. Obstet Gynaecol 1040-1044.

ERRATA CORRIGE

Issue No 13, Autumn '89

Pg. 2 Fig. 2 'Terminals (eg In GP romms/wards)' to read ' ... in GP rooms ...)'

Pg 5 Col. 1 line 18 'tests' to read 'test'
Col. 3 line 12 'erythoucytes' to read erythrocyte'
Col. 3 line 46 'I Gm' to read 'IgM'

Pg 26 Table 2 'Familiar hyperlipedaemia' to read
'Familial hyperlipidaemia'

Pg 31 Fig 4 '(a tipeptide: yglu - cys - gly)' to read '(a tipeptide: glu - cys - gly)'

Pg 32 Table 2 'asthenia' to read 'aesthenia'
'diarrhea' to read 'diarrhoea'

Pg 36 Col. 3 line 23 'ATT' to read anti-tetanus toxoid
'ATG" to read anti-tetanus globulin

GUIDLINES FOR AUTHORS

Authors are encouraged to submit material for publication in Medi-Scope hoping that the work is original and is not intended for publication elsewhere. All authors must give signed consent to publication. The Editor retains the customary right to style and, if necessary, to shorten material accepted for publication.

Acceptable material includes review articles, reports of studies (mostly those carried out in Malta), case presentations, aides memories for students, articles on practical subjects not usually well discussed in standard text-books and quiz material. Manuscrips should not be lengthy: one may consider that three type-written pages on A4 size paper, with one inch margin on either side and double spacing will occupy one page in the journal.

The number of authors should be kept to one or two: further acknowledgements can be added to the text. The author's appointments and qualifications at the time of writing the article should be given and the Editor informed of any change of appointment. It should be made clear on the manuscript which author is responsible for correcting gally proofs and answering queries and correspondence. His/her address and telephone number must be stated. Proof corrections must be kept to a minimum; sizeable alterations should be discussed with the Editor.

A summary of about 80 words should precede the article giving the main argument of findings. The manuscript submitted MUST be typed with double spacing and one inch of margin on either side of the text. Articles should be typed on only one side of the paper; sheets shoiuld be numbered and the end of the article denoted by a double line. Authors are strongly advised to keep a copy. Acceptance of material sent for publication is at the sole discretion of the Board.

Drugs should be given their approved name. Abbreviations may be used provided that what they signify is clearly expressed at least once, on their first appearance in the article. Scientific measurements should be given in SI units with traditional units in parenthesis if necessary.

References:
References should be limited to approximately half a dozen. They should be in alphabetical order of the Authors' names and should conform to the following style:

Articles in Journals:
Authors' names and initials; year of publication; title of article; title of journal; abbreviated to the style of Indes Medicus: volume number; first and last page numbers e.g.:
Birth, C. (1910): Phlebotomus Fever in Malta and Crete. J. Royal Arym Med. Corp. p. 238-260.
Roberts, S.A. and Soothill, J.F. (1982): Provocation of Allergic Response by Supplementary Feeds of Cow's Milk. Arch. Dis. Child. 57: 127.

Articles in Books:
Author's names and initials; year of publication: title of article; Editor of book; title of book; publisher; place of publication; first and last page numbers. e.g.:
Feroze, R.M. (1981): Benign Tumours of the Uterus. Dewhurst, J. (ed): Integrated Obstetrics and Gynaecology for Postgraduates. Blackwell Scientific Publ., London. p. 698-703.

Books:
Authors' names and initials; year of publication; title of book; publisher; place of publication; pages of reference e.g.:
Cuschieri, A., Giles, G.R. and Moossa, A.R. (1982): Essential Surgical Practice. Wright. PSG. Bristol. P3-14.

Illustrations:
Tables, illustrations and graphs should be submitted on separate sheets of paper from the text proper. A reference must be made clear and highlighted in the text. Each should be accompanied by a caption. Graphs must contain all the relevant information including properly labelled axes. Line drawings and rough sketches may also be supplied. Photographs are most useful in the form of prints rather than slides. The top left hand corner should be marked. Patients shown in photographs should have their identity concealed or should give their written consent to publication. Photographic material will only be returned to the authors if specifically requested in writing on submission of manuscripts. If any tables or illustrations submitted have been published elsewhere, written concent to republication should be obtained by the author from the copyright holder (usually the publisher) and the authors.

Letters:
Letters to the Editor are welcome, particularly those which take up points from material published in the journal. They should not normally exceed one type-written page in length and may include an illustration or table.

The Editorial Board would like to take this opportunity to thank all those who help in materialising each issue of **Med-Scope** as well as those who by their kind words, constructive criticism and suggestions are helping in making this a fine journal. The Board will be pleased to discuss any problem or difficulties as may arise in connection with **Medi-Scope**.

International Committee of Medical Journal Editors. Uniform Requirements for Manuscripts Submitted to Biomedical Journals.
Br. Med. J. (1982) 284: 1766-70.
List of Journals Indexed – printed in the *Index Medicus*.

3M HEALTHCARE LTD.

Acupan – Non narcotic analgesic

Dorbanex – the gentle way to treat constipation

Duromine – for the control of simple obesity

Hiprex – an effective treatment for urinary tract infection

Medihaler Range – bronchodilators in aerosol form

Pholtex – a sustained release cough suppressant

Pulmadil – a fast acting aerosol bronchodilator

Nuelin S.A. – a long acting theophylline preparation for the routine control of bronchospasm

Rauwiloid – for the long-term management of hypertension

Rikospray Group – a range of topical antiseptic aerosol products

Supplamins – one-a-day multivitamin and mineral

Full details of these and other products are available from...

JOSEPH CASSAR LIMITED
54 Melita Street
Valletta, Malta

or direct from...

All product names; Riker; 3M: trade marks

3M HEALTHCARE LTD.
Loughborough England

3M

MEMORY
Part 1: Neurochemistry and Spatial Organisation

PIERRE MALLIA
Medical Student

Substantial research has been done and is still being done on the biochemical aspects of memory (microphysiology). Furthermore many experiments on sub-human mammals have localized centres in the brain responsible for specific aspects of memory (macro-physiology). Research into computational networks provides models on how neurons associate together to produce the advanced functions of thinking and memory. The aim of this paper is to put together the material relevant to the field of memory gathered from physiology and biochemistry and use computational networks as a model to propose a hypothesis on the functioning of memory.

Early experiments on rats and assessment of lesions in the human brain showed that memory can be divided into short term memory (STM) and long term memory (LTM). It has been shown that structures relating to the limbic system (hippocampus, amygdala etc) are all important but there is no organ which can be classified as the organ of memory. It is generally agreed that memory functionally involves the cooperation of many structures together. This is brought about by plasticity at the level of synapses which permits the establishment of circuits between relevant areas, to memorise percepts.

The hippocampus is necessary to transfer STM to LTM, but both types of memory can still exist without this part of the brain. The amygdala are important in emotional experiences. Thus a monkey whose amygdala have been excised no longer fears human beings. Moreover it is also involved in the establishment of memory. Due to their connections with the hypothalamus, they are probably the organs which permit the establishment of individual experiences in the course of one's life.

Neurochemistry

Early experiments showed that memory can be resolved to a molecular level and that it involves protein. Such proteins have been 'transplanted' and the experience carried from one animal to other. Drugs too can have an effect on memory. These show a state-dependency, in that, if a memory is learnt under the action of a drug, it will only be recalled optimally under the influence of the same drug. The early belief that the 'memory molecule' is Ribonucleic acid is now, not in vogue, its only role being relegated to protein synthesis. Blocking RNA will block protein synthesis, and hence the establishment of memory.

Long term potentiation (LTP), is a long lasting increase in the effectiveness of synaptic transmission. This is triggered by high frequency stimulation of certain presynaptic axons. LTP is produced by a few brief, high frequency bursts of presynaptic action potentials. Larger excitatory postsynaptic potentials (EPSP), enhance the ability of the synapse to trigger action potentials in the postsynaptic neuron; this could be a memory forming mechanism. Note that LTP means a long lasting increase in the EPSP. This has been shown to occur in the hippocampus.

Kauer et al have shown LTP to be divided into two processes: slowly decaying potentiation (SDP) which is short term, and disappears after thirty seconds, and a true LTP which lasts for hours or days. They induced slowly decaying potentiation by applying glutamate, an excitatory neurotransmitter, over the surface of the snyapse. However, the establishment of a true LTP also required electrical excitation of the presynaptic terminals. This demonstrated the need for a second unknown neurotransmitter. Malinow et al have shown that one or more protein kinases are involved in maintaining a true LTP, but these seem not to be involved in the less persistent SDP.

LTP has traditionally been divided into a phase of induction, that includes several seconds during and after tetanic stimulation when the event is initialised and a second phase, maintenance, in which the presynaptic terminal achieves plasticity: (i.e. release of more neurotransmitter during excitation). Induction involves an interplay between pre- and postsynaptic membranes. Hyperpolarization of the postsynaptic membrane during tetanic stimulation of a presynaptic membrane blocks induction of LTP. Thus even though maintenance depends on the presynaptic membrane, induction also occurs postsynaptically.

Induction requires glutamate receptor activation; two types of these are found in the brain: quisqualate/kainate (Q/K) and N-methyl D-

aspartate (NMDA). Blockade of Q/K eliminates the postsynaptic potential normally produced by a single stimulation.

Blockade of NMDA does not affect the postsynaptic potential but blocks induction of LTP during tetanic stimulation.

Strong membranes depolarization and the presence of glutamate are both required to activate NMDA receptors, hence tetanic stimulation is necessary for induction of LTP in a pathway. This could provide a mechanism for associative learning.

The ion channel linked to Q/K is highly selective for Na^+ and Ka^+ ions, while that linked to NMDA also admits Ca^{++}. Activation of NMDA can thus produce a rise of intraneuronal Ca^{++} which is known to be a second messenger that can activate different effector molecules. Three mechanisms of LTP provoking Calcium-activated enzymes have been proposed, all having their limitations.

1. C-kinase hypothesis.

Ca^{++} ions and/or diaclyglycerol activate a C-kinase. C-kinase can also be activated by phorbol esters which act as diacylglycerol analogues. The application of phorbol ester to a slice of hippocampus produces an increased potentiation of synaptic transmission, with many LTP characteristics. This was the first indicator that C-kinase is involved. Membranes of neurones prepared an hour after induction contained twice as much C-kinase as the unpotentiated tissue. C-kinase binds to membranes on activation. The hypothesis is that tetanic stimulation activates C-kinase which phosphorylates proteins, producing LTP (e.g. GAP-43, a protein which is a prominent substrate to C-kinase). However how such a substrate brings about LTP is missing from the hypothesis.

2. CaM kinase hypothesis:

Activation of type II Ca^{++}/calmodulin-dependent protein kinase (CaM kinase), occurs when an increase in calcium, concentration causes the calmodulin Ca^{++} complex to bind to a regulatory domain within the kinase. In the forebrain and hippocampus CaM kinase seems to be a major postsynaptic component (and is found in high concentrations in tissue sections). It is presumably exposed to NMDA receptor-mediated calcium flux. On in vitro activation the kinase phosphorylates appropriate substrate proteins. It also autophosphorylates a threonine residue, this inhibits refolding and allows CaM kinase to remain activated long after the calcium concentration has fallen. This hypothesis has the same weaknesses as above.

3. Calpain hypothesis

Calpain is a calcium activated protease in synaptic membranes. It cleaves cytoskeletal proteins fodrin and MAP2. In vitro it proteolyses several protein kinases, including C-kinase and CaM-kinase, freeing the catalytic domains and producing active kinase molecules that could persist in vivo until destroyed by other proteases. Greenberg et al suggest that enhanced gene expressions for the calpains could increase the level of constitutive kinases in neurons, producing long lasting changes. Malinow et al show that increased concentrations of protein kinases are needed for LTP. When the regulatory domains of the C-kinase and CaM-kinase are blocked by Sphingosine and H7 (a synthetic organic inhibitor) induction of LTP is blocked. (Except in hippocampal synapses).

No one of these hypotheses explains the feedback mentioned above from postsynaptic to presynaptic terminals. Dumuis et al demonstrated that binding of NMDA to its receptors releases arachidonate into the extracellular space. This could be the transynaptic messenger, this is able to travel back.

Dumuis et al experimented on the striatum of 14 to 15 day old mouse embryos. They proposed that glutamate and NMDA, acting at typical NMDA receptors, stimulate the release of arachidonic acid probably by stimulation of a Ca^{++}- dependent phospholipase A2. The results show that glutamate and NMDA responses are mediated by NMDA receptors. It is likely that influx of Ca^{++} through the NMDA receptors triggers the arachidonic acid cascade system. This is also dependent on the activation of a phospholipase A2 (PLA2) on the postsynaptic membrane. When this was blocked by a potent inhibitor (mepacrine) the effects of glutamate were completely abolished. The involvement of a G protein in the coupling between NMDA receptors and PLA2, similar to that described in thyroid cells between alpha-adrenergic receptors and PLA2 is unlikely but cannot be totally excluded, because in the latter system the coupling is also dependent on external Ca^{++}.

It is postulated that arachidonic acid and/or its metabolites (AAM) are released from the postsynaptic cell and act on the presynaptic terminal to trigger an increase in glutamate release or inhibition of glutamate re-uptake.

Combinatorial Systems

There are two known patterns of neuronal communication. These are the topographical and the combinatorial modes of connection. In the topographical arrangement, an input into one neuron makes contact with a second neuron in another region via limited contacts, in approximately a one to one arrangement. This is shown in A in figure 1. Additional input to this arrangement needs only the insertion of a new target neuron without affecting the previous neurons, as shown in B. In a combinatorial arrangement, the neurons are interconnected such that, the input of one neuron affects all the neurons at the target end. A new input to this network will disrupt the combinatorial character of the previous arrangement (D). Thus expansion of topographical networks, only requires addition of neurons whilst that of combinatorial networks also requires the expansion of axons and dendrons.

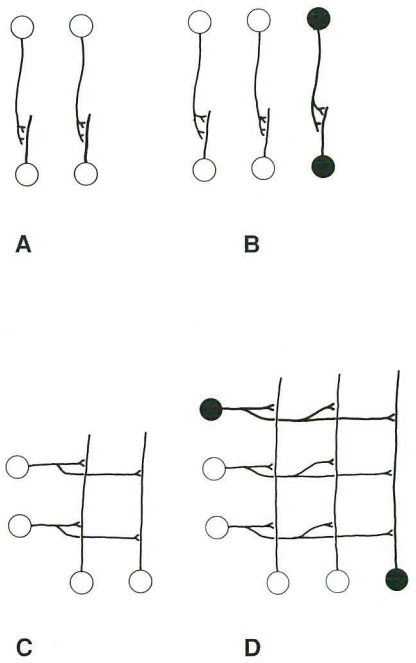


Figure 1. Diagramatic representation of expansion of topographical A → B and combinatorial C → D modes of connection.
(Additional neurones in black)

Evolutionary evidence indicates that most of the organisation of the mammalian cortex is of the combinatorial type (Lynch). Retrograde transport of labels and neuroanatomical studies show that the pyriform cortex is an excellent example of a combinatorial organisation.

The deep layer of the pyriform cortex has connections with the dorsomedial nucleus of the thalamus, which communicates with the frontal cortex. Layer 2 of the pyriform cortex (which communicates with the deep layer) also has projections of its own to the frontal cortex. The deep layer of the entorhinal cortex projects to the neocortex. Its layer 2 however sends fibres to the hippocampus. The dentate gyrus, the primary target of the lateral perforant path communicates profusely with thousands of granule cells – again a combinatorial system. The output of the dentate gyrus is restricted to the regio inferior (CA3) of the hippocampus proper, which itself communicates with a massive commissural association network with itself and the regio superior (CA1). The output of the hippocampus is the deep layer of the entorhinal cortex and the subiculum. The latter sends fibres back to the regio superior and also, to the entorhinal cortex, the ventral forebrain, the anterior thalamus, and the mammillary bodies; whilst the entorhinal cortex sends axons to the temporal neocortex.

Also, the fibres that the DMN sends to the cortex terminate in layers I and III of the cortex in a combinatorial manner as that found in the pallium of the lizard. It seem likely that both vertical and horizontal interactions occur. From comparative studies it can be expected that combinatorial systems are found throughout the cortex and possibly other regions of the forebrain.

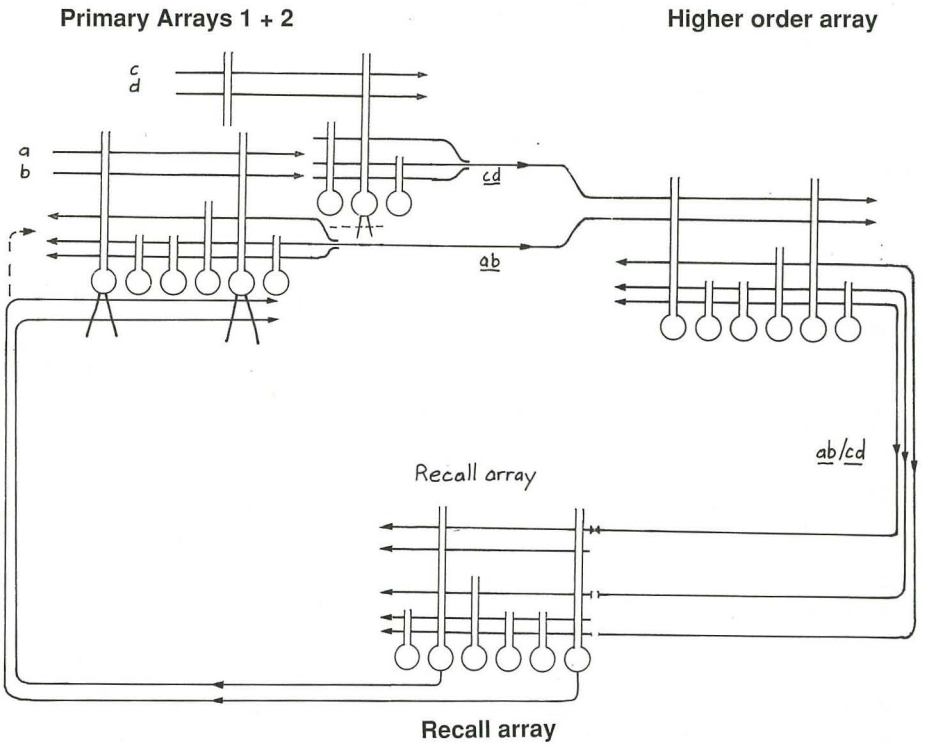


Figure 2: In this circuit (Fig. 2), we have two primary arrays: one where the signals for a and b are generated and another where the signals for c and d are generated. These are associated in a higher order array which produces the signal ab/cd and this then projects feedback fibres on a separate 'recall array'. This recall array projects fibres onto the primary arrays. These produce a discharge at a frequency which is not enough to generate LTP on their own. Potentiation occurs on the primary arrays and does so on those cells which are activated when the recall signal arrives. On subsequent occasions, projections from the second array (that which produces the ab/cd signal) would trigger only those cells in the primary array which had been temporarily associated with the recall fibres the first time the association of ab had occurred with cd. Lynch has also proposed experiments to test the hypothesis, which although still posing problems is a step to understanding how the high frequency required for LTP may be brought about.

Recall

From a physiological point of view the crossing of two chains in combinatorial systems solves many problems. But to be more exact the model must solve psychological problems. Thus the input of B will recall a previous event, A. For example, the smell of cheese will recall from memory the shape, colour and other perceptory identifications of cheese. Lynch has forwarded models of arrays of neurons, one of which is summarized below. These provide suggestions how potentiation can occur in the hippocampus.

Lesions to the hippocampus would not impede short term memory and not even already established long term memories. However the function of forming new long term memories, that is, the capability of transferring STM to LTM is disrupted. The combinatorial hypothesis provides a good explanation for this. Since the hippocampus is the site where connections between various parts of the brain occur, its importance in combinatorial connections with the various regions is established. Thus it is important in establishing long term potentiation of the concerned synapses in the memory circuits. However, damage of the hippocampus will not alter the already established potentiated synapses and thus established LTM will not be disrupted. Short term memory need only involve certain centers which will not include hippocampus directly. There is still the memory of words etc. This shows that the hippocampus is not needed for certain long term memories and it is only the combinatorial network which is disrupted, that is the ability to recall one event from the imposition of another.

In fact, psychologists have concluded that humans use two memory systems, one that stores information or data and a second that processes this according to a new set of "rules" or "procedures". The combinatorial arrays running through the hippocampus provide the second system, while neurons connected through the dorso-medial nucleus of the thalamus (e.g. olfactory-DMN) provide the first.

The hypothesis of combinatorial networks is "firmly grounded" in the field of neuroanatomy but it is still short on data.

The Amygdaloid Complex in Relation to Memory

Experiments by Mishkin and Appenzeller showed that the amygdala are as important, in memory, as the hippocampus. Bilateral removal of the hippocampus and amygdala produced a complete amnesic animal. The animal was completely impaired in experiments regarding association of objects with reward The visual pathways were not affected, as structures with connections to these paths were tested. The amygdala and hippocampus have extensive connections, with the visual pathways, (the latter indirectly). In fact it is the capability of positively associating the reward with the visual system which was impaired. Removal of the hippocampus alone had no effect on this ability. Bilateral removal of the amygdala produced an animal with poor ability to associate, but although slow to learn, was still able to do so. It is removal of both structures, which produces the lack of ability to associate. The following experiment demonstrated this and that the visual path was not damaged:

The animal was presented with an object under which was a reward (food). In a second trial the previous object and another one were presented and the food was put under the new object. The animal thus should learn to associate the food with the novel object. To do this it must remember the previous object. Whenever the trials were performed the two objects were always changed so that the monkey only learned to associate reward with the second object, irrespective of what is was. Animals with bilateral removal of hippocampus and amygdala performed well when the delay between the first and second trial was short, showing that the visual path was not affected. If the interval between the two trials was lengthened however the scores fell to the level of chance.

Moreover the amnesia was global. If the experiment was performed using the ability of touch to recognize instead of sight, the results were the same. Thus the hippocampus and amygdala have the same importance, removing either alone has little or no effect.

Higher Stations

Damage to hypothalamus and thalamus alone impair memory as much as damage to the limbic structures. In fact the limbic system and the diencephalon participate in a circuit rather than independently. This can be shown by damaging the pathways connecting the two areas, producing the same amnesic results.

Tracing the circuit to its possible end, Bachevalier found that surgical lesions to the ventromedial prefrontal cortex also produced this loss of recognition memory. At minimum we have thus these three sites as stations for memory.

Puzzle solved?

We have seen the importance of the limbic system in converting short term memory into long term memory. Here we find its importance in forming associations. A model of how long term potentiation by feedback circuits occurs, has been discussed. Memory occurs in combinatorial circuits which are established by LTP, that causes the plasticity in synapses to "fix" circuits. Damage to any of the above centres thus impedes impulses passing through these combinatorial circuits, preventing long term potentiation. This also explains why previous long term memory is preserved. Long term potentiation has already occurred before damaged to any station is done. When the damage is done the circuits are already "fixed" (synapses have been potentiated) and are thus established. Short term memory will remain intact as this requires paths other than the limbic or diencephalic regions. Damage to these stations however impedes communication with higher combinatorial arrays and hence LTP.

Types of memory

There are other functions of memory, further to simple recognition, for instance spatial relations, e.g. if one visits the Academy of Arts museum in Florence and recognises the statue of David, besides the shape of the statue, one will also remember its relation to the museum. He will remember, or have an idea even where the statue lies even if the museum was visited only once. This "spatial memory" was found to be located in the parietal cortex. Recognition memory, however, is not impaired, if this is damaged. In an experiment performed by Pohl, monkeys were presented with two wells, one of which contained food. The one containing the food was put near a cylinder. Thus the monkeys would learn to associate food, as being in the well, near the cylinder. This was relatively simple for monkeys with infero-temporal lesions, but those with damage to the parietal cortex had impaired spatial memory.

Although the hippocampus and the amygdala can substitute each other in association experiments, the hippocampus is also important in spatial memory, whilst the amygdala are not. Parkinson found this in similar experiments to Pohl performed on these regions.

Amygdala and previous memories

The amygdala, which are really a collection of nuclei have connections with all the sensory systems in the cortex. They are a sort of crossroads in the brain. The same parts of the amygdala which have sensory inputs also send fibres deeper into the brain into the hypothalamus, which is thought to be the source of emotional responses.

Mishkin and Appenzeller give results of experiments which suggest the amygdala as being the site where memory recalls other memories, hence a second candidate, probably more plausible, for combinatorial arrays of recall which may fall into Lynch's model discussed earlier.

In the experiment, monkeys with bilateral removal of the amygdala were allowed to examine objects both in the light (using sight and touch) and in the dark (using touch only). They then had to recognise the object from a pool of forty. The animals performed well. Their visual and tactile memories had remained intact, in keeping with the earlier finding that the hippocampus and amygdala can substitute for each other.

In a second experiment however, the monkeys were allowed to examine the object in the dark and then made to recognise it in the light using their visual system. The group with damage to the amygdala were unable to correlate tactile with visual memory. A control group with damage to the hippocampus were able however to perform the distinction quite well (ninety percent of the time).

Memory and emotion

Kluver and Bucy noticed that monkeys with damage to temporal lobe also lost their fear of humans. This was traced down to the amygdala. The link with familiar objects and their emotional associations had been severed. This observation goes hand in hand with the fact that monkeys without amygdala are slow in learning to associate an object with reward, as pointed out before in this section. In fact Mishkin and Appenzeller found that the amygdala not only receive fibres from all the sensory systems but also in turn send fibres to them. the amygdala are rich in neurons synthesising opium like neurotransmitters known as endorphins. Evidence shows that there are endorphin containing fibres from the amygdala to the sensory systems where they may serve "gatekeeping functions" influencing what is perceived and learned. In this way it is not foul to classify the amygdala as the motivation centre, especially when we know that without motivation, our chances of memorising are much reduced.

Speculation

It was noted initially that current thought of memory formation is the building of input onto previous memories or experiences. The analogy of streams being formed by water rolling down a hill has often been used. The passage of further water will follow the path created by the previous stream but will add onto it, creating new pathways. This is done by the force of gravity acting on the water. The water tries to occupy ever lower energy states (in this case potential energy) and in so doing it seeks new paths which are made possible by the property of the soil in allowing new paths to be formed by the currents.

Something on similar lines is thought to occur in the brain. Considering the combinatorial circuit model suggested before: if for simplicity we take a brain with no information in it, incoming information creates paths, that is synapses are potentiated to create circuits to a great extent at random, within the anatomical pathways described. We have already seen how two separate inputs can affect each other by feedback neurons. Thus new information will follow the same paths but will create more circuits. This is how ideas build on one another and hence learning. The part of understanding is thus nothing but the evaluation of previous knowledge in order to incorporate into this knowledge, the new knowledge that is being perceived. This new knowledge can thus be viewed as following through the paths already there. Correlating previous information is in fact creating combinations between circuits by means of long term potentiation. Naturally, this process can lead to what we define as 'misunderstanding', if either the previous or incoming knowledge was not organised well into the brain network. This can also be due to a state of fatigue of the person, which may implicate that incoming information is led voluntarily by the person along certain paths. An analogy would be respiration which is normally effortless but at any point the person can control the rate of respiration and thus the volume of air entering the body. Similarly in the brain, perceptions are continuously being introduced but unless some effort is made or unless under some emotional state, whatever enters is usually forgotten. An effort to understand will however bring the circuitry into action and incoming information is correlated to what was previously learnt (is led along correct circuital paths).

All this speculation is possible for the combinatorial circuitry model described. Thus as water fell along lines led by potential energy, perceptions enter the brain along potentiated circuitry led by energy states of the neurons. The thoughts fall along 'hills' of energy states and in the process new paths are created.

This is a good way however of demonstrating how to visualise that not all we know is continuously in our presence of mind. Hence the distinction between what is conscious and what is subconscious. Waves of hills are continuously being created and one leads to the others - just as a train of thoughts occurs when one is sitting in a state of 'daydreaming'. Information from the environment can stimulate the formation of energy hills. These can be pursued and thus lead to the activation of other hills (memory) and in some instances potentiate if there is enough evaluation of the perception. This is brought about by the recall mechanisms mentioned earlier. In other instances they are simply omitted; a previous memory may be aroused (an energy hill), that is a previously potentiated circuit, but the perception is not voluntarily evaluated enough to arouse previous experience or curiosity and thus enhance LTP. Let us take the example of memorising the path of the radial nerve in the arm, assuming that the previous knowledge is a memory of the anatomy and relations of the bones and muscles in the region. At the start of the procedure, assuming that the student is active and not simply performing passive reading, what was previously known is remembered. That is, action potentials have passed through the potentiated circuits and various energy hills have been

Continued from page 8

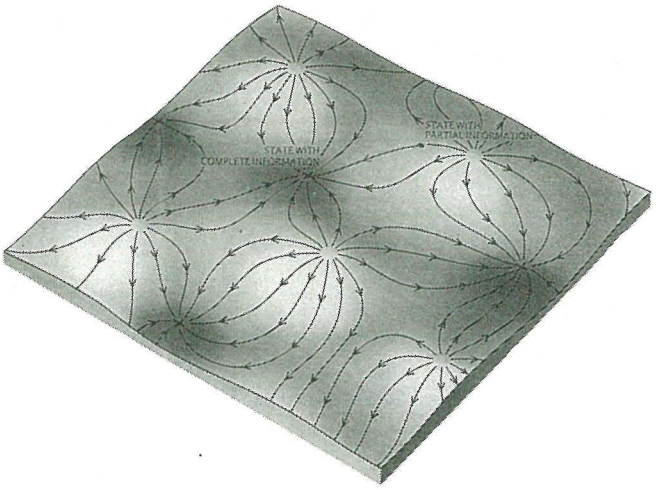


Figure 3: For a clearer understanding of why some thoughts remain and others do not, one can imagine that these energy levels are all in a resting state; 'flat' (as a carpet). *The passage of action potentials through a circuit arouses the energy state of that circuit and an energy 'hill' is created on this imaginary 'carpet'. When one is interested in what is happening around him, he thus activates previous knowledge (fig 3).* The carpet can be viewed as being lifted (forming a hill). That is, the energy levels are created and the incoming information will flow 'downhill'. Thus a medical student on a bus may be hearing conversation but will remember nothing. However if he overhears something relevant to his studies his curiosity is aroused (an energy hill is created) and the information is understood. There is more chance of his remembering the information now. Whether he remembers it weeks after depends on how much he allowed that information to affect his energy states, e.g. he might have been prompted to go and study more about what he had heard. Thus whenever he remembers this topic he will recall the experience on the bus. This experience has been potentiated into his memory store.

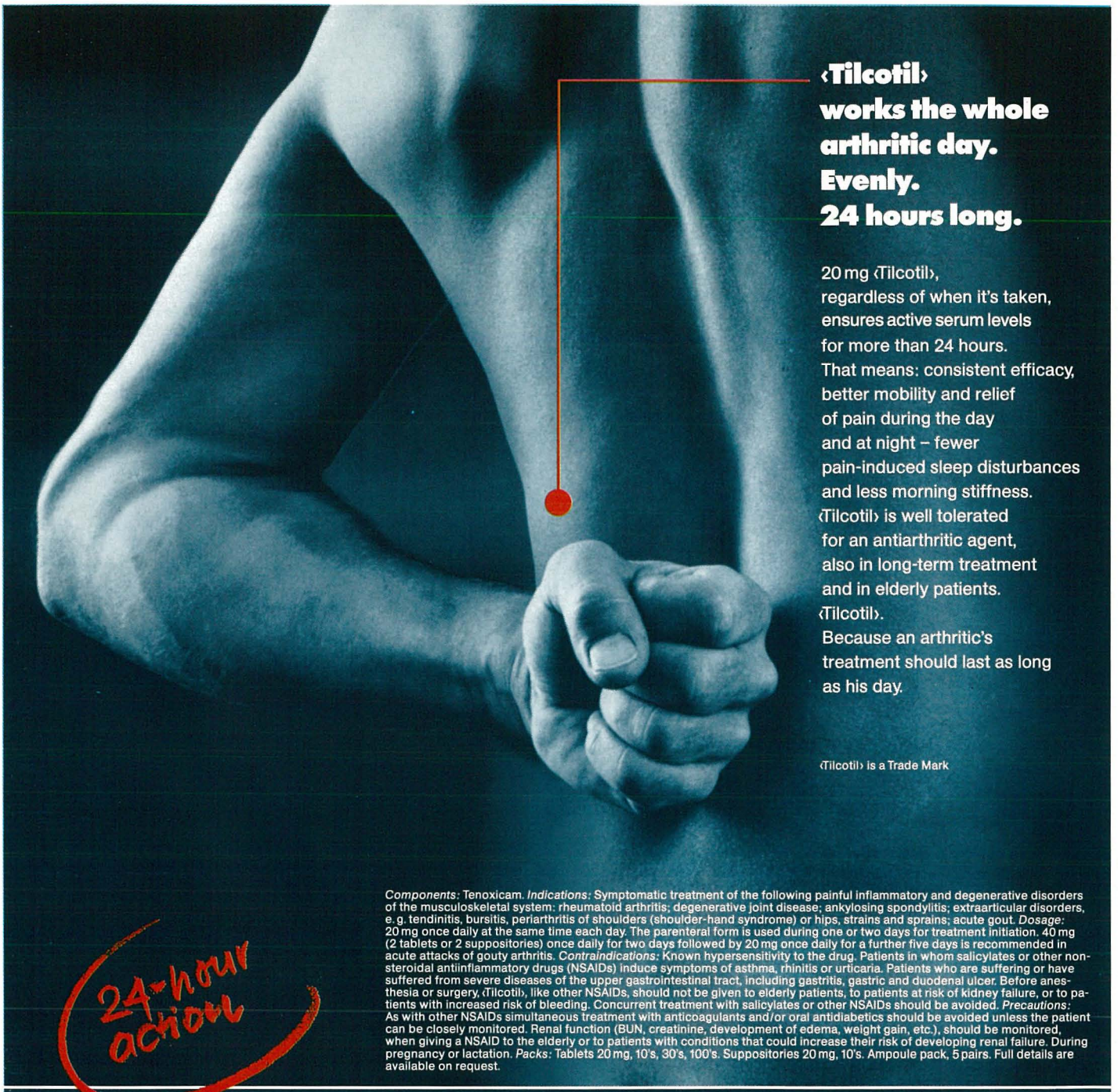
'aroused' (again remember that one hill may produce another by the feedback model) producing what one may call a landscape of energy hills. The incoming information relating to the course of the nerve must be understood in relation to what was previously learnt. That is, the information is flowing along the hills, creating new networks in the meantime. These new networks are the basis for the memory of "the course of the radial nerve", and its future recall depends on the potentiation this circuit gets in the presence. Some people potentiate by repetition (but note that this does not mean that a previous effort of understanding was not necessary); others by as much understanding as possible, that is relating what is being learnt to as much previous knowledge as possible (thus the student might compare the upper limb with the lower limb).

It is also known that long term potentiation can decay in certain synapses which shows why the longer time passes, the less detail one tends to remember. However most of the circuit is still intact (not all synapses of the circuit need decay at once because indeed some may be being used in other circuits) and therefore a revision of something will enhance memory. Thus people having seen a film a few years back may still have a 'vague idea' of the film but if on reviewing it they 'will start' remembering and indeed there will be parts which they have completely forgotten. During the film other intact memories will be aroused (a creation of energy hills). One will anticipate what is going to happen next because the action potential flow is led into going down these energy hills. An analogy to computational networks shows this is feasible.

The second part of this article will be published in the following issue.

References

1. Beck, AC (1951) Obstetrical Practice 5th Ed. Williams & Wilkins; Baltimore p.774-785
2. Brews, A (1963) Holland & Brews Manual of Obstetrics 12th ed. Churchill Ltd.; London, p. 490-494.
3. Butigiec. F (1804) Trattato dell' arte ostetrica dettato e spiegato del Perille Signor Dr. Francesco Butigiec nello studio publico del Grand Ospedale Nazionale de' Malta, Principiato li 18 Ottobre 1804 manuscript in Cassar, P (1973) "Teaching of midwifery in Malta at the beginning of the nineteenth century" St. Luke's Hosp. Gaz. 8(2):91-111.
4. Cassar, P. (1987) "Clinical teaching in Malta fifty years ago" Medi-scope 11:24-29.
5. Chisholm, AE (1923) "Symphysiotomy, craniotomy and Caesarean section" Lancet Aug. 11th p.276-278.
6. Department of Health (1938) Annual report on the health conditions of the Maltese Islands and on the work of the Medical and Health Department for the year 1937 Govn. Printing Off.; Malta p.119-126.
7. Department of Health (1939) Annual report on the health conditions of the Maltese Islands and on the work of the Medical and Health Department for the year 1938 Govn. Printing Off.; Malta p.106-127.
8. Department of Health (1953) Report on the health conditions of the Maltese Islands and on the work of the Medical and Health Department for the year 1951 Govn. Printing Off.; Malta p.92-93.
9. Department of Health (1954) Report on the health conditions of the Maltese Islands and on the work of the Medical and Health Department for the year 1952 Govn. Printing Off.; Malta p. 82-84.
10. Donald, I. (1959) Practical Obstetric Problems 2nd ed. Lloyd-Luke; London p.270-275.
11. Macafee, CHG (1945) "Placenta praevia. A study of 174 cases" J. Obstet. Gynaecol. Br. Commonw. 52:313-324.
12. Macafee, CHG (1960) "Placenta praevia" Lancet 1:449-452.
13. Malmstrom, T (1957) "The vacuum extractor, an obstetrical instrument" Actra Obstet. Gynaecol. Scand. 36 (Suppl.3):5-50
14. Pisani, SL (1883) Ktieb il qabla Govn. Printing Off.; Malta p.101.
15. Schembri GB (1891) "Prima operazione cesarea in Malta" Rivista di Obstetricia e Ginecologia p.1 In Cassar, P. (1964) Medical History of Malta Wellcome Hist. Med. Lib; London p.538.
16. Schembri, GB (1896) The Midwife's Guide Book Govn. Printing Off.; Malta p.96-101.
17. Spiegelberg, O (1887) Textbook of Midwifery vol.1 p.534-551 New Sydenham Soc.; London.
18. Spiegelberg, O (1888) Textbook of Midwifery vol.2 p.607-625 New Sydenham Soc.; London.
19. Tait, L (1899) "On the treatment of 'unavoidable haemorrhage' by removal of the uterus" Lancet 1, 364.
20. Willett, JA (1925) "The treatment of placenta praevia by continuous weight traction" Proc. Royal Soc. Med. 18:90.



‹Tilcotil› works the whole arthritic day. Evenly. 24 hours long.

20 mg ‹Tilcotil›, regardless of when it's taken, ensures active serum levels for more than 24 hours. That means: consistent efficacy, better mobility and relief of pain during the day and at night – fewer pain-induced sleep disturbances and less morning stiffness. ‹Tilcotil› is well tolerated for an antiarthritic agent, also in long-term treatment and in elderly patients. ‹Tilcotil›. Because an arthritic's treatment should last as long as his day.

‹Tilcotil› is a Trade Mark

24-hour action

Components: Tenoxicam. *Indications:* Symptomatic treatment of the following painful inflammatory and degenerative disorders of the musculoskeletal system: rheumatoid arthritis; degenerative joint disease; ankylosing spondylitis; extraarticular disorders, e.g. tendinitis, bursitis, periarthritis of shoulders (shoulder-hand syndrome) or hips, strains and sprains; acute gout. *Dosage:* 20 mg once daily at the same time each day. The parenteral form is used during one or two days for treatment initiation. 40 mg (2 tablets or 2 suppositories) once daily for two days followed by 20 mg once daily for a further five days is recommended in acute attacks of gouty arthritis. *Contraindications:* Known hypersensitivity to the drug. Patients in whom salicylates or other non-steroidal antiinflammatory drugs (NSAIDs) induce symptoms of asthma, rhinitis or urticaria. Patients who are suffering or have suffered from severe diseases of the upper gastrointestinal tract, including gastritis, gastric and duodenal ulcer. Before anesthesia or surgery, ‹Tilcotil›, like other NSAIDs, should not be given to elderly patients, to patients at risk of kidney failure, or to patients with increased risk of bleeding. Concurrent treatment with salicylates or other NSAIDs should be avoided. *Precautions:* As with other NSAIDs simultaneous treatment with anticoagulants and/or oral antidiabetics should be avoided unless the patient can be closely monitored. Renal function (BUN, creatinine, development of edema, weight gain, etc.), should be monitored, when giving a NSAID to the elderly or to patients with conditions that could increase their risk of developing renal failure. During pregnancy or lactation. *Packs:* Tablets 20 mg, 10's, 30's, 100's. Suppositories 20 mg, 10's. Ampoule pack, 5 pairs. Full details are available on request.

Tilcotil

Tenoxicam

nonsteroidal antirheumatic

Roche

F. Hoffmann-La Roche Ltd,
Basel, Switzerland

1989/30 221

clio

Streaks ahead... the Renault Clio is different. With its concentration of talent and energy it is more spacious than any other car in its class. Quiet and comfortable, the Renault Clio is available in 3 or 5-door versions. Warm and generous, the Renault Clio adds a new dimension to your life.

RENAULT CLIO

CAR OF THE YEAR 1991

RENAULT

PART-EXCHANGE ACCEPTED

clio

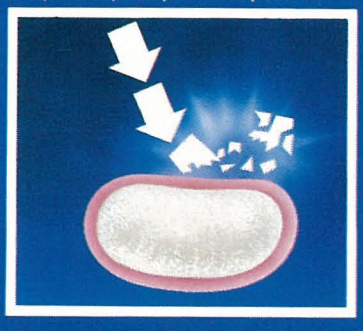
Enquiries: KIND'S SHOWROOMS:
Lija. Tel: 433601/2/3. Gżira. Tel: 330031.
GOZO AGENT: Tasika Auto Ltd., Victoria, Gozo. Tel: 553288.

AUGMENTIN

clavulanate-potentiated amoxycillin

CLAVULANATE POWER AGAINST INFECTION

The most important bacterial defence mechanism is the production of ß-lactamase enzymes. These are produced by an increasing number of bacteria and destroy many oral cephalosporins and penicillins.



Amoxycillin can now penetrate and destroy the pathogen

Clavulanate inhibits and then destroys the majority of ß-lactamases

ß-lactamase

- **A broader spectrum than cefuroxime[1], cephalexin[2], co-trimoxazole[2] or ampicillin[2]**
- **Excellent activity against aerobes and anaerobes, including Bacteroides[2]**
- **Consistently high success rates in a variety of community and hospital infections**

Prescribing Information

Indications: Upper/lower respiratory tract infections: sinusitis, tonsillitis, otitis media, acute and chronic bronchitis, pneumonia, empyema, lung abscess. Skin and soft tissue infections: boils/abscesses, cellulitis, wound infections, intra-abdominal sepsis. Genito-urinary tract infections: cystitis, urethritis, pyelonephritis, septic abortion, pelvic infections, chancroid, gonorrhoea. Osteomyelitis, septicaemia, peritonitis, surgical prophylaxis.
Oral dosage: Adults and children over 12 years: One tablet tds. Children 7-12 years: 10ml of 156mg syrup tds. Children 2-7 years: 5ml of 156mg syrup tds. Children 9 months-2 years: 2.5ml of 156mg syrup tds. Children below 9 months: No suitable presentation currently available. In severe infections the dosage may be doubled.
Intravenous dosage: Adults and children over 12 years 1.2g 6-8 hourly. Children 3 months-12 years 30mg/kg 6-8 hourly. Children below 3 months see pack insert leaflet. Surgical prophylaxis: Adults 1.2g at induction of anaesthesia. Procedures longer than 1 hour require subsequent doses (up to 4 in 24 hours). Treatment with AUGMENTIN should not be extended beyond 14 days without review.
Contra-indication: Penicillin hypersensitivity. **Precautions:** A number of studies at high dosages have shown AUGMENTIN to be free from teratogenicity in animals; however its safety in human pregnancy has not yet been established. There is no experience of AUGMENTIN I.V. in human pregnancy therefore its use in pregnancy cannot be recommended. Changes in liver function tests have been observed in some patients receiving intravenous AUGMENTIN. The clinical significance of these changes is uncertain but AUGMENTIN should be used with care in patients with evidence of severe hepatic dysfunction. Dosage for patients with moderate or severe renal impairment should be adjusted as described in the pack insert leaflet. **Side-effects:** Uncommon, mainly mild and transitory eg. diarrhoea, indigestion, nausea, vomiting, candidiasis. If gastro-intestinal side-effects occur with oral therapy they may be reduced by taking AUGMENTIN at the start of meals. In the event of an urticarial or morbilliform rash discontinue treatment. Phlebitis at the site of injection has been reported. As with some other antibacterial agents, a few cases of transient hepatitis and cholestatic jaundice have been reported.
Availability: 375mg AUGMENTIN tablets containing 250mg amoxycillin/125mg clavulanic acid. 156.25mg AUGMENTIN syrup each 5ml containing 125mg amoxycillin/31.25mg clavulanic acid. 600mg AUGMENTIN intravenous vials each containing 500mg amoxycillin/100mg clavulanic acid. 1.2g AUGMENTIN intravenous vials each containing 1g amoxycillin/200mg clavulanic acid. Not all presentations are available in every country.
Storage and Stability: See pack insert leaflet.

References: 1. Med Int., (1984), **2**, (2), 41. 2. Excerpta Medica, (1980). **ICS 544**, 58.

AUGMENTIN is a trademark.

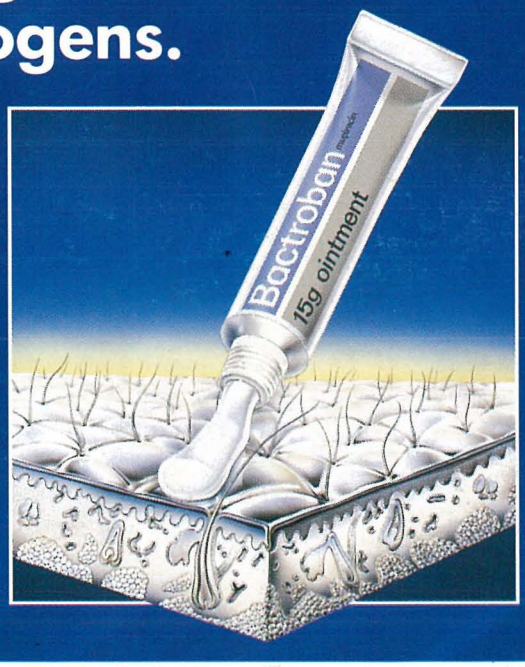
Beecham Pharmaceuticals
BRENTFORD ENGLAND

Further information is available on request.
01/1272/9/88

Bactroban mupirocin

rapid success

- Fast and effective in bacterial skin infections.[1-5]
- Highly active against the causative pathogens.
- Remarkably low incidence of side effects.[6]
- 96% success in a variety of skin infections.[1]



PRESCRIBING INFORMATION

Presentation BACTROBAN ointment: mupirocin 2% w/w in polyethylene glycol base. 5g or 15g tubes.

Activity BACTROBAN is a topical anti-bacterial agent, active against those organisms responsible for the majority of skin infections, e.g. Staphylococcus aureus, including methicillin–resistant strains, other staphylococci and streptococci. It is also active at concentrations attainable on the skin against Gram-negative skin pathogens such as Escherichia coli and Proteus spp.

Indications Bacterial skin infections, e.g. impetigo, folliculitis and furunculosis.

Dosage and Administration Adults and children: BACTROBAN should be applied to the affected area up to three times daily, for up to 10 days.

Precautions Avoid contact of BACTROBAN ointment with the eyes. Use BACTROBAN with caution in patients with moderate or severe renal impairment.

Use in Pregnancy: There is inadequate evidence of safety to recommend the use of BACTROBAN during pregnancy.

Contra-indications Hypersensitivity to BACTROBAN or other ointments containing polyethylene glycols. This BACTROBAN formulation is not suitable for opthalmic or intra-nasal use.

Side-effects Some minor localised effects such as burning, stinging and itching have been reported.

Storage BACTROBAN should be stored at room temperature (below 25°C). Not all presentations are available in every country. Further information is available on request. BACTROBAN is a trademark.

Beecham Pharmaceuticals
BRENTFORD · ENGLAND

001/34/2/10/89

References 1. Contemporary Dermatology, 1987, **1** (2): 32. 2. Proc. Int. Symp. on Bactroban, Excerpta Medica, 1984, 190. 3. Int. J. Derm., 1987, **26** (7): 472. 4. Curr. Ther. Res. Exp., 1987, **41** (1): 114. 5. Proc. Int. Symp. on Bactroban, Excerpta Medica, 1984, 141. 6. Roy. Soc. Med. Int. Cong. and Symp. 80, 173.