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MEDICAL AND PHARMACEUTICAL PRODUCTS.

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YOUR REF.

OUR REF. RRC/K

DEPARTMENT. Medical

MIDDLE EAR DISORDERS

Dear Sir,

we take this opportunity of bringing to your notice "OTOSCLEROL", a preparation which has occupied the attention of the medical Profession for some years in the treatment of middle ear diseases.

"OTOSCLEROL" is an active agent for the treatment of all subjective ear symptons, the active principles consisting of Bromide and phosphorus in combination with Cimicifugin which has a pronounced action on the general nervous system.

Recent Communication :- M.D., F.R.C.S., London, May 1929

> "From the private and institutional trials I have made with Otosclerol I have found same excellent in the treatment of auricular buzzings".

We enclose descriptive leaflet, and, for your information, Otosclerol is stocked by our depots as mentioned on the leaflet who will gladly supply you with samples or stocks as required.

Yours faithfully,

Coates & Cooper.

R.R. Coates

P.S .We also enclose literature re our new introduction "CALCIMINT".

CORTROPHIN "Z"

LONG-ACTING A. C. T. H.

FORM AND ADMINISTRATION

Cortrophin 'Z' is issued in a twin pack : a rubber-capped vial containing the A.C.T.H. and an ampoule holding the buffer which converts it into a long-acting suspension.

Exactly 1 cc. is withdrawn from the ampoule in a syringe and added to the contents of the rubber-capped vial. The 2 cc. of suspension which results then contains 40 i.u. of long-acting A.C.T.H. This is stable for at least a week under normal room conditions.

Dosage—In the clinical trials carried out most patients gave a full adrenocortical response to 20 i.u. Cortrophin 'Z' every second day. A very few required a larger dose but quite a number were maintained on half this dose or less. The average duration of activity was a full two days but again it was found that the response lasted considerably longer in some patients. The dose and frequency should therefore be adjusted by trial in each case ; reliance upon the patient's clinical response is usually satisfactory but where necessary the tests suggested overleaf will provide evidence of the response of the adrenal cortex.

FOR ALL INDICATIONS

Cortrophin is not a specific remedy for any disease but an agent for altering the response of the patient to disease.

An adrenal cortex already under the influence of stress may respond more or less than expected to exogenous Cortrophin. Sufficient should be given initially to produce the fullest possible remission. The technique of maintenance will depend on the needs and response of the patient, i.e. :

1. Full courses repeated at intervals as required.
2. Small maintenance doses every few days.
3. Combinations with courses of cortisone given alternatively or concurrently.

Cortrophin should never be omitted abruptly. If the treatment is stopped suddenly a short period of relapse and weakness constituting a rebound phenomenon may occur immediately, to be followed by an interval before the real relapse sets in.

INDICATIONS

Conditions in which life may be saved

Status asthmaticus
(Status asthmaticus is consistently interrupted and life often saved. Patients become more responsive to bronchodilators, e.g. adrenalin)

Snake bite (Dramatic relief of pain and local oedema.)

Delirium tremens

Agranulocytosis

Acute phases of dermatomyositis

Periarteritis nodosa

Acute phases of lupus erythematosus
(Prompt improvement in systemic manifestations. Skin lesions fade in a few weeks.)

Serum sickness and severe drug hypersensitivity

Acute pemphigus

Purpura haemorrhagica

Acute leukaemia (lymphatic) in children (with folic acid antagonists).

Severe burns

Conditions in which pain is relieved and function restored

Sympathetic ophthalmia (with local cortisone)

Acute self-limiting skin disease while awaiting remission

Severe gout in conjunction with colchicine (rapid relief of pain and inflammation)

Rheumatoid arthritis

"Frozen shoulder" (peri-articular fibrositis)

Shoulder-hand syndrome

CONTRA-INDICATIONS

1. Several cases of acute peritonitis originating from perforated peptic ulcers and from appendicitis have occurred during treatment with A.C.T.H., and the loss of pain-sense conferred by the hormone complicates diagnosis.
Cortrophin should therefore be used with great care in the presence of peptic ulcer, ulcerative colitis or diverticulitis.
2. Cortrophin should be used with great caution in the presence of bacterial infections. There is evidence that resistance to invasion is reduced.
3. Cortrophin should not be administered to patients suffering from diabetes or hypertension, including Cushing's syndrome, in which osteoporosis is a further contra-indication.

POSSIBLE UNDESIRABLE FEATURES

(a) Filling out and rounding of the face (so called moon-face), development of striae, hirsutism and pigmentation of the skin particularly in association with scar tissue, can usually be disregarded, and generally regress when treatment is withheld.
(b) Delay in healing of biopsy wounds or injuries or the breakdown of scar tissue may occur when large doses are given, but it is not common.
(c) Frank psychotic responses are unusual and only occur in unstable patients.
(d) Blood pressure increases in hypertensives and in all conditions where there is renal disease, but not apparently in other cases.
(e) Significant alkalosis is uncommon, but apparently more likely to occur in women.
(f) Excessive or undesirable oedema from sodium retention can be treated with oral or injectable diuretics. It is usually only a feature of the early days of treatment.
(g) Hypopotassaemia can be controlled by the administration of potassium salts.
(h) Nitrogen loss can be controlled by simultaneous administration of one of the nitrogen-retaining androgens such as testosterone or methylandrostenediol.

PRECAUTIONS IN ADMINISTRATION

It is advisable to X-ray the chest whenever possible before commencing treatment with Cortrophin. Dissemination of pulmonary tuberculosis has been recorded.

To avoid over-dosage the following observations may be valuable :—

1. Blood pressure observations.
2. Weight record.
3. Observations of oedema and other signs of hyper-corticalism (Moon-face, hirsutism, red striae, osteoporosis.)
4. Urine analysis, especially for sugar and calcium excretions.
5. E.C.G. for evidence of coronary inadequacy and potassium deficiency.
6. Laboratory investigation including blood counts, uric acid/creatinine ratio, serum sodium and potassium levels, 17-ketosteroid excretion.

A.C.T.H. THERAPY——

The effect of Cortrophin on the body, whether secreted or injected, depends upon the existence of sensitive adrenocortical tissue. The adrenal cortex

(continued on back cover

CONDITIONS IN WHICH A.C.T.H. HAS BEEN USED

INDICATION	EFFECTIVE IN	POSSIBLE USE IN	INEFFECTIVE IN	CONTRA-INDICATED IN
Allergy and Hypersensitive States	Allergic dermatitis	Lepra reaction	Epidermolysis bullosa	
	Allergic rhinitis and Polyposis	Paroxysmal haemoglobinuria		
	Angioneurotic oedema	Tropical eosinophilia		
	Asthma, status asthmaticus			
	Atopic dermatitis			
	Drug sensitisation			
	Exfoliative dermatitis			
	Hay fever			
	Loeffler's syndrome			
	Neurodermatitis			
	Serum sickness			
	Urticaria			
Blood	Agranulocytosis	Acute leukaemia	Acute porphyria	Sickle-cell anaemia
	Anaemia with other amenable listed diseases	Eosinophilic leukaemia	Aplastic anaemia	
	Cooley's anaemia	Erythroblastosis foetalis	Monocytic leukaemia	
	Haemolytic anaemias	Idiopathic hypochromic anaemia	Myelocytic leukaemia	
	Hypersplenic syndromes	Idiopathic thrombopenic purpura	Myelophthisic anaemia	
	Hypoferraemia of infection	Infectious mononucleosis	Primitive cell leukaemia	
	Lymphatic leukaemia in childhood (temporary effect)	Periodic neutropenia		
	Tropical eosinophilia	Pernicious anaemia		
		Thrombocytopenia		
Cardiovascular	Cranial arteritis	Non-thrombocytopenic purpura	Frostbite	Arteriosclerosis obliterans
	Periarteritis nodosa	Raynaud's disease	Hypotension, orthostatic	Congestive heart failure
	Phlebitis migrans	Temporal arteritis		Hypertension
	Thromboangiitis obliterans			Polyarteritis
				Vascular thrombosis
Endocrine	Non-Addisonian hypoglycaemia in children	Hyperinsulinism	Addison's disease	Acromegaly
		Hyperthyroidism	Adrenocortical insufficiency	Adrenal hyperplasia
	Thymic masses	Panhypopituitarism	Myxoedema (primary)	Adrenogenital syndrome
		Pituitary myxoedema	Ovarian agenesis	Cushing's syndrome
		Thyroiditis	Pancreatic fibrosis	Diabetes mellitus
			Thyrotoxicosis	Hirsutism in females
				Primary hypothyroidism
Eye	Cyclitis	Behcet's syndrome	Angiospastic retinopathy	Syphilitic interstitial keratitis
	Iridocyclitis, acute	Chorioretinitis	Cataract	
	Iritis	Choroiditis	Corneal oedema	
	Keratitis (non-syphilitic)	Disciform degeneration		
		Endophthalmitis	Keratoplasty	

INDICATION	EFFECTIVE IN	POSSIBLE USE IN	INEFFECTIVE IN	CONTRA-INDICATED IN
	Ocular surgery, trauma	Iridocyclitis, chronic	Optic and retrobulbar neuritis	
	Ocular tuberculosis	Keratoconjunctivitis		
	Sclerokeratitis	Reiter's syndrome		
	Secondary glaucoma	Retinitis pigmentosa		
	Sympathetic ophthalmia	Retrolental fibroplasia		
	Uveitis following herpes zoster	Scleromalacia		
	Uveitis, non-granulomatous	Sjögren's syndrome		
	Vernal conjunctivitis	Thyrotoxic ophthalmopathy		
		Tuberculous uveitis		
		Uveoparotid tuberculosis		
Gastro-Intestinal	Non-tropical sprue	Pseudopolyposis of colon	Polyposis of colon	Peptic ulcer
	Regional enteritis	Regional ileitis	Rectocolitis haemorrhage	
		Regional jejunitis		
		Ulcerative colitis		
Infection		Chagas' disease (Brazilian trypanosomiasis)	Diphtheria	Blastomycosis
		Leprosy	Equine encephalomyelitis	Malaria
		Newcastle disease	Influenza virus	Peritonitis } except for shock
		Viral encephalitis (e.g. post-vaccinal)	Moniliasis	Septicaemia } except for shock
		Smallpox	Pneumococcal pneumonia	Streptococcal infections
		Trichinosis	Poliomyelitis	Tuberculosis
		Typhoid fever	Rickettsial infections	Varicella
			Virus pneumonia	
Liver		Chronic viral hepatitis	Acute infectious hepatitis	
		Homologous serum hepatitis	Alcoholic cirrhosis	
		Laennec's cirrhosis	Biliary cirrhosis	
Metabolism	Gout	Calcinosis universalis		
		Essential lipaemia	Intermediary metabolism	Scurvy
		Glycogenosis (v. Gierke's disease)		
Muscular	Dermatomyositis	Myotonia atrophica	Polymyositis	
	Shoulder-hand syndrome	Myotonia congenita	Progressive muscular dystrophy	
	Subacromial bursitis			
	Tendinitis—"Frozen shoulder"			

INDICATION	EFFECTIVE IN	POSSIBLE USE IN	INEFFECTIVE IN	CONTRA-INDICATED IN
Neurological and Neuromuscular	Menopausal myopathy	Dystrophia myotonica	Amyotrophic lateral sclerosis	
	Tabes dorsalis			
		Epilepsy—grand mal	Diabetic neuropathy	
			Epilepsy—petit mal	
		Guillain-Barré syndrome (radiculoneuritis)		
			Meningitis	
		Myasthenia gravis (some improvement has been observed after the end of a course of ACTH)	Multiple sclerosis	
			Otitis	
			Otosclerosis	
		Postherpetic neuralgia	Parkinsonism	
			Polyneuritis	
			Progressive muscular atrophy	
			Tay-Sachs disease	
			Wilson's disease	
Neuropsychiatry	Acute alcoholism	Anxiety states	Alcoholism with ascites	
	Anorexia nervosa	Chronic alcoholism	Depression	
	Delirium tremens		Korsakoff's psychosis	
	Drug addiction		Manic depressive states	
			Schizophrenia	
Respiratory (see also under Allergy)	Berylliosis	Laryngeal oedema	Bronchiectasis	Pulmonary tuberculosis (cases showing hypersensitivity to streptomycin and P.A.S. may be treated with these substances under the protection of Cortrophin)
	Bronchial asthma	Laryngeal tuberculosis	Chronic lung disease with pulmonary emphysema	
		Silicosis	Laryngeotracheitis	
Rheumatism and Arthritis	Felty's syndrome	Osteoarthritis	Rheumatic carditis with congestive heart failure	
	Gout	Panniculitis (Weber-Christian disease)		
	Mumps arthritis		Tuberculous arthritis	
	Rheumatic fever	Psoriatic arthritis		
	Rheumatoid arthritis	Reiter's syndrome		
	Spondylitis	Sydenham's chorea		
	Schoenlein's disease			
	Still's disease			
Skeletal	Osteitis pubis	Infantile cortical hyperostosis	Eosinophilic granuloma of bone	Osteoporosis
				Osteomalacia
Skin (see also under Allergy)	Chronic discoid lupus	Alopecia	Discoid and lichenoid dermatoses	Acne
	Erythema multiforme	Dermatitis herpetiformis	Herpes simplex	Hyperpigmentation
		Herpes gestationis	Herpes zoster	
	Erythema nodosum			

INDICATION	EFFECTIVE IN	POSSIBLE USE IN	INEFFECTIVE IN	CONTRA-INDICATED IN
		Keloids	Kaposi's disease (xeroderma pigmentosum)	
	Exfoliative dermatitis	Lichen planus		
	Hodgkin's disease of skin	Lupus vulgaris	Mycosis fungoides	
		Pemphigus vegetans	Pemphigus foliaceus	
	Leukaemia cutis	Pemphigus vulgaris	Psoriasis vulgaris	
	Lupus erythematosus disseminatus (acute)	Pruritus, anogenital		
	Nummular eczema	Psoriasis		
	Scleredema	Sarcoidosis ; Boeck's sarcoid		
	Seborrhoeic dermatitis	Schamberg's disease (progressive pigmentary dermatosis)		
	Sumac dermatitis			
		Scleroderma		
Surgery	Burns	Adhesions	Postoperative anorexia	**Wound healing**
	Shock from acute infections, including fulminating pneumonia, acute peritonitis, and septicaemia	Craniopharyngioma (surgery of)		
		Radiation sickness		
	Surgical shock			
	Traumatic shock			
Tumours, Malignant	Lymphoma	Ewing's tumour	Breast cancer	
	Malignant thymoma	Hodgkin's disease	Cancers, various	
		Lymphogranuloma	Lymphoblastoma	
		Lymphosarcoma	Melanoma	
		Multiple myeloma	Neuroblastoma	
		Pancreatic adenoma	Non-lymphomatous sarcoma	
		Plasma cell myeloma	Paget's disease of nipple	
		Squamous cell carcinoma	Sarcoma, reticulum cell	
Urogenital	Urethritis of Reiter's syndrome	Interstitial cystitis (Hunner's ulcer)	Acute glomerulonephritis	
		Nephrotic syndrome	Chronic glomerulonephritis	
Miscellaneous	Snake bite	Arachnidism		**Pregnancy toxaemia**
		Barbiturate poisoning	Infertility	
		Geriatrics, general	Peritonitis, benign paroxysmal	
		Hyperemesis gravidarum	Polyserositis	
		Lipomelanotic reticulosis	Prematurity	
		Secondary amenorrhoea	Wasp stings	

NOTE. As references to ACTH now amount to over 6,000 it is impracticable to list them all, but bibliographies can be supplied on special subjects.

continued from front cover)
is stimulated both as regards quantity and quality of output of its steroidal hormones. Of these the most important for the protection of the body against toxins, the effects of stress, shock, starvation, etc., are the gluco-corticoids or carbohydrate-metabolism-affecting hormones. These steroid hormones possessing an oxygen atom attached at the conventional carbon-11, in their turn modify the reactions of the body, controlling undesirable over-response both of tissues and senses. The loss of pain is one of the most striking features. The most potent substance belonging to this group which occurs in the human is probably Kendall's compound F, which is structurally but very slightly different from the synthetic compound E, cortisone.

TESTS OF ADRENOCORTICAL SENSITIVITY TO CORTROPHIN AND BIOCHEMICAL CHANGES INDUCED

1. Direct—estimation of the excretion rate of 11-oxysteroids (from the adrenal cortex).

2. Probably direct—estimation of 17-ketosteroids (degradation products of androgens from the adrenal cortex and gonads and probably also of 11-oxycorticoids).
Both these tests require accurately collected urine samples and the tests are tedious.

3. Indirect—due to changes brought about in the body by an increased adrenocortical function.

(a) Clinical remission of symptoms.

(b) Eosinophil cell depletion in the peripheral blood (Thorn test). Circulating eosinophils should be reduced by 50% in 4 hours after Cortrophin 25 i.u.; in 8–12 hours after Cortrophin Z 20 i.u.

Other blood cell changes occur but are less characteristic ; lymphocytes tend to be diminished and polymorphs to be increased.

(c) Biochemical changes which occur with considerable regularity, but are not specific :—
Uric acid increased in blood and urine.
Free and esterified cholesterol increased in serum.
Sodium retention with resultant oedema in many cases, often observed only early in treatment and followed by diuresis.

Increased potassium excretion to the stage at which interference with muscle activity may be serious ; the first indication of this may be electrocardiographic changes. Administration of potassium salts by mouth is advisable during Cortrophin therapy.

Decreased sugar tolerance and increased insulin tolerance.
Disturbed albumin/globulin ratio reverts towards normal. Elevated serum globulin decreased.
Other effects of greatly increased adrenocortical function are :—
1. Interference with the normal barriers to infection.
2. Interference with healing processes or even breaking down of scars. This appears to be due to a direct effect upon the fibroblasts and collagen fibres.
3. Hyaluronidase is destroyed or checked : it is possible that this is an important element in the effects of adrenocortical hormones on joint stiffness.
4. Haemopoiesis is stimulated. Haemoglobin and erythrocytes are increased.
5. Lymphocytic tissue throughout the body is depressed.
6. Mental changes may result ; euphoria usually occurs initially with restlessness. Manic or depressive psychotic changes take place in some cases usually after prolonged treatment.

All the conditions which have been found to be brought into remission by Cortrophin or cortisone relapse more or less quickly upon cessation of treatment, unless the illness is self-limiting or spontaneous remission happens to coincide with treatment. Continued treatment induces the clinical picture of Cushing's syndrome with all its disadvantages. Unless, therefore, it can be found possible to control the symptoms completely or partially by intermittent or small doses, Cortrophin (and cortisone) should at present only be regarded as a life-saving measure in the acute phases of many of the conditions listed.

Evidence of depression or exhaustion of the adrenal cortex may be suggested by any or all of the biochemical tests described above during any acute or prolonged illness, and in some of these cases it may be considered advisable to administer cortisone substitutively before attempting to stimulate the patient's own adrenal cortex.

CORTROPHIN (A.C.T.H.) & CORTISONE

Although the effects of Cortrophin are brought about by increased adrenocortical secretion, certain differences have been shown in the clinical use of Cortrophin and cortisone.

Cortrophin is a more economical therapeutic agent for most purposes than cortisone, the international standard material being from three to eight times as effective as cortisone weight for weight.

Cortrophin stimulates the adrenal cortex, but cortisone, being but substitutional, has the reverse tendency.

Eosinophil depression is less consistent with cortisone than with Cortrophin, tending to revert to pre-treatment levels during continued dosage.
Sodium retention occurs more regularly with Cortrophin than with cortisone.

17-Ketosteroid excretion is reduced by cortisone unless very large doses are given.

Cortrophin produces less change in the concentration of serum lipids and cholesterol than does cortisone.

Whenever cortisone is given, Cortrophin should be given also to avoid the atrophy of the patient's own adrenal cortex which results from pituitary depression by cortisone. This dose of Cortrophin should be stepped up just before withdrawal of cortisone, and thereafter reduced only slowly.

CONSTIPATION IN - INFANCY -

THE satisfactory results obtained with Mellin's Food in constipation in Infancy is common knowledge to a vast number of physicians; but to those who are not familiar with the use of Mellin's Food in such conditions, the following suggestions, based upon careful observations, may be helpful.

CONSTIPATION IN THE VERY YOUNG.

In the hand rearing of infants, constipation is at once perhaps the commonest and most baffling difficulty which has to be dealt with. At one time or other it will arise, generally at first in a mild form, and every effort to remove the condition seems to be a failure, even in certain cases to provoke a greater virulence of the attack.

This apparent intractability of constipation in spite of drastic and complete changes in the diet is more readily understood when it is recognised that the condition can be set up by a variety of causes of the most diverse character, practically all at the root being errors in the food constituents.

In the following notes the principal deficiencies are indicated in the hope that light thrown upon the digestive processes may assist in dealing with particular cases as they arise.

Excessive Protein Splitting. This form of constipation is extremely common. It is easily recognised by the dry, hard, stools, generally accompanied by much wind and odour often of a most

offensive kind. The child suffers much from colic, and is subject to great discomfort. The stools may vary in colour from brown to green. The condition is due to a preponderance of those forms of bacteria which decompose protein with formation of gas. Thus the proteins, instead of being digested and used in the system, are broken up by the bacteria into products largely valueless for nutrition; these are expelled with difficulty and the child, although receiving plenty of food, becomes starved.

To remedy this condition it is necessary to induce the growth of healthy acid-forming organisms in the intestinal tract. These will gradually suppress the unhealthy gas-forming variety and a return to normal health will follow.

To carry out this object the use of sterilised, dried or condensed milks should be stopped and fresh raw milk substituted, modified by addition of a thoroughly malted carbohydrate. In bad cases even fresh milk must be diluted with much water.

Fat Wastage.

The stools in this case are generally of a greyish colour, soap-like and greasy. The odour is sour but not usually offensive. This form of constipation is also

caused by improper fermentative action, though not necessarily by the same variety of bacteria. It is more commonly noticeable when whole milk or rich milk foods are being given.

Briefly, the bacterial action causes a separation of lime from the milk ; this lime combining with the fats present, produces hard, curdy, insoluble soaps. These curds form the white cheesy particles noted in the stools. As a consequence of this action the child is both fat and lime starved, and in very pronounced cases the daily loss of lime may even equal the total intake. The general methods for removing this type of constipation consist in a reduction of the fat by removal of some of the cream, dilution of the milk to attenuate the proteins, and addition of Mellin's Food, the maltose and dextrine of which will rectify this form of constipation.

Maltose by stimulating the acidic fermentation, is a protein sparer and prevents both the saponification of fats and precipitation of lime. Maltose is most readily assimilated by children and is the only sugar which can be prepared by purely biological methods.

Unsuitable Carbohydrates. Not all carbohydrates or sugars are fit for use as an adjuvant to milk for infants' use. Only such as are readily available to the digestive ferments as developed in the infant can safely be employed. Starchy foods are most unsuitable and very likely to induce constipation by reason of the low power possessed by the infant in transforming starch into soluble forms.

Cane sugar again is unsuitable because young infants do not secrete invertase. Manufactured milk sugar is not physiologically identical with the fluid carbohydrates of milk and the process of its manufacture involves the use of strong reagents.

Malt sugar, however, possesses many advantages. It is possible to prepare it from cereal products by purely natural processes and without any chemical addition. It is readily used by the infantile digestive powers.

It strongly favours the development of healthy acidic fermentation and forms a good medium for the growth of lactic ferments. It is, therefore, the best modifier which can be employed to adjust the

balance of food constituents in cow's milk to human needs.

Lack of Energy.

Constipation may appear to be the result of sluggish muscular activity in the intestines. This, however, is only a secondary effect of the activation of deleterious bacteria. The products of their activity act as poisons upon the muscular walls, causing toxaemia and hence the whole system is reduced to a torpid condition. The cultivation of healthy acid-forming organisms is the only means of removing this lethargy.

The general treatment of constipation turns, therefore, upon the extirpation of those types of gas-forming and protein-destroying bacteria, which lower the intestinal tone, and cause food wastage by their activities.

This can only be done by encouraging the development of those other forms of bacteria which produce healthy lactic fermentations; these will in time suppress the noxious forms and acting as protein, fat, and lime sparers, will secure the complete utilisation of these important bodies for the full nutrition of the system.

Prevention of constipation is only to be secured by careful attention to proper balance in the diet so as to ensure that the correct type and quantity of carbohydrates are present to maintain healthy fermentations.

The best to use, and one which has already been proved during many years to be of the highest possible value in all cases of constipation, whether recent or old standing, is Mellin's Food, a pure malted cereal extract perfectly free from starch and other difficultly digestible carbohydrates.

Mellin's Food with fresh milk in properly regulated proportions has been proved in numberless instances to give the best results in all types of constipation.

Samples willingly sent free on request by :—

MELLIN'S FOOD, LTD., Peckham, London, S.E.

For the Medical Profession only.

TRADE "OTOSCLEROL" MARK

CIMICIFUGIN . . .	6·66%
BROMUM	36·3%
PHOSPHORIC SALTS . .	40%

INDICATED IN THE TREATMENT OF

Buzzing in the Ear, Deafness and other EAR SYMPTOMS

arising from nervous or sclerotic causes or from auto-intoxication; also for

Middle Ear Disorders and Nervous Sleeplessness

Sole Concessionnaires for the United Kingdom and Dominions:

COATES & COOPER

IMPORTERS & EXPORTERS OF MEDICAL AND PHARMACEUTICAL PRODUCTS

41, GREAT TOWER STREET, LONDON, E.C. 3.

Telephone No.: Royal 2968. *Telegrams:* "Synthetica," Bilgate, London.

TRADE **"OTOSCLEROL"** MARK

OPINIONS still differ as to the nature of the otosclerotic processes in the ear. Many authors, including Cornel, Werhofsky, Heimann and Schier consider that otosclerosis is not merely a local condition. Manasse; in his well-known work on the subject, states also that otosclerosis cannot in any way be looked upon as merely a local condition, but as arising from some derangement of the nervous system.

Since the etiology of a disease must always provide the suggestion for the scientific treatment, it is obvious that a main point of treatment must be to induce a change in the nervous system. Otosclerol provides a means of scientific treatment and has been thoroughly tried by many clinicians.

The following are selected from a large number of published reports on the preparation :—

MEDICAL OPINIONS.

Prof. Cav. GIUSEPPE TURTUR, *Graduate Teacher of the Otorinolaringojatric Clinic of the Royal University of Rome, Chief Specialist at the Fate-Bene-Fratelli Hospital.*

. . I do not hesitate in stating that I have always been satisfied with same in cases where there was a clear indication and as assistant to the usual remedies, whether in form of chronic catarrh with adherencies and initial anchylosis of the stapes, or in the internal original form and otosclerosis.

" In particular in the latter case, in which pathogenesis must still be carefully considered, it would seem that the Otosclerol preparation exercises the greatest influence in regard to a general action of its component parts and perhaps also with regard to a

modification or attenuation of what is to be defined and stabilised through the osteospongiotic process.

" . . . the Otosclerol preparation represents for the moment a useful combination of medicines responding to a scientific and objective indication. Even in cases of painful iperacusis and general iperestesia accompanied by tormenting auricular buzzings, without injury to the hearing organ, I have found it to be equally good."

Dr. SANTO VEZZINI, *Otorinolaringojatric Clinic Royal University of Genoa.*

" Otosclerol is indicated in chronic ear diseases including those cases which have proved refractory to other carefully carried out treatments and which are accompanied by buzzing noises in the ears (subjective noises)—whether their origin is the sequela of a purulent ear disease, whether due to a general disturbance of the whole organism or caused by an infectious toxic association . . . . and it should be tried in every case of otosclerosis."

Prof. RICCARDO PAOLUCCI, *Florence.*

" I have pleasure in stating that in two cases of ear affections, of nervous and inflammatory origin, I have successfully used Otosclerol, ordinary and iodised.

" I have been in particular amazed at the rapid disappearance of the subjective troubles (buzzing and giddiness) and decrease of the local symptoms."

Dr. THEIMER, *Oest. Aerz. Zeit. No. 7.*

" Otosclerol certainly has an influence on the subjective ear symptoms. I give one tablet thrice daily and increase this dose to five tablets thrice daily, the latter dose being continued for some time."

Dr. ZALESKY, *Prague University Ear-Clinique.*

" As a result of investigations in a large number of cases of pure otosclerosis I am convinced of the value of Otosclerol. I give one tablet half-an-hour after each meal, later increase this dose and continue the medication for two to three years."

Dr. DENKER'S Text-Book on Ear Diseases.

" Otosclerol has a favourable influence on the subjective ear symptoms."

Dr. SENATOR, *Med. Klinik No.* 46.

"Otosclerol does not deserve to be treated with the scepticism inevitable with other ear remedies. In my hands it has been attended with very satisfactory results. I give one to five tablets three times daily."

Dr. NATHAN, *Ars. Medici. No.* 4.

"For the relief of the subjective symptoms of otosclerosis Otosclerol can be thoroughly recommended."

Dr. TRAUGOTT, *Nervous Sleeplessness.*

"Otosclerol removes the sleeplessness associated with subjective ear symptoms."

Hitherto no agent has been available which provides the active combination of phosphorus and bromide, together with the special action on the nervous system of cimicifugin. *Otosclerol is an active agent for the treatment of all subjective ear symptoms; even in chronic cases the preparation should be tried. It may be employed in conjunction with the local treatment of the ear affection. The administration of Otosclerol can be continued as long as circumstances demand it.*

M.D., F.R.C.S., LONDON. May, 1929.

"From the private and institutional trials I have made with Otosclerol, I have found same of excellent service in the treatment of auricular buzzings."

Doses of Otosclerol.

At first one tablet three times a day, increased gradually to five tablets three times a day, taken after meals.

Packings and Prices of Otosclerol in U.K.

Otosclerol tablets (each 3 gr.) in original tubes of 50 tablets 4/6
Hospital packings, bottles of 500 tablets 40/-

Physicians' Samples on application to Agents.

Dominion Depots:

India.—Calcutta: Frank Ross, Ltd., 15, Chowringhee.
Bombay: Thomson & Taylor, Ltd., Esplanade Road.
Canada.—W. Lloyd Wood, Ltd., 64/66, Gerrard Street, E., Toronto.
Australia.—Australian Medical and General Distributors, Ltd., 9, Bligh Street, Sydney.
South Africa.—Lennon, Ltd., Capetown, Johannesburg and Branches.
New Zealand.—The Dominions Dental Supply Co., Box 205 G.P.O., Wellington and Branches.

Manufactured by

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1926, Nummer 30, pp 1236/1237.
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Intestinol

A new remedy for dyspepsia and flatulence

By Prof. Dr. R. Hirsch, Berlin

Although dyspeptic derangements are common amongst all classes of the community, the dwellers in what are otherwise quite healthy towns and cities, are particularly liable to these disturbances accompanied by the undue generation of gases in the digestive tract.

Charcoal plays an important part in the medicamental treatment of these conditions frequently however without success and for the obvious reason that it does not combat the cause of the ailment, but merely absorbs the toxic products of metabolism.

Intestinol should be welcomed as representing a medicament which acts on the causative, and promotes the digestive process.

Intestinol is a pancreatic preparation combined with animal charcoal, its pancreatic content being dosaged according to Fuld-units. It furthermore contains secretin (the hormone of the duodenal mucous membrane) and fellinic acid salts:

each tablet: –

0.1	gram	Pancreatinum sicc.
0.15	„	Carbo animalis.
0.05	„	Secretin.
0.05	„	Fellinic acid salts.

The secretin contained in the preparation, stimulates pancreatic secretion of the digestive ferments and encourages the elimination of bile by the liver. The fellinic acid salts as is well known, possess the property of supporting the digestive efficiency of the ferments and stimulating an increased motoric and peristaltic function of the intestines.

The pharmacological and biological tests on Intestinol were carried out by Prof. Joachimoglu at the Pharmacological Institute of Berlin University. Firstly to determine whether the digestive action of the ferments contained in Intestinol was affected by the simultaneous presence of charcoal. The researches both, in vitro, and on animals showed that the digestive action of the pancrin ferments contained in Intestinol is not influenced by the charcoal.

This is in accordance with the researches of Winckel with regard to the digestive power of the trypsin absorbed by charcoal.

Winckel proved that the presence of animal charcoal does not influence the effect of trypsin, he even demonstrates as a result of his observations that the charcoal absorbed trypsin, is more efficient in use than the pure ferment which is almost totally destroyed by the gastric juice. The charcoal protects the ferments from attack by the gastric juice, so that they are able to exert their full effect in the alkaline intestine.

As is seen, even a charcoal trypsin absorbate is physiologically effective. The pancrin ferments contained in Intestinol are present in a form

which protects them against the gastric juice; they are not however absorbed by the charcoal but form a dry mixture with the animal charcoal.

Prof. Joachimoglu has very kindly placed the following tests carried out by him at our disposal.

Test. 1. A saturation of Intestinol was tested to determine its digestive power according to the American Pharmacopoeia and this was compared with the digestive power of an equivalent quantity of a saturation of pure pancrin. No difference in the digestive effect of Intestinol and pancrin was observable.

Test. 2. 3.5 grm. Intestinol tested according to the Fuld-Gross method, yielded a digestive effect of 20,000 units, corresponding to the same amount of pancrin contained in Intestinol.

1 grm. pancrin tested in the same manner also yielded 20,000 units. This indicates that despite its admixture of animal charcoal Intestinol entirely gives off its ferments to the weak alkaline water. The animal charcoal does not disturb the fermentative action.

Test. 3 In order to prove the chief factor viz. that the ferments contained in Intestinol also exert their effect on the human body in the presence of charcoal, a dog weighing 10 kg was given Intestinol mixed with meat. After 24 hours the black faeces were suspended in a buffer solution of pH 7.8; (glycocol and sodium hydrate) the suspension with its entire charcoal content was then tested according to the American Pharmacopoeia. The result showed that the suspension no longer possessed any digestive power whatever. The Intestinol had therefore transferred its entire ferments to the organism of the test animals. No ferments could be detected in the charcoal residue of the faeces.

The results of these experiments are in keeping with the practical clinical experiences obtained since last autumn.

The generation of gas in the intestines connected with severe digestive disturbances accompanied by nausea, headache, sensations of abdominal pressure etc. etc. are more beneficially influenced by Intestinol than by a simple charcoal preparation. Intestinol permits ailing individuals to partake of even such foods as are difficult of digestion and otherwise to be avoided, without the usual resulting disturbances. It is advisable to take these tablets, which are quite convenient to swallow: —

One or two tablets 3 times daily after the principal meals. If taken fasting in the morning, they also exert a beneficial effect.

In special cases where dietary treatment alone or physical procedures, particularly abdominal gymnastics in the way of breathing exercises, are not applicable, Intestinol medication forms a valuable addition to our pharmaceutical treasury.

DR. GEORG HENNING, BERLIN-TEMPELHOF
KOMTURSTRASSE 19-20

Chemische und pharmazeutische Fabrik. Dr. Georg Henning, Berlin-Tempelhof

Intestinol «Henning»

Nuevo preparado de fermentos pancreáticos y secretina duodenal.

En los trastornos de la digestión y alteraciones del metabolismo, con malestar, dolor de cabeza, sensación de presión en el vientre, flatulencias y exceso de formación de gas en general, tómese Intestinol.

Bajo la acción del Intestinol pueden disfrutarse sin temor alguno hasta los alimentos más difíciles de digerir.
Con los alimentos son absorbidos hidratos de carbono, grasas y albúmina. Para poder aprovechar estas sustancias nutritivas en necesario que sean digeridas antes, es decir, desintegradas en sus diferentes componentes químicos, porque el cuerpo no es capaz de asimilar productos de composición complicada sino las sustancias de su desdoblamiento.
Las grageas de Intestinol contienen los fermentos de la glándula pancreática y del duodeno, carbón animal y sales de ácido colálico.
El Intestinol es un producto de composición tan adecuada para el tratamiento de los trastornos de la digestión y del metabolismo, que con él puede normalizarse la digestión consiguiéndose así un aprovechamiento completo de los alimentos y evitándose las enfermedades del estómago, hígado, bilis e intestinos.
La actividad o función digestiva es posible gracias a la acción de fermentos, en particular pancreáticos, que desdoblan en sus componentes tanto las grasas como las albúminas y los hidratos de carbono; los fermentos del páncreas son auxiliados eficazmente en esta actividad por la bilis, mediante la cual son hechos activos.
El fermento del duodeno, la secretina, excita al páncreas a la formación de fermentos digestivos y al hígado a la secreción de bilis.
El carbón animal absorbe los productos venenosos del metabolismo, las sustancias en putrefacción y los gases, haciéndolos así inofensivos.
El Intestinol se encuentra en el comercio en tabletas grageadas, fáciles de tragar.

Dosificación: Después de cada comida 1—2 tabletas
En casos especiales 3—4 tabletas.
El Profesor R. Hirsch ha comprobado la buena tolerancia del Intestinol también por parte del estómago en ayunas.
Cada tableta contiene:

0,1 gr. Pancreatina sicc.	0,05 gr. sales de ácido colálico
0,05 gr. Secretina	0,15 gr. carbón animal

El Prof. R. Hirsch considera la medicación por el Intestinol como un enriquecimiento precioso de nuestro arsenal terapéutico.

Literatura: Prof. Dr. R. Hirsch, Berlino, Münch. Mediz. Wochenschrift 30/1926. Dr. O. Nemetz, Viena, Fortschritte der Medizin 6/1926, Dr. M. Winkel, M. M. W. 50/1912. Dr. Carl Müllern, Viena, (Ambulancia Central del Ejército) Medizinische Klinik Nr. 11/1928. Dr. Giesemann, Eisenach, Fortschritte der Therapie, Heft 17/1928. Dr. Kadletz, Viena, Wiener Klinische Wochenschrift 37/1928. Dr. Obstmayer u. Dr. Molnar, Viena, Medizinische Klinik Nr. 50/1928. San. Rat Dr. Kittsteiner, Hanau, «Der Praktische Arzt» Heft 15/1928. Dr. Baumwell, Alland, «Die Tuberkulose» Nr. 7/1928. Dr. Böhm, Berlino, Münch. Med. Wochenschrift Nr. 6/1929.

Chemische und pharmazeutische Fabrik. Dr. Georg Henning, Berlin-Tempelhof

Intestinol «Henning»

une nouvelle préparation de pancréas-sécrétine.

Contre les douleurs de la digestion et les troubles des échanges nutritifs qui se manifestent par des malaises, des maux de tête, une sensation de pesanteur dans le ventre, du ballonnement et une quantité de gaz exagérée qu'on prenne de l'intestinol.

Grâce à l'action de l'intestinol on peut prendre sans douleurs même des aliments difficiles à digérer. Les aliments contiennent de l'albumine, des graisses et des hydrates de carbone. Avant d'être assimilés ces corps doivent tout d'abord être digérés c. à d. être décomposés en leurs éléments chimiques parce que l'organisme n'est pas capable d'assimiler des substances à composition compliquée, mais seulement leurs éléments. Les dragées d'intestinol contiennent les ferments du pancréas et du duodénum, du charbon animal et des sels biliaires.

L'intestinol est un médicament si judicieusement composé pour le traitement des troubles de la digestion et les échanges nutritifs, qu'il peut régler la digestion, faire assimiler entièrement la nourriture et prévenir les affections de l'estomac, du foie, de la bile et de l'intestin.

La digestion se fait par les ferments et en grande partie par les ferments du pancréas, qui décomposent la graisse, l'albumine et les hydrates de carbone en leurs éléments; l'activité des ferments du pancréas est efficacement secondée par la bile dont la présence leur est nécessaire pour devenir actif.

Le ferment du duodénum, la sécrétine, provoque la sécrétion des ferments de digestion du pancréas et celle de la bile dans le foie.

Le charbon animal se combine aux produits des échanges nutritifs toxiques, tels que les produits de décomposition et les gaz de l'intestin et les rend inoffensifs.

L'intestinol se trouve dans le commerce sous forme de pastilles-dragées agréables à prendre.

Mode d'emploi: Après chaque repas 1—2 pastilles.
Dans certains cas 3—4 pastilles.
Le Prof. R. Hirsch-Berlin a constaté que l'intestinol peut aussi être pris à jeun.

Chaque pastille contient:

0,1 gr de pancréas sèche	0,05 gr de sel biliaires
0,05 „ „ sécrétine	0,15 „ „ charbon animal.

Le Prof. R. Hirsch déclare que la médication à l'intestinol est un précieux enrichissement de notre arsenal thérapeutique.

Littérature: Prof. Dr. R. Hirsch, Berlin, Münch. Medizin. Wochenschrift, 30/1926. Dr. O. Nemetz, Vienne, Fortschritte d. Medizin 6/1926. Dr. M. Winkel, Münch. Med. Wochenschr. 50/1912. Dr. Carl Müllern, Vienne (Zentralfachambulatorium des Bundesheeres) Medizinische Klinik Nr. 11/1928. Dr. Giesemann, Eisenach, Fortschritte der Therapie, Heft 17/1928. Dr. Kadletz, Vienne, Wiener Klinische Wochenschrift 37/1928. Dr. Obstmayer u. Dr. Molnar, Vienne, Medizinische Klinik Nr. 50/1928, San. Rat Dr. Kittsteiner, Hanau, «Der Praktische Arzt» Heft 15/1928. Dr. Baumwell, Alland, «Die Tuberkulose» Nr. 7/1928. Dr. Böhm, Berlin, Münch. Med. Wochenschrift Nr. 6/1929.

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Chemische und pharmazeutische Fabrik. Dr. Georg Henning, Berlin-Tempelhof

Intestinol »Henning«

Pankreas-Sekretin-Kohle-Präparat

Zusammensetzung	Wirkung
Sekretin Hormon der Duodenalschleimhaut	fördert Pankreas- und Gallensekretion
Pankreatin	spaltet Fett, Eiweiß und Kohlehydrate
Gallensaure Salze	steigern Pankreas- und Gallensekretion
Tierkohle	bindet Fäulnisstoffe und Darmgase

1 Tablette enthält: 0,1 g Pankreatinum sicc.
0,05 g Sekretin
0,05 g gallensaure Salze
0,15 g Tierkohle

Intestinol „Henning" hat fermentative und adsorbierende Eigenschaften. Darauf beruht seine therapeutische Überlegenheit den reinen Pankreas- und Kohlepräparaten gegenüber.

Intestinol „Henning" wirkt nicht nur durch Substitution von Pankreas und Galle. Sein Gehalt an Sekretin macht es zu einem physiologischen Stimulans der Anhangdrüsen, die für die Verdauung wichtig sind.

Intestinol „Henning" verbessert und reguliert also die Gesamtverdauung!

Indikationen: akute, subakute und chronische Verdauungsstörungen ohne anatomische Grundlage, Fermentschwäche, Meteorismus, Labiler Gastro-Intestinal-Traktus, Gasbildung im Darm mit Übelkeit, Kopfschmerz, Druckgefühl im Leib — Flatulenz, Diätfehler bei Kindern, arteriosklerotisch bedingte Verdauungsstörungen, Rekonvalescenz nach Darminfektionen, Dyspepsie der Herzkranken.

Dosierung: 3 mal täglich 1—2 Tabletten nach dem Essen mit Wasser, Tee oder ähnlichem zu nehmen. In besonders hartnäckigen Fällen Steigerung der Einzeldosis bis zu 4 Tabletten.

Literatur:

Prof. Dr. R. Hirsch, Berlin, M. M. W. 30/1926.
Dr. Nemetz, Wien, Fortschritte der Medizin Nr. 6/1926.
Dr. M. Winkel, M. M. W. 50/1912.
Dr. Müllern, M. Kl. 11/1928.
Dr. Giesemann, Eisenach, Fortschritte der Therapie, Heft 17/1928.
Dr. Kadletz, Wien, Wiener Klinische Wochenschrift 37/1928.
Dr. Obstmayer u. Dr. Molnar, Wien, Medizinische Klinik Nr. 50/1928.
San. Rat Dr. Kittsteiner, Hanau, „Der Praktische Arzt", Heft 15/1928.
Dr. Baumwell, Alland, „Die Tuberkulose„ Nr. 7/1928.
Dr. Böhm, Berlin, Münch. Med. Wochenschrift Nr. 6/1929.

Chemische und pharmazeutische Fabrik. Dr. Georg Henning, Berlin-Tempelhof

Intestinol "Henning"

A new preparation of Pancreas-Secretin.

Take Intestinol in cases of lack of assimilation or digestive troubles which are accompanied by sickness, headaches, pressure in the abdomen, flatulence, and increased formation of gases in general.

Under the influence of Intestinol even heavy food can be taken with impunity. As is well known we take with our food albumen, fats, carbohydrates, and in order to utilize these food stuffs they must be digested, that is to say, they must be split up into their chemical components, because the body is not able to assimilate variously compounded substances as such, but only their elements.

The Intestinol-dragées contain the ferments of the Pancreas gland and of the Duodenum, animal charcoal and cholic acid salts.

Intestinol is a remedy so well adapted for the treatment of assimilatory troubles and disturbances that digestion can be regulated, food can be utilized and complaints of the stomach, liver, gall and intestines can be avoided.

The action on the digestive system takes place through the ferments and especially through the ferments of the Pancreatic gland which split up albumen, fats and carbo-hydrates into their ingredients; in this action the pancreatic ferments are effectively assisted by the gall with the help of which they become active.

The ferment of the Duodenum, the "Secretin", stimulates the Pancreas in the production of the digestive ferments and the liver in the production and the flow of bile.

Animal charcoal neutralizes poisonous products arising during the process of assimilation, decomposed substances and intestinal gases and makes them harmless.

Intestinol is put on the market in easily swallowed, sugarcoated tablets.

Dosage: After every meal 1—2 tablets,
In special cases 3—4 tablets.

Professor Dr. R. Hirsch has also discovered the beneficial qualities of Intestinol when taken fasting.

Each tablet contains:

0,1 g Pancreatinum sicc.	0,05 g cholic acid salts (gall salts)
0,05 g Secretin	0,15 g animal charcoal.

Prof. Dr. R. Hirsch pointed out that the medication of Intestinol forms a valuable addition to our medicinal achievements.

Literature: Prof. Dr. R. Hirsch, Berlin, Münch. Medizinische Wochenschrift 30/1926. Dr. O. Nemetz, Vienna, Fortschritte d. Medizin 6/1927, Dr. M. Winkel, M.M.W. 40/1912 Dr. Carl Müllern, Vienna, (Zentralfachambulatorium des Bundesheeres) Medizinische Klinik Nr. 11/1928. Dr. Giesemann, Eisenach, Fortschritte der Therapie, Heft 17/1928. Dr. Kadletz, Vienna, Wiener Klinische Wochenschrift 37/1928. Dr. Obstmayer u. Dr. Molnar, Vienne, Medizinische Klinik Nr. 50/1928. San. Rat Dr. Kittsteiner, Hanau, "Der Praktische Arzt" Heft 15/1928. Dr. Baumwell, Alland, "Die Tuberkulose" Nr. 7/1928. Dr. Böhm, Berlin, Münch. Med. Wochenschrift Nr. 6/1929.