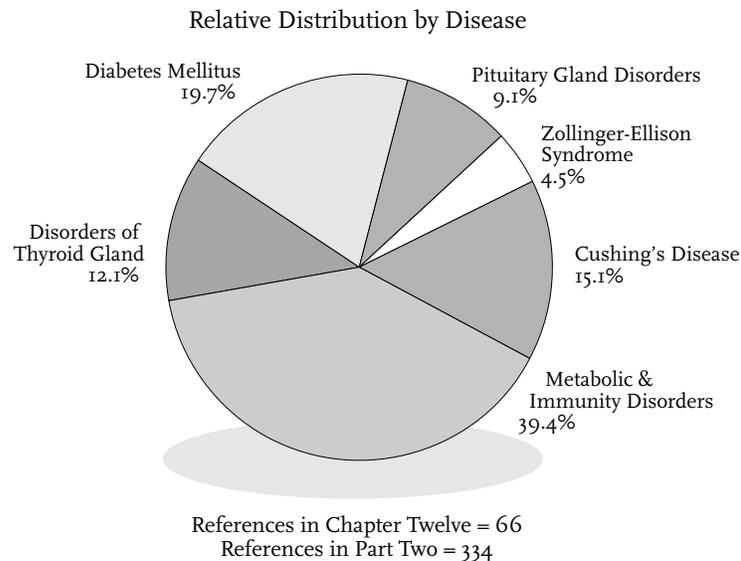


12. Remission of Endocrine, Nutritional and Metabolic Diseases, and Immunity Disorders



Remission of Endocrine, Nutritional and Metabolic Diseases, and Immunity Disorders



Endocrine, nutritional and metabolic diseases, and immunity disorders include diseases that affect the endocrine glands (thyroid, parathyroid, pituitary, adrenals, thymus, islet cells of the pancreas, ovaries, and testicles), nutritional deficiencies such as vitamin deficiencies and malnutrition, and disorders of lipid, carbohydrate, amino acid, and plasma protein metabolism and other metabolic disorders. Other endocrine, nutritional and metabolic diseases include cystic fibrosis, amyloidosis, and acute and chronic histiocytosis. Disorders that involve deficiencies of humoral and cell-mediated immunity and some autoimmune disorders are also included in this broad division.

Endocrine, nutritional and metabolic diseases and immunity disorders are assigned the code numbers 240-279 in the International Classification of Diseases 9th Revision (ICD-9-CM)*, a volume that provides an international standard for the classification of diseases.

There are 66 references in Chapter 12 (19.8% of the 334 references in Part Two)—24 annotated and 42 supplemental. Full text of 22 case reports is included. A summary of the chapter contents is presented in Table One.

Table One: References and Case Reports in Chapter Twelve †

Disease/Disorder	References (number)	Cases (number)	Cases (%)
Diseases of the Thyroid Gland (total)	8	2	1.7%
Hashimoto's Thyroiditis	3	2	1.7%
Primary Hypothyroidism	5	0	0.0%
Disorders of Other Endocrine Glands (total)	32	5	4.2%
Diabetes Mellitus	13	2	1.7%
Pituitary Gland	6	0	0.0%
Zollinger-Ellison Syndrome	3	1	0.8%
Cushing's Disease	10	2	1.7%
Other Metabolic and Nutritional Disorders (total)	23	13	10.8%
Macroglobulinemia	3	1	0.8%
Histiocytosis	18	11	9.2%
Amyloidosis	2	1	0.8%
Deficiencies of Humoral Immunity	3	2	1.7%
Totals	66	22	18.4%

† Total number of case reports in Part Two is 120.

* Commission on Professional and Hospital Activities [Ann Arbor, Michigan: Edwards Brothers, Inc.], April 1986.

Disorders of the Thyroid Gland

HASHIMOTO'S THYROIDITIS

Spontaneous Remission of Hypothyroidism Due to Hashimoto's Thyroiditis

HOW J; KHIR ASM; BEWSHER PD
Lancet 2(8191): Aug 23 1980; 427

Extracted Summary

Hypothyroidism due to Hashimoto's (chronic lymphocytic) thyroiditis is generally regarded as an irreversible disorder requiring life-long thyroid hormone replacement therapy. Two non-puerperal cases of spontaneous remission of hypothyroidism due to Hashimoto's thyroiditis are reported.

SELECTED CASE REPORT

Case 1: A 31-year-old woman was referred to the thyroid clinic with a 3-month history of general tiredness, cold intolerance, and enlargement of the thyroid gland. There was no history of fever or neck pain, and she had not been on any drug treatment. Examination revealed a moderate-sized, firm, non-tender, diffuse goitre without any other definite abnormal physical signs. Serum thyroxine (T₄) 43 nanomoles/l (normal 70-150), serum thyrotrophin (TSH) 19 mU/l (normal 0-4), and antithyroid microsomal antibodies ++++. The patient was seen again 2 months later, when

the intention was to start thyroxine replacement treatment for the documented primary hypothyroidism. She reported, however, spontaneous improvement of her symptoms. Serum T₄ was now within the normal range (82 nanomoles/l) as was the serum TSH (1.8 mU/l). Over the next 12 months and on no treatment, she remained symptom-free and biochemically euthyroid with the serum TSH levels repeatedly less than 1 mU/l. Tests for antithyroid microsomal antibodies became weakly positive (+), and there was a marked reduction in the size of the goitre.

Recovery of Thyroid Function with a Decreased Titre of Antimicrosomal Antibody in a Hypothyroid Man with Hashimoto's Thyroiditis

YAMAMOTO M; KAISE K; KITAOKA H; YOSHIDA K; KAISE N; FUKAZAWA H; SAKURADA T;
SAITO S; YOSHINAGA K

Acta Endocrinologica 102: 1983; 531-534

Extracted Summary

A 36-year-old man with diffuse goitre, signs of mild hypothyroidism, strikingly low levels of T₄ (0.9 micrograms/dl) and T₃ (24 nanograms/dl), elevated TSH (140 microU/ml) and elevated microsomal haemagglutination antibody (MCHA, 1:409,600), subsequently became nongoitrous and euthyroid with a decreased titre of antimicrosomal antibody without any medication. At the time of surgical biopsy, serum levels of T₄ and T₃ had risen to the normal range (4.6 micrograms/dl and 73 nanograms/dl, respectively), serum TSH had decreased to 30 microU/ml and the titre of MCHA to 1:25,600. Thyroid specimens showed Hashimoto's thyroiditis. The activity of thyroid peroxidase (TPO) was normal. The latest examination, 1 year and 3 months after initial evaluation, showed that the patient remained euthyroid with no goitre, that serum thyroid hormones were within the normal range (T₄ 7.7 micrograms/dl and T₃ 97 nanograms/dl), and that TSH was not detectable. The titre of MCHA decreased strikingly to 1:400.

SELECTED CASE REPORT

A 36-year-old man presented on February 28, 1980, with swelling at the front of the neck, hoarseness and oedema of the face. Two of his relatives had Graves' disease.

On physical examination, his height was 165 centimeters, weight 61 kilograms, body temperature 36°C and pulse rate 60 beats/minute. His skin was slightly dry, his face puffy and his voice husky. The slightly enlarged thyroid gland was diffuse, symmetrical and firm. The deep tendon reflex was regarded as normal. The electrocardiogram disclosed a regular sinus rhythm without a low voltage QRS complex in the standard leads. The chest x-ray gave a cardiothoracic ratio of 53.4%. The laboratory tests showed the following results: serum total protein 8.4 gm/100 ml (gamma globulin 16.4%); SGOT, 26 IU; SGPT, 18 IU; LDH, 263; CPK, 112 U and serum total cholesterol, 200 mg/100 ml. The thyroid function tests: BMR, 15%, T_4 , 0.9 micrograms/dl, T_3 , 24 nanograms/dl, ^{131}I T_3 resin sponge uptake, 21.1%, TSH, 140 microU/ml, titre of MCHA, 1:409,600 and TGHA, negative (<1:100). On March 7, thyroidal ^{131}I 24 hour uptake was 20.6% and a further decreases in the serum level of thyroid hormones was observed subsequently (T_4 , 0.3 micrograms/dl and T_3 , n.d.).

When he was admitted to our clinic on April 14, 1980, 6 weeks after the first examination, serum T_4 and T_3 were slightly elevated without any treatment compared with those of first examination (1.8 micrograms/dl and 47 nanograms/dl, respectively). At this time the titre of MCHA was slightly decreased (1:102,400).

A KSCN discharge test performed on May 8, showed a percent discharge of ^{131}I from the thyroid gland of only

5.2% 2 hours after administration of KSCN, indicating the absence of an iodine organification defect in the thyroid gland.

On April 28, further elevation in both serum T_4 and T_3 values, and decrease both in titre of MCHA and serum level of TSH occurred together with an increase in ^{131}I uptake (43.7%).

When surgical biopsy was performed on May 12, TSH decreased to 30 microU/ml, and both T_4 and T_3 were normalized, at 4.6 micrograms/dl and 75 nanograms/dl, respectively. The titre of MCHA also decreased (1:25,600).

On histological examination, the thyroid tissue obtained by surgical biopsy consisted of small thyroid follicles. Almost all thyroid follicles contained vesicular architecture but a small area was broken up into formless masses. Swollen cells with clear and eosinophilic cytoplasm. Ashkanazy cells were observed. But the extreme hyperplasia of cells, characteristic of thyrotoxicosis, was not found. Lymphocytic infiltration was present and lymphoid follicles with germinal centres were formed. Slight interstitial fibrosis was observed. These findings appeared to be consistent with mild changes of Hashimoto's thyroiditis. The activity of TPO was 66.7 U which was in the high normal range.

On May 22, T_4 and T_3 were slightly elevated, at 5.3 micrograms/dl and 91 nanograms/dl, respectively. TSH and the titre of MCHA decreased respectively to 20 microU/ml and 1:6,400 without any medication. Although he was clinically euthyroid and the thyroid gland was not palpable, L-thyroxine (125 micrograms/day) was administered before his discharge because of the slightly elevated TSH.

Spontaneous Remission of Hypothyroidism in Hashimoto's (Autoimmune) Thyroiditis

SASAKI H; YAMAMOTO T; OKAMURA M; EIMOTO T; ASANO T
Israel Journal of Medical Sciences 20(7): July 1984; 625-629

Extracted Summary

Two patients with goitrous hypothyroidism due to Hashimoto's thyroiditis who were followed up for relatively long periods are discussed. Thyroid function fluctuated spontaneously during the course of the disease, unrelated to an associated pregnancy.

Spontaneous Remission from Primary Hypothyroidism

YAMAMOTO T; SAKAMOTO H

Annals of Internal Medicine 88(6): June 1978; 808-809

Extracted Summary

Primary hypothyroidism in adults has been thought to be an end result of the destructive process of chronic thyroiditis, for which life-long replacement therapy with desiccated thyroid or its equivalent has been an accepted method of treatment. In a recent issue of this journal, Amino et al. (*Annals of Internal Medicine* 87 (1977) 155-159) described their experience with transient hypothyroidism, which they observed in 14 postpartum women. The authors report the case of a 24-year-old woman who spontaneously recovered from hypothyroidism accompanied by goiter which was not associated with pregnancy. Twenty-one months after she was first evaluated she remained euthyroid without goiter. Serum thyroid hormones and TSH were normal. (Permission to reproduce case report denied by publisher.)

SUPPLEMENTAL REFERENCES—DISORDERS OF THE THYROID GLAND

Spontaneous Remission of Hypothyroidism [letter]
CARLSON HE

Archives of Internal Medicine 140(12): 1980; 1675-1676

Spontaneous Remission of T₄-Thyrotoxicosis Caused
by Multiple Autonomous Thyroid Nodules

GOROWSKI T; LAZICKA-FRELEK M; CHOMICKI O

Journal of Nuclear Medicine and Allied Sciences 26:
1982; 135-137

Spontaneous Remission of T₄-Toxicosis Caused By
Multiple Hot Thyroid Nodules

GOROWSKI T; LAZICKA-FRELEK M

Polski Tygodnik Lekarski 38(4): Jan 24 1983; 125-126

Natural Course of Intermittent Chronic Autoimmune
Thyroiditis: A Case Report

RIDDERVOLD F

Acta Endocrinologica 102: 1983; 46-48

Disorders of Other Endocrine Glands

DIABETES MELLITUS

Complete Remission of Severe Diabetes

PECK FB JR. KIRTLEY WR; PECK FB SR

Diabetes 7: March-April 1958; 93-97

Extracted Summary

The findings are reported in a 41-year-old male admitted to the hospital on October 12, 1954, in severe diabetic coma. There was no history of diabetes until the onset of illness one day before admission, when he was found unconscious. On admission, the blood sugar was 1,280 mg%, Carbon dioxide was 3 mEq, the Rabinowitch Severity Index was 24, and the patient was in

circulatory collapse. Nineteen hundred and ten units of insulin were administered during the next twelve hours, and subsequently insulin resistance developed requiring 200 to 400 units of insulin daily in order to maintain normal glycemia.

After approximately ten days in the hospital responsiveness to insulin suddenly improved and severe hypoglycemia ensued. Regulation was then established with 90 units of NPH insulin, which was reduced to 30 units daily until November 27, 1954, when insulin was entirely discontinued and the patient's blood sugars remained normal. Intensive study of the patient's endocrine and metabolic status subsequently disclosed no significant abnormalities, and clinical evidence of diabetes is not revealed even to the provocative cortisone glucose tolerance test of Fajans-Conn. The case represents an unusual instance of temporary severe diabetes accompanied by coma and acidosis with apparently complete recovery as far as can now be determined. Until a five-year period has elapsed, it should be regarded as a remission rather than a cure.

SELECTED CASE REPORT

A 41-year-old Negro male, R. W. (325653), was admitted to the Emergency Ward of Indianapolis General Hospital on October 12, 1954, in profound diabetic coma. He had been in good health until one week before admission, when he had an upper respiratory infection, loss of appetite, and loss of weight. There is no history of diabetes in the family. The day before admission he remained at home because of nausea and vomiting, and was found unconscious.

The physical findings were of a patient in deep coma and a shock-like state, with Kussmaul respiration and an acetone odor to his breath. The eyeballs were soft and funduscopic findings were normal, as were the lungs, heart and abdomen. Generalized hypoactive deep reflexes were noted, and there was no response to painful stimuli. The blood pressure was 0-80/60 mmHg, pulse 120, respiration 32.

The urine was strongly (4 plus) positive for sugar and acetone. Blood sugar was 1,280 mg% (Somogyi method); plasma carbon dioxide was 3 mEq and blood urea nitrogen 60 mg%. Calculation of the Rabinowitch severity index gave a numerical value of twenty-four (any rating of twenty-one or over is exceptionally severe and carries with it a mortality rate of 80 to 90%).

Vigorous treatment over the first twelve hours necessitated venous incisions in the lower extremities in order to combat circulatory collapse by intravenous infusions with norepinephrine added to maintain the blood pressure. During this period 1,910 units of insulin were administered, and a total of 6.5 liters of normal saline, 2 liters of 5% dextrose and 65 mEq of potassium. It was on the advice of Dr. D. D. Van Slyke, who was visiting our laboratories that day, that an additional 15 grams NaHCO_3 was given intravenously as the patient was obviously not responding to treatment. In retrospect, we believe this was probably lifesaving, as the carbon dioxide values then began to rise, and the patient's general condition began to improve. During the hours when blood pressure was minimal, pressure of the patient's weight on his buttocks resulted in a large area of sacral decubitus which subsequently required surgical debridement before healing occurred. Unconsciousness persisted for two full days.

Electrolyte balance was greatly disturbed, the serum sodium being 170 mEq, with serum chlorides 138 mEq despite adequate urinary output. It was thought at the time that this might be the result of too vigorous administration of sodium chloride, although adequate urinary output was present during most of the stormy initial course.

The patient responded poorly during the first few days. Weakness of the left arm and leg was noted, which in conjunction with the altered electrolyte pattern suggested cerebral thrombosis. Spinal fluid was normal. Insulin resistance appeared on October 14, subsequently requiring 200 to 400 units daily in order to maintain normal glycemia. Regulation of glycemia between 70 to 90 mg/100 ml of blood sugar was finally established with 90 units NPH insulin per day. A severe insulin shock occurred on the fifth day, with blood sugar of zero, and another insulin shock occurred on the tenth day. There was prompt response to glucose intravenously and then several days of satisfactory regulation with 30 units of NPH insulin daily. The patient was transferred to the Lilly Research Ward on November 3, 1954, for further study of his metabolic state. Clinical evidence of diabetes completely disappeared.

Insulin was entirely discontinued on November 27. The blood sugar level remained normal in both fasting and postprandial periods. The decubitus healed under treatment with penicillin and Varidase. A glucagon test gave a lower-than-normal blood sugar elevation (usually 30 to 40 mg% by our methods). Oral glucose tolerance tests and a triple glucose tolerance test consisting of two orally administered priming doses followed by an intravenous glucose curve were essentially normal except for delayed return in two hours. In fact, a sharp hypoglycemic reaction occurred one and one-half hours after the intravenous glucose. This "Staub-Traugott" phenomenon appears in normals, and the less severe the diabetes, the more nearly does the curve approach normal. An insulin tolerance test displayed some initial slight delay in responsiveness to insulin, but was otherwise within normal limits. The glucose insulin tolerance test was not abnormal since in normals the hyperglycemia is greater

than after the administration of the same amount of glucose without insulin, ranging from 25 to 75% increase from initial blood sugar values. The Thorn eosinophil test for adrenal function was normal. Three basal metabolic rates were within normal limits. A four-day ACTH stimulation test did not show a normal increase in 17-ketosteroids and 11-oxysteroids in the urine. Later a high eosinophil count (50%) was attributed to his long term penicillin Varidase therapy, and the count fell rapidly toward normal limits when these agents were discontinued. Skull films of sella turcica were normal, the blood count, liver and kidney function studies were all within normal limits. Evidence of the initial severe diabetes having disappeared, the patient was released to the out-patient Diabetes Clinic for long-term observation, with

instructions to maintain his diet within the range of 1,500 to 1,800 calories to avoid gain in weight.

Subsequent visits to the Diabetes Clinic have confirmed the continued absence of any signs or symptoms of diabetes. The blood sugar levels have remained entirely normal since 1954, and there has not been a single positive test for glycosuria, either in the clinic or under home and working conditions.

Periodic rechecks of the patient's glucose tolerance have been continued. Further evidence of the dormant nature of the diabetes in this case is shown by the response to the cortisone-glucose tolerance test of Fajans and Conn, performed according to their methods on June 29-30, 1957.

Spontaneous Remission in Diabetes

Journal of the American Medical Association 196(12): June 20 1966; 1085

Extracted Summary

Diabetes is rarely thought of as a remitting disorder. In the June Archives of Internal Medicine, O'Sullivan and Hurwitz suggest that this view may have to be modified. Having studied sequential glucose tolerance tests in 83 nonpregnant young diabetic women six months to two years after the onset of the disease, these investigators found an improvement in 54% and a return to normal in 28%. This would suggest that a reassessment of therapy and diagnostic screening is necessary. What causes diabetes to submerge? O'Sullivan and Hurwitz, having found no apparent cause for the remissions, have designated them as "spontaneous."

Spontaneous Remissions in Early Diabetes Mellitus

O'SULLIVAN JB; HURWITZ D

Archives of Internal Medicine 117(6): June 1966; 769-774

Extracted Summary

Sequential oral glucose tolerance tests on 83 nonpregnant, untreated women with early diabetes mellitus are described. Spontaneous improvements were found to range from 25% to 89%, a large proportion of which were remissions to normal. A normal fasting blood sugar level proved to be the single most important factor favoring improvement, although the number of remissions in persons with fasting hyperglycemia is impressive. Weight reduction also favored improvement but did not occur in a sufficient number of patients to affect the conclusion that the changes were spontaneous. Two-thirds of the patients with remissions had no change in weight or in a few instances had a weight gain. Diabetics, as a group, were found to be more overweight in both number and degree than the 83 non-diabetic control patients. The diabetics were also gaining weight more rapidly than the controls in the two years preceding their diagnoses. Our data indicate that spontaneous remissions in both obese and nonobese diabetic patients occur frequently enough to indicate the need for carefully controlled studies before ascribing such results to any specific form of treatment.

Spontaneous Disappearance of Insulin-Resistant Diabetes Mellitus in a Patient with a Collagen Disease

A Case Report, with Review of the Literature for Conditions Associated with Insulin Resistance

BRUCE DH; BERNARD W; BLACKARD WG
American Journal of Medicine 48(2): Feb 1970; 268-272

Extracted Summary

Insulin resistance causing insulin requirements greater than 1,000 units a day is reported in a 39-year-old woman with signs and symptoms of a collagen disease. After ten months insulin resistance regressed and glucose tolerance and insulin sensitivity returned to normal. A review of the literature indicates that this is only the second well-documented case of disappearance of diabetes. The conditions associated with insulin resistance and the possible causes of insulin resistance in this patient are discussed.

SELECTED CASE REPORT

A 39-year-old Negro housewife (B. H.) was admitted to the Flint-Goodridge Hospital on October 23, 1967, for evaluation of weakness, fatigability, palpitations and dyspnea on exertion, all of which had been present for two months. Despite a good appetite, she had lost 23 pounds over the preceding two years. Two months prior to admission she noticed urinary frequency and nocturia, pain in her right shoulder, dryness of mouth and growth of hair over the temples. She suffered a chronic rash with dryness, crusting and pruritus over her face and scalp. She also complained of pain in her fingers associated with blanching on exposure to cold. Roentgenograms of the gallbladder obtained previously for symptoms of mild dysphagia and fat intolerance revealed cholelithiasis. After having four children of normal birth weight, she delivered an erythroblastotic child in 1959 and a stillborn child at six months' gestation in 1966. There was no past history of arthritis, asthma, endocrine, hepatic, renal or skin disease. No relatives had diabetes mellitus, allergic disease or collagen diseases.

Physical examination revealed a thin, alert and intelligent Negro woman who appeared chronically ill. Vital signs were normal and weight was 57 kilograms. A seborrheic eruption involving the face and scalp and an eczematoid eruption involving the neck were present. Funduscopic examination was normal. The submaxillary glands were enlarged and nontender. The right shoulder was tender, with limitation of motion. Peripheral pulses were normal, but both hands blanched on immersion in cold water and after exercise. Cervical lymph nodes were slightly enlarged and nontender without other evidence of lymphadenopathy. The liver and spleen were not enlarged. Physical examination was otherwise within normal limits.

Laboratory studies showed a normal hemoglobin

with a white blood cell count of 5,198/mm³. A sickle cell preparation was negative. C-reactive protein was absent from the serum; the erythrocyte sedimentation rate was 21 mm/hour. Urinalysis showed 3+ glucose, 3+ albumin and moderate acetone with normal microscopic examination. Blood glucose was 267 mg%, blood urea nitrogen 10.2 mg%, uric acid 2.6 mg% serum sodium 130 mEq/L, potassium 4.0 mEq/L, carbon dioxide capacity 20 mEq/L and chloride 105 mEq/L. A test for rheumatoid factor was positive, but lupus erythematosus preparations, a serologic test for syphilis and tests for cold agglutinins and cryoglobulins were negative. Serum glutamic pyruvate transaminase and bilirubin were normal, alkaline phosphatase was 4.8 units (normal: 1.5 to 4.0 units), cephalin flocculation 2+ and total cholesterol 123 mg%. Serum protein electrophoresis showed a moderate, nonhomogeneous increase in gamma globulin and a moderate decrease in albumin. Immunoelectrophoresis showed an increase in IgG and IgM with normal IgA and complement levels. Protein-bound iodine, twenty-four hour urine for 17-hydroxysteroids, urinary vanillylmandelic acid, and plasma growth hormone levels by radioimmunoassay were normal. Bone marrow aspirate was hypocellular with moderate erythroid hyperplasia. Biopsy of a cervical node showed atypical reticuloendothelial hyperplasia. Skin biopsy specimens showed minimal and nonspecific changes. Roentgenograms of the right shoulder were normal. Esophagram and roentgenograms of the upper gastrointestinal tract were normal except for prominence of the mucosal folds of the duodenum and delayed gastric emptying.

Serum was tested for insulin antibodies on several occasions by a qualitative assay. The patient's serum and control serum were incubated separately with tracer ¹²⁵I labelled insulin for twenty-four hours and then placed on GX5 Sephadex[®] columns to separate free

from bound tracer. By this method the presence of insulin antibodies was indicated by radioactivity in the antibody containing fraction of the patient's serum in excess of that found in the same fraction from control serum. Serum specimens obtained during the patient's initial hospitalization in October 1967 were negative for insulin antibodies, whereas serum obtained in October 1966 and March 1969 (four and nine months after cessation of insulin therapy) indicated the presence of substantial binding. Measurements of insulin-like activity and immunoreactive insulin in our patient were vitiated by the presence of antibodies.

When glycosuria and hyperglycemia were discovered, insulin therapy was initiated on a sliding scale for the glycosuria, with 50 units of NPH insulin being given initially, and an 1,800 calorie diabetic diet was instituted for the hyperglycemia. Despite progressive increases in insulin dosage to 80 units of crystalline insulin three times a day, blood glucose levels ranged from 210 to 249 mg% with persistent 3+ to 4+ glycosuria and variable acetonuria. The patient was treated with prednisone, 60 mg/day, for eight days and tolbutamide, 2 gm/day, for fifteen days without apparent effect on blood glucose. A trial of pork insulin proved no more effective than beef insulin. Feeling improved but with the diabetes under no better control than on admission, the patient was discharged on December 2, 1967, on a regimen consisting of a 3,000 calorie diabetic diet

and 240 units of NPH insulin each morning.

From December 1967 to May 1968 the patient continued to improve symptomatically with less weakness and a 22 pound weight gain. Urine samples continued to be strongly positive for glucose, and fasting blood glucose levels ranged from 176 to 253 mg% despite progressive increases in insulin dosage to 1,050 units of crystalline insulin per day in divided doses. At the end of May 1968 when the patient reported that her morning urine specimen was negative for sugar, insulin therapy was discontinued; neither the diabetic symptoms nor glycosuria recurred. A year later she was still symptom-free without medication or diet. The results of oral glucose tolerance tests during remission yielded a flat but nondiabetic response. An insulin tolerance test performed in March 1969 during which she displayed marked symptoms of hypoglycemia revealed normal insulin sensitivity. At present, she complains only of occasional weakness before meals. Erythema over the malar areas of her face and dorsum of her phalanges has persisted. In addition, patchy hyperpigmentation over the upper part of her chest, hypopigmentation and telangiectases of her cuticles, and small stellate scars on her finger tips have developed. The submaxillary glands are smaller and firmer. Urinalysis is normal, and liver function studies are within normal limits except for persistent hyperglobulinemia.

SUPPLEMENTAL REFERENCES DIABETES MELLITUS

Spontaneous Disappearance of Diabetes

JOHN HJ

Journal of the American Medical Association 85(21): Nov 21 1925; 1629-1631

Recurrent Diabetes: Spontaneous Remissions and Exacerbations

GLASSBERG BY

Journal of Clinical Endocrinology and Metabolism 6: May 1946; 369-382

Extreme Hyperglycemia and Severe Ketosis with Spontaneous Remission of Diabetes Mellitus

CHENG TO; JAHRAUS RC; TRAUT EF

Journal of the American Medical Association 152(16): Aug 15 1953; 1531-1533

Severe Diabetes with Remission: Report of a Case and Review of the Literature

HARWOOD R

New England Journal of Medicine 257(6): Aug 8 1957; 257-261

Severe Diabetes with Remission: Report of a Case

STUTMAN LJ; HAYES JD

Diabetes 8: May-June 1959; 189-191

Serum Insulin in a Case of Severe Diabetes Mellitus Showing Remission

TAYLOR KW

British Medical Journal 1: June 18 1960; 1853-1855

Insulin-Resistant Diabetes Associated with Increased Endogenous Plasma Insulin Followed by Complete Remission

FIELD JB; JOHNSON P; HERRING B

Journal of Clinical Investigation 40: 1961; 1672-1683

Remission in Diabetes Mellitus: A Case Presentation

BRERETON RB

Delaware Medical Journal 40: Feb 1968; 37-41

Degos' Disease Associated with a "Spontaneous Cure of Diabetes"

SALOMON MI; MANDEL EH; GALLO G

American Geriatric Society. Journal 19(11): 1971; 923-32

Spontaneous Regression of Enlargement of the Sella Turcica and of Associated Panhypopituitary Symptoms

VOGT JH

Acta Endocrinologica 85(4): 1977; 684-691

Extracted Summary

The case history of a woman born in 1946 is given. In 1968 she developed a syndrome of headache, fever, elevated antistreptolysin titer, enlarged and ballooned sella turcica, hypothyroidism secondary to TSH deficiency, secondary amenorrhoea of pituitary genesis, probable growth hormone deficiency, and secondary adrenocortical insufficiency. From 1972 all the mentioned pituitary defects of function disappeared, and the sella turcica gradually became normal in size as shown by x-ray examination.

SUPPLEMENTAL REFERENCES DISORDERS OF THE PITUITARY GLAND

Regression of the Forbes-Albright Syndrome After Pituitary Apoplexy

MCLAREN EH; KEET PC

British Medical Journal 2(860): Apr 28 1973; 214-215

A Case of Pituitary Apoplexy with Spontaneous Recovery

KASAI K; SUZUKI H; NAKAMURA T; KIKUCHI T; IERI T; TAKEMURA Y; SHIMODA S-I; UEDA Y; CHIEN T; NAGAI M
Endocrinologia Japonica (Nihon Naibunpi Gakkai) 25(3): June 1978; 209-216

Spontaneous Remission of Cranial Diabetes Insipidus Due to Concomitant Development of ADH-Producing Lung Cancer: An Autopsied Case

TAKEDA R; HIRAIWA Y; HAYASHI T; YASUHARA S; YANASE E; SAKATO T; NAKABAYASHI H; TAKEGOSHI T; NISHINO T; TANINO M; YAMAJI T
Acta Endocrinologica 104(4): Dec 1983; 417-422

Spontaneous Recovery from Hypopituitarism Due to Postpartum Hemorrhage

OHYAMA T; NAGASAKA A; NAKAI A; AONO T; MASUNAGA R; KATAOKA K; NAKAGAWA H; KATO S; KAWABE T; MAJIMA H; KOMETANI K; FUKUSHIMA M
Hormone and Metabolic Research (Stuttgart) 21(6): Jun 1989; 320-323

Diabetes Insipidus with Spontaneous Remission
OHSHIMA K; OKADA S; ONAI T; UMAHARA M; MORI M; KOBAYASHI I; KOBAYASHI S; KATAKAI S
Journal of Endocrinological Investigation (Milano) 12(10): Nov 1989; 713-715

Spontaneous Remission of Zollinger-Ellison Syndrome

MELNYK CS; KRIPPAEHNE WW; BENSON JA JR; DUNPHY JE
Archives of Internal Medicine 115: Jan 1965; 42-47

Extracted Summary

A unique case of the Zollinger-Ellison syndrome is described with chronic diarrhea, multiple peptic ulcerations, gastric hypersecretion, and a mild malabsorptive state, undergoing spontaneous remission for 20 months after laparotomy and single lymph node biopsy of an invasive islet cell carcinoma of the head of the pancreas. The possible reasons for this result are discussed.

SELECTED CASE REPORT

A 50-year-old welder developed profuse, watery diarrhea in 1960, immediately after a hemorrhoidectomy. The diarrhea consisted of 5-15 loose, watery stools daily without mucus, pus, or blood. This was reduced by large doses of paregoric to four to six movements per day. By June 1962, he had lost 15 pounds (6.8 kilograms) and was hospitalized elsewhere for his first symptoms of duodenal ulcer. An upper gastrointestinal series revealed a duodenal ulcer crater with a very rapid small bowel transit time (one hour to cecum). Family history disclosed no evidence of peptic disease, endocrine disorder, or malabsorption. A complete physical examination was negative except for moderate right rectus muscle spasm and tenderness.

The stool was consistently negative for occult blood and pus cells. Fecal fat measured 4 gm/24 hours (5% of oral fat intake) and 6 gm/24 hours (7% of intake). Gastric aspirate revealed substantial free acid, but no quantitative study was performed. Abnormal studies included urinary xyloses of 1.1 grams and 0.8 grams in five-hour specimens (normal, greater than 5 grams) and serum carotene of 15 micrograms/100 ml (normal, 45-65 micrograms). Two percent of ingested radioactive triolein ^{131}I had been absorbed into the blood by five hours and had increased to 10% following the addition of pancreatic extract (normal value, greater than 10% absorption). A secretin test was abandoned because of difficulty in obtaining alkaline secretions.

At gastroscopy, the gastric mucosa appeared normal. The proximal jejunum biopsied by Rubin tube appeared normal. Sigmoidoscopy was unremarkable except for a polyp at 25 centimeters which proved to be benign after removal.

Roentgenograms of the chest, gallbladder, and colon were normal. Upper gastrointestinal and small bowel series on August 27, 1962, still demonstrated a duodenal ulcer crater and the rapid small bowel transit time. The small bowel was dilated and bore coarsened mucosal markings which were most notable proximally.

The patient was treated in the hospital for two months with a bland diet, hourly antacids, anticholinergics, and sedation. He experienced moderate improvement in the pain and some decrease in the diarrhea but required analgesics periodically for relief of severe right upper quadrant pain. He was discharged from the hospital on September 10, 1962, with instructions for a bland diet and received the following medications: an antacid (Aludrox: aluminum hydroxide gel with magnesium hydroxide), two tablespoons every one to two hours while awake; an anticholinergic (Belaps No. 1: phenobarbital and belladonna) four times daily; meprobamate, 200 mg four times daily; a water absorbent material (Siblin: material from plantago plus thiamine), one tablespoon daily; and an analgesic (Darvon Compound: dextropropoxyphene, aspirin, acetophenetidin, caffeine) to be taken as needed. The discharge diagnoses were duodenal ulcer, improved, and suspected pancreatic insufficiency.

The patient continued to have intermittent attacks of right upper quadrant pain which he controlled by oral analgesics. He had four to five diarrheal stools per day.

On October 23, 1962, he presented himself to the Multnomah Hospital and was admitted with severe right upper quadrant pain radiating to his back and right shoulder. He was a well-nourished, 165 pound (74.8 kilogram) man with spasm of the right rectus muscle and point tenderness in the right epigastrium.

Laboratory studies were all normal except for serum phosphorus of 6 mg/100 ml (normal, 2-4 mg/100 ml) and two diabetic oral glucose tolerance curves (two-hour glucose, 166 mg%). Because of the copious gastric secretions and the difficulty in neutralization, a histamine stimulation test was not performed preoperatively.

Upper gastrointestinal x-ray study showed a large ulceration of the first portion of the duodenum, a new ulceration near the esophagogastric junction, and a questionable lesser curvature ulcer. Gastric rugal folds were very prominent. The small bowel had coarsened folds with segmentation and flocculation of barium.

Another cholecystogram and an intravenous pyelogram were normal.

Continuous nasogastric suction returned volumes of 4,000 to 7,500 ml/24 hours with pH 1-2. Since this aspiration presented difficulty in electrolyte management and had minimal effect on the pain, hourly aspirates were neutralized with 2 to 4 grams of calcium carbonate and returned to the stomach. In addition, atropine sulfate (0.4 milligrams every four hours), narcotics, and sedative drugs were given. In 48 hours he was somewhat improved and the nasogastric suction was discontinued. He was then fed 2 grams of calcium carbonate powder, alternating with milk every half hour.

With a preoperative diagnosis of Zollinger-Ellison syndrome, an exploratory laparotomy on November 7, 1962, under cyclopropane anesthesia, revealed a large tumor mass of the head of the pancreas with extension to encompass the porta hepatis up to approximately 0.5 centimeters from the liver, the distal part of the stomach, the first portion of the duodenum, and the proximal third of the gallbladder. The duodenal ulcer was observed at surgery to be encased in tumor. There were no obvious liver or peritoneal metastases. Biopsy of a lymph node from along the lesser curvature of the stomach disclosed 80% replacement by islet cell carcinoma. Because of the extensiveness of the tumor, a total gastrectomy or any other gastric procedure was not thought to be technically feasible. A gastrostomy tube was inserted to facilitate postoperative gastric acid neutralization.

Microscopic examination of the lymph node by Robert A. Cooper, MD, was reported as follows. "The total mass of neoplastic cells was subdivided into poorly defined lobules by persistent lymph node trabeculae extending into the mass from the capsule. These lobules were further subdivided into numerous nests and interconnecting trabeculae by a delicate, highly vascular fibrous connective tissue network. Approximately 95% of the tumor cells were arranged in this pattern. The remaining 5% formed well-defined ducts containing finely granular eosinophilic intraluminal material. The gland lumens were bordered by an average of 30 cells, whose nuclei were oriented with their long axes perpendicular to the lumen. At their nonluminal border the lining cells were continuous with the cells of the solid nests and were not separated from them by a basement membrane. Individual tumor cells were characterized by sharply delineated, finely granular eosinophilic cytoplasm and a nuclear to cytoplasmic ratio of 1:1. Nuclei were round to oval, averaged 15 microns in diameter, and were moderately hyperchromatic. Chromatin was dispersed in small, regular, angular masses. Most nuclei had more than one chromo-

center. Eosinophilic nucleoli were present. Approximately 10% of nuclei were significantly larger than the average with some measuring up to 50 microns. In addition, there were occasional binucleate forms. Morphologically normal mitoses, generally in metaphase, were present at a rate of one per four high-power fields. Occasional fields contained as many as three mitotic figures. Abnormal mitoses were rarely seen. In scattered areas the basic pattern was modified by the formation of perivascular pseudo-rosettes, vacuolar spaces secondary to individual tumor cell degeneration, and by ectasia of thin-walled vascular channels with compression of surrounding tumor cells."

A biopsy of gastric mucosa taken at this time did not demonstrate recognizable parietal cell hyperplasia.

Immediately after surgery the patient experienced less pain, and gastric secretion diminished to 800 to 1,600 ml/24 hours with pH 2-6. The diarrhea ceased. His postoperative period was complicated by a mild pneumonia which cleared with penicillin and tetracycline therapy, and he was discharged on November 27, 1962, entirely asymptomatic. His therapy consisted of a bland diet and hourly antacids which were discontinued by the patient after two months. The gastrostomy tube was removed two months after his surgery without incident.

Laboratory studies performed after surgery and at three-month intervals with normal results were complete blood cell count, urinalysis, serum bilirubin, serum proteins, alkaline phosphatase, serum amylase, serum glutamic oxaloacetic transaminase, and sulfobromophthalein (Bromsulfalein) dye test.

The following studies were performed six months after surgery. Fecal fat was 0.7 gm/24 hours. Repeat oral glucose tolerance curve and serum phosphorus were normal. Serum carotene was 48 micrograms/100 ml, and a five-hour urinary xylose value was 4.1 grams. Aspiration needle biopsy of the liver showed no evidence of tumor. Small bowel and gastric mucosal biopsies by Rubin tube were normal. X-ray study of the stomach and small bowel showed complete healing of the multiple ulcers but persistence of hyperrugosity of the stomach and moderate edema and coarseness of the duodenum...

As of July 1964, the patient continued to feel very well, had gained 50 pounds (22.7 kilograms) and did not desire a second laparotomy. He was then receiving tincture of belladonna, 18 drops, four times daily, and calcium carbonate (1.2 grams) tablets hourly. Barium study of the stomach and small bowel had remained unchanged for the past year. There was no radiographic evidence of tumor.

SUPPLEMENTAL REFERENCES ZOLLINGER–ELLISON SYNDROME

Zollinger-Ellison Syndrome: Spontaneous Regression of Advanced Intra-abdominal Metastases with 20 Year Survival

DAVIS CE JR; VANSANT JH

Annals of Surgery 189(5): May 1979; 620-626

Malignant Zollinger-Ellison Syndrome: Remission of Primary and Metastatic Pancreatic Tumor After Gastrectomy—Report of a Case and Review of the Literature

MOROWITZ DA; LEVINE AE

American Journal of Gastroenterology 81: 1986; 471-73

CUSHING'S DISEASE

Spontaneous Remission in a Case of Cushing's Syndrome

PASQUALINI RQ; GUREVICH N

Journal of Clinical Endocrinology and Metabolism 16: March 1956; 406-410

Extracted Summary

Cushing's syndrome is usually caused by hyperplasia or carcinoma of the adrenal cortex; less frequently it is associated with a basophil tumor of the pituitary, with or without adrenal hyperplasia; exceptionally it is observed in the presence of an ovarian or a thymic tumor; and in rare instances autopsy of typical cases of Cushing's syndrome reveals no organic lesion in the endocrine glands. Irrespective of its original cause, the evolution of all known cases has followed a progressive course which could only be delayed by means of pituitary irradiation, ample adrenalectomy, or death of the patient due to some intercurrent infection. Spontaneous remission in cases of Cushing's syndrome with well-defined somatic alterations is mentioned only exceptionally in the literature, and for this reason we consider as most interesting the description of a typical case, including adrenal hyperplasia, in which there was spontaneous evolution to complete cure.

SELECTED CASE REPORT

The patient was an unmarried woman, 21 years old, born in the Province of Catamarca, Argentina. The family history was non-contributory. When she was 11 years old, she had a fever for two months which resembled that of brucellosis. When she was 16 she had measles and mumps; at 20 she had German measles. Menses began at the age of 14 1/2; the interval was twenty-five days and the bleeding lasted for three days.

She was admitted to the Clinical Ward on July 2, 1953, suffering from a disease characterized by the following symptoms: two months of amenorrhea after two years of irregular menses with periods of oligomenorrhea associated with hypomenorrhea and hypermenorrhea; headache with elective retro-ocular localization during the preceding year; and an increase in weight from 62 to 69 kilograms during the same period. She had noticed that obesity was most prominent in the face and was associated with substantial changes in features and expression. There had been a gradual increase in facial and body hair, and marked shedding of scalp hair. During the previous six months she had noticed atrophic striae in dif-

ferent parts of the body, which increased gradually in number and size. During the previous two weeks she had felt pain in the interior thorax, spreading forward in the form of a belt. She had no other complaint.

Physical examination revealed obesity of moderate degree. Her weight was 69 kilograms and height, 158 centimeters. Adipose tissue had accumulated in the face, neck (especially in the posterior part) and thorax. The abdomen was moderately prominent and the gluteal regions definitely flattened. The arms and legs appeared normal. The general body configuration was of the buffalo type. The features showed the characteristic moon shape, with drooping of the corners of the mouth and an increase in adipose padding of the cheeks. The eyes, nose and mouth were normal. There was no pigmentation of the buccal mucous membrane. The skin was brown, plethoric and seborrheic. There were extensive violet-red striae (more than 2 centimeters in width) with telangiectasia in the external surface of the upper arms, axillae, hands, anterior and lateral abdominal walls, iliac and trochanteric regions, and antero-medial surfaces of

both thighs. There was a marked increase in facial hair, especially on the cheeks and upper lip; body hair was abundant in the dorsal region and on the shoulders and arms; axillary and pubic hair was very thick, and the latter had a masculine distribution. The scalp hair receded over the temples and, although it remained abundant, shedding was appreciable. The muscular system was normal, as was the skeletal system, except for dorsal kyphosis. The thyroid gland was normal in size. The mammary glands were large, with deeply pigmented areolae; the mammary tissue was of normal consistency. A study of the cardiovascular system revealed normal heart sounds with a rate of 96, an arterial blood pressure of 152/100 and a heart of normal size by roentgenography. The respiratory system was normal. Abdominal findings were negative. Gynecologic examination showed no abnormalities; the clitoris was of normal size. Results of examination of the nervous system were negative.

Roentgenograms of the sella turcica showed normal characteristics; those of the spine showed diffuse osteoporosis of moderate degree. Adrenal radiography, after the injection of air by the precoccygeal route, revealed a bilateral increase to double the normal size; the increase was diffuse and symmetrical. Pelvipneumography showed the ovaries and uterus to be of normal dimensions.

The patient retained a good appetite, having reduced voluntarily the amount of carbohydrates and sodium chloride consumed, for the purpose of losing weight. She had polydipsia and polyuria of moderate degree.

Laboratory data: RBC 4,620,000; hemoglobin 14.2 gm%; WBC 7,000 with neutrophils 75%, eosinophils 22%, lymphocytes 18% and monocytes 5%. The level of blood urea was 30 mg/100 ml, cholesterol 286 mg/100 ml, chloride 400 mg/100 ml, sodium 344 mg/100 ml, potassium 20 mg/100 ml, total calcium 8.3 mg/100 ml, phosphorus 3.6 mg/100 ml, and alkaline phosphatase 2.6 Bodansky units/100 ml. The urine was normal, without albumin or glucose and with a specific gravity of 1.015. Three successive glucose tolerance tests, with 100 grams of glucose orally, yielded the following results: July 8, 1953: 0 minutes-Blood sugar level (BSL) (mg/100 ml)=70; 60 minutes-BSL=95; 120 minutes-BSL=90; 180 minutes-

BSL=80. August 3, 1953: 0 minutes-BSL= 80; 60 minutes-BSL=80; 120 minutes-BSL=90; 180 minutes-BSL=80. November 2, 1953: 0 minutes-BSL=80; 60 minutes-BSL= 115; 120 minutes-BSL=100; 180 minutes-BSL= 85. An insulin tolerance curve with 0.1 unit/kg. subcutaneously was as follows: 0 minutes-85; 15 minutes-45; 30 minutes-40; 60 minutes-60; 80 minutes-70; 120 minutes-75; 180 min-80. Urinary 17-ketosteroids were 24.2 mg/24 hours. 11-oxycorticosteroids on both July 3 and July 16, 1953 were 1.2 mg/24 hours. The urinary gonadotropin titer was less than 48 mouse units/24 hours. Thorn tests with 25 mg of ACTH resulted in an eosinophil count of 223/mm³ before, and 190/mm³ after four hours, a drop of 14.8%.

Clinical course: No treatment was instituted except for a restriction in caloric intake. In August 1953 menstruation, although scanty, reappeared and continued monthly. In December her weight was 66.4 kilograms, with a general decrease in adipose tissue and a decrease in the symptoms typical of Cushing's syndrome. At that time, methyltestosterone in a dosage of 10 milligrams daily was given for a few days. In January 1954, all pathologic somatic characteristics had become much less pronounced, the cutaneous striae were becoming pale and the skin was more normal in appearance. In April the improvement was marked. The patient's weight was 61.9 kilograms, the blood pressure was 110/75, and there was a great change in her facial expression. In July 1954 her features and somatic configuration were completely normal in spite of an increase in weight to 65.5 kilograms, the cutaneous striae were completely pale and the blood pressure was 90/60.

Determinations of urinary 17-ketosteroids gave the following results: August 28, 1953, 14.9 mg/24 hours; November 3, 1953, 9.4 mg/24 hours; and May 10, 1954, 12.5 mg/24 hours. The 11-oxysteroid values were: November 3, 1953, 0.95 mg/24 hours; and May 10, 1954, 1.04 mg/24 hours.

After suffering from Cushing's syndrome for almost a year, the patient had returned to her physical status prior to the disease and was completely free of symptoms. Menstruation was normal.

Spontaneous Remission of Cushing's Disease

HAYSLETT JP; COHN GL

New England Journal of Medicine 276(17): April 27 1967; 968-970

Extracted Summary

The natural course of Cushing's disease has been obscured by the difficulties of diagnosis of the milder forms and the relative infrequency of the disorder. The case confirms earlier clinical observations that spontaneous remission may occur. Although most patients with Cushing's disease require surgical or radiologic intervention, continued observation may be preferable in a case, like the one reported, with mild clinical disease and without evidence of osteoporosis, diabetes mellitus and other complicating features.

Cushing's Disease with a Spontaneous Remission

PUTNAM TI; ACETO T JR; ABBASSI V; KENNY FM
Pediatrics 50(3): Sept 1972; 477-481

Extracted Summary

Since its description in 1932, Cushing's disease has become a therapist's disease. With the discovery of its existence came the natural reaction of destroying the cause or supposed cause as quickly as possible lest the more dangerous complications of the syndrome manifest themselves.

As a result of therapy, the natural history of the disease is unknown in children. Also apparent from the complications and secondary effects of surgery and or irradiation is the fact that the ideal treatment is yet to be found. Our experience with the patient described herein establishes that a spontaneous remission is possible. Therefore, we propose that no treatment be given to patients with mild Cushing's disease.

SELECTED CASE REPORT

The propositus presented to the Endocrine Clinic in December 1965, at the age of 11 years, 10 months, with the single complaint of short stature. At age 5, Eugene's height had been in the 85th percentile and had fallen from the 50th percentile at age 8 years to the 3rd percentile when he presented. At 8 years of age his appearance had been that of a normal prepubertal boy; however, in the ensuing three years he had grown only 3.1 centimeters but gained 21 kilograms. His parents depicted him as a pleasant, happy individual of bright intellect. Eyesight had not deteriorated, and no history of headaches could be obtained. Physical examination revealed marked obesity, mild acne, moon facies, "Buffalo hump," supraclavicular fat pad and pubic hair despite small prepubertal testes.

The elevated urinary 17-hydroxycorticosteroids (17-OHCS) in December 1965 and elevated cortisol secretory rate in March 1966, clearly established the diagnosis of Cushing's disease. The urinary 17-OHCS did decrease during the administration of 1.5 milligrams dexamethasone per day, but they did not fall below 4.0 mg/24 hours.

Subsequent studies were done to confirm the impression of Cushing's disease, to locate the site of the abnormality, to document effects and course of the disease. The suppression of urinary 17-OHCS with dexamethasone and the rise in plasma cortisol and urinary 17-OHCS following stimulation with ACTH tended to rule out an adrenal tumor. Air insufflation of the retroperitoneal spaces, intravenous pyelogram, and laminograms done at the same time showed normally sized adrenals without aberration in shape or position. Roentgenograms for the sella turcica size, brain scan, electroencephalogram, and pneumoencephalogram likewise were unproductive. Visual fields showed no defect and visual acuity has remained 20/25.

In order to document the presence or absence of the usual effects of the disease, additional studies were done.

Of note was a diabetogenic oral glucose tolerance curve (fasting sugar: 74 mg/100 ml; 1 hour: 170 mg/100 ml; 3 hours: 140 mg/100 ml). The following studies were normal: serum pH, CO₂ content and electrolytes; growth hormone response to arginine (peak value, 20 nanograms/ml of plasma) and growth hormone response to insulin-induced hypoglycemia (peak value, 19 nanograms/ml plasma); serum thyroxine iodine (5.4 micrograms/100 ml); urinary 17-ketosteroids (9.9 and 13.5 mg/24 hours); urinary catecholamines (56.0 micrograms/24 hours) and urinary vanillylmandelic acid (3.1 mg/24 hours). Bone age, estimated from roentgenograms, was the same as chronological age.

During the next year, Eugene never demonstrated the disturbing stigmata of Cushing's disease, for example, hypertension, osteoporosis, emotional lability, renal calculi or the like. Because of the absence of the "dangerous" problems, neither subtotal adrenalectomy, hypophysectomy, nor irradiation of the pituitary was performed. In addition, since all available therapy was potentially "destructive" and his disease was mild, it was felt that treatment might be more detrimental to the patient's health than the disease itself, if the latter did not progress.

When the urinary 17-hydroxycorticosteroids became normal in 1967, we suspected that Eugene was in biochemical remission and confirmed this repeatedly over the next four years. In 1970 his tolerance to orally administered glucose was normal (fasting blood sugar: 76 mg/100 ml; 1 hour: 149 mg/100 ml; 3 hours: 98 mg/100 ml). Also, plasma cortisol levels showed the usual circadian rhythm. Eugene had grown from 55 inches in 1967 to 62 inches in October 1971, a growth rate of approximately 1 3/4 inches per year, a marked improvement to the earlier rate of 3/8 inch per year. He has lost the stigmata of Cushing's disease and matured sexually.

Cushing's Syndrome and Pregnancy with Spontaneous Remission after Delivery

VERDUGO C; DONOSO J; MEZA H; DOMKE G; ESTERIO H; MARTINEZ A; CRUZ G
Revista Medica de Chile 110(6): Jun 1982; 564-569

Extracted Summary

To this date there have been 27 cases of Cushing's syndrome and its relation to pregnancy published. This low frequency of association can be attributed to the fact that, generally speaking, suprarenal glucocorticoid hyperfunction is accompanied by problems with menstruation and/or infertility. Occasionally Cushing's syndrome can undergo unexpected evolutive changes and various cases have been described of spontaneous remission in persons who weren't pregnant, regardless of the cause of the syndrome. The period of gestation has been recognized as a factor that can modify the evolution of Cushing's syndrome. In the majority of cases one observes an exacerbation or initiation of the clinical syndrome with remission following childbirth. But sometimes attenuation of the syndrome has been seen in the course of gestation. Following is a case of Cushing's syndrome that appeared during pregnancy and disappeared after childbirth.

(Noetic Sciences translation)

SUPPLEMENTAL REFERENCES CUSHING'S DISEASE

Spontaneous Remission in a Case of Cushing's Syndrome Presumably Due to Adrenal Tumor

OVLISEN B; ANDERSEN HJ

Journal of Clinical Endocrinology and Metabolism 26(3): Mar 1966; 294-298

Cushing's Disease with Spontaneous Recovery Lasting 30 Years and Then Relapsing (Maladie de Cushing avec Rétrocession Spontanée Pendant 30 Ans et Réchute)

MORNEX R; GAGNAIRE JC; BERTHEZENE F; STEFANINI F; PROST G

Semaine des Hopitaux 48(4): Jan 20 1972; 276-278

Exacerbation of Cushing's Syndrome During Pregnancy

CALODNEY L; EATON RP; BLACK W; COHN F

Journal of Clinical Endocrinology and Metabolism 36(1): 1973; 81-86

Spontaneous Remission of Cushing's Syndrome After Termination of Pregnancy

RESCHINI E; GIUSTINA G; CROSIGNANI PG; D'ALBERTON A
Obstetrics and Gynecology 51(5): 1978; 598-602

Spontaneous Remission of Cushing's Disease: A Case Report and Review of the Literature

KAMMER H; BARTER M

American Journal of Medicine 67(3): Sep 1979; 519-523

Intermittent Cushing's Disease with Spontaneous Remission

SCOTT RS; ESPINER EA; DONALD RA

Clinical Endocrinology 11(5): Nov 1979; 561-566

Metabolic Disorders

DISORDERS OF PLASMA PROTEIN METABOLISM

Macrocryoglobulinemia

Report of a Case with Unusual Spontaneous Recovery

NUTTER DO; KRAMER NC

American Journal of Medicine 38: March 1965; 462-469

Extracted Summary

A case of clinical Waldenström's macroglobulinemia associated with cryoglobulin of $S_{20W}9.8$ is described, and the clinical and laboratory features of the macroglobulinemias commented on. The presence of a defect in renal concentrating ability corresponding to the degree of serum viscosity is reported. There was complete spontaneous remission.

SELECTED CASE REPORT

The patient, a 57-year-old Negro man, was admitted to the District of Columbia General Hospital for the first time on April 3, 1962, because of disorientation and confusion. He related having had vague anterior chest pain, dyspnea on exertion, dizziness, blurring of the vision of several weeks' duration and bleeding gums and hemoptysis for several days. He had noted impotency of insidious onset and mild weakness. The patient denied excessive use of alcohol. He had taken an unknown medication for relief of chest pain recently. At the time of admission to the psychiatry service he had a syncopal episode with cardiovascular collapse which responded rapidly when he was placed in the Trendelenburg position.

There was no history of infections, metabolic diseases or blood dyscrasia. The family history included carcinoma of the breast in his mother and death of a sibling from pulmonary tuberculosis.

Examination revealed a stuporous, muscular, well-nourished man. The blood pressure was 120/70 mmHg, pulse 80/minute and respirations 16/minute. The temperature was normal. A fine, maculopapular, seborrheic rash present over the back was the only abnormality noted on the skin or nails. The pupils were dilated and reactive, and old conjunctival hemorrhages were apparent. The optic fundi demonstrated fresh flame-shaped hemorrhages with venous engorgement and beading and a few small, soft exudates. Gingival bleeding without hypertrophy and small firm lymph nodes palpated in the left posterior cervical area were the only abnormalities observed in the head and neck. The lungs were normal and examination of the heart demonstrated accentuation of the second sound with physiologic splitting in the pulmonic area. A grade 2 (on six bases) systolic ejection murmur was heard at the left sternal border. The venous pattern was generally prominent. Slight abdominal distention

was present, and a smooth liver edge was palpated at the right costal margin, a splenic tip on the left. There was no edema, purpura or joint abnormality. The neurological examination was within normal limits. Psychiatric evaluation revealed impairment of memory, judgment and mentation, with confusion and poor orientation; these findings were considered to be compatible with an acute brain syndrome.

The white blood cell count was 5,000/mm³ with 79% neutrophils, 14% lymphocytes and 7% monocytes; the hematocrit was 30%, hemoglobin 10.7 gm%, red blood cell count 3.32 million/mm³, reticulocyte count 1.1% and platelet count 100,000/mm³. The peripheral smear was normochromic and normocytic. The blood was extremely viscous and gel formation occurred at room temperature. Results of the Sia water test were positive. The corrected sedimentation rate was 0 millimeters at 20°C. The Rumpel-Leede test and bleeding and clotting times were normal, and the prothrombin time was 19 seconds (control 15 seconds). Urinalysis was within normal limits with a pH of 5.0 and specific gravity of 1.010; Bence Jones proteinuria was not present. Stools were guaiac-negative. The reactions to intermediate tuberculin and histoplasmin skin tests were negative, as were the results of the test for syphilis. Blood urea nitrogen was 32.5 and nonfasting blood sugar 150 mg/100 ml. Serum sodium was 131, potassium 4.6, chloride 90 and carbon dioxide 34 mEq/L. The level of bromide in the blood was 4.7 mg/100 ml and of salicylates 1.75 mg/100 ml; there was no trace of barbituates. The serum amylase was less than 180 units and serum total protein was 7.9 with albumin 2.4 and globulin 5.5 gm/100 ml. The serum total bilirubin was 0.2 mg/100 ml, cholesterol 70 mg/100 ml, alkaline phosphatase 7.2 Bodansky units and acid phosphatase 0.7 Bodansky units. Results of a cephalin floccu-

lation test were trace and 1+, and the lupus erythematosus cell preparation was negative. A chest roentgenogram demonstrated generalized cardiomegaly with a dilated and calcified aorta. An ileus pattern was observed on abdominal x-ray film. Roentgenograms of the skull, lumbosacral spine and hip showed no abnormalities. Evidence of left ventricular hypertrophy and strain was observed on the electrocardiogram. A specimen of bone marrow from the iliac crest was normocellular and contained increased numbers of lymphoid cells and a slight increase in the number of plasma cells.

During the hospital course the patient was afebrile and his blood pressure was normal. His mental symptoms subsided gradually to a state of lethargy and slow mentation. Gingival bleeding stopped, and there was no evidence of cardiovascular, hematological or neurological disease. The optic fundi demonstrated almost complete regression of the initial lesions. Management consisted of bed rest, fluid and caloric supplements and the oral administration of 300 milligrams of ferrous sulfate daily after the completion of blood studies.

Further laboratory studies on the ninth hospital day yielded the following values: serum sodium 136 mEq/L, potassium 4.8 mEq/L, chloride 95 mEq/L, carbon dioxide 24 mEq/L, total bilirubin 0.3 mg/100 ml, alkaline phosphatase 4.2 Bodansky units, bromsulfalein retention 35%, serum glutamic oxaloacetic transaminase (SGOT) 140 units, thymol turbidity 12 units and total protein 8.3 gm/100 ml, with albumin 3.5 and globulin 4.8 gm/100 ml. On the twenty-fifth day the blood urea nitrogen was 13 mg/100 ml, fasting blood sugar 100 mg/100 ml, alkaline phosphatase 6.4 Bodansky units, cholesterol 242 mg/100 ml, bromsulfalein retention 25%, thymol turbidity 14 units and serum total protein 8.6 gm/100 ml, with albumin 3.1 and globulin 5.5 gm/100 ml. On the fifty-ninth day total bilirubin was 0.25 mg/100 ml, alkaline phosphatase 9.6 Bodansky units, cholesterol 221 mg/100 ml, SGOT 68 units and thymol turbidity 14.8 units. The hematocrits varied between 25 and 30%, white blood cell counts from 2,000 to 3,000/mm³ and blood platelets from 125,000 to 195,000/mm³. Barium enema and roentgenograms of the gastrointestinal tract revealed no abnormalities. A second specimen of bone marrow by sternal biopsy showed no changes.

Renal function studies were performed on May 2, 1962, with the following results: C_{IN} 81 ml/minute/1.73 m²; C_{PAH} 515 ml/minute/1.73 m²; U_{MAX} 630 mOsm/kg; Serum osmolality 287 mOsm/kg; U:P osmolality 2.19; T_m^c H₂O 6.0 ml/minute.

Additional studies of the serum proteins were performed. Vertical starch gel electrophoresis in a tris-citric acid borate discontinuous buffer system revealed a large homogenous component just behind the point of insertion, compatible with a macroglobulin or a gamma₁ myeloma protein. Further examination of the serum by agar immunoelectrophoresis against horse antihuman serum revealed a decrease in normal gamma globulin with an

increase in the precipitin arc due to the beta 2M macroglobulin. Serial electrophoretic studies showed a diminution in quantity of this abnormal protein to the 57th hospital day. Ultracentrifugal evaluation of this serum disclosed a major component of S_{20W} 9.8 which was 20% of total serum protein. A diminished normal gamma globulin component with a sedimentation constant of S_{20W} 6.4 was observed.

Studies of the viscosity of the patient's serum in a Cannon-Fenske Viscometer at 37°C revealed a transit time of 55 seconds (normal 65 seconds) and a water time of 45 seconds. Thus the serum had a relative viscosity of 9.1 (normal 1.4). On standing at room temperature the serum separated into two layers: the lower layer was a viscid gel and the upper layer was more fluid. Electrophoretic studies revealed that the gel layer contained the greatest amount of the abnormal protein. No evidence of cryoprecipitating protein was present on refrigeration. At 37°C. the gel became more fluid and could be mixed with the supernatant.

Two 500 cc trials of plasmapheresis were performed on the fifty-seventh and fifty-eighth hospital days, after the clinical symptoms and signs had essentially cleared. The patient was transferred to a lodging home June 26, 1962; at this time he was asymptomatic with no physical abnormalities, although still lethargic.

The patient returned to the medical clinic on August 12, 1962, with complaints of low back pain which developed after he had done heavy lifting three weeks previously. The pain was midline, dull aching, without radiation and most pronounced in the early morning while he was at rest. There was some improvement with exercise. He was otherwise asymptomatic and was referred for admission and re-evaluation at this time. On readmission the patient was lethargic, slightly confused and mentally dull, but oriented and well-maintained. The blood pressure was 135/70 mmHg, pulse 60/minute and respiration 16/minute. He was afebrile. The cervical adenopathy was unchanged; the head and neck were normal otherwise. The skin was seborrheic and without lesions. The lungs were normal and cardiac examination revealed a grade 2/6 systolic, ejection murmur at the left sternal border and accentuation of the second sound with splitting in the pulmonic area. Hepatosplenomegaly, purpura, edema, and pain or deformity of the back were not present. The neurological examination was within normal limits.

The white blood cell count was 5,800/mm³ with neutrophils 54%, lymphocytes 38%, monocytes 6%, hematocrit 42% the red blood cell count 3.34 ml/mm³, reticulocyte count 0.3%, and platelets 142,000/mm³. The peripheral smear revealed no abnormalities. The corrected sedimentation rate was 44 mm/hour at 20°C. Bleeding and clotting times were normal and the prothrombin time was 17 seconds (control 14 seconds). Urinalysis was within normal limits, with a specific gravity of 1.025, and pH 6.0. Three determinations for

protein were negative. The blood and serum appeared normal, and Sia water and formal gel test results were negative; cryoglobulin precipitation was not present. Results of the test for syphilis were negative. Blood urea nitrogen was 9.5 and fasting blood sugar 65 mg/100 ml. Serum sodium was 133, potassium 4.2, chlorides 105 and carbon dioxide 26 mEq/L. Serum calcium was 9.6 and phosphorus 2.4 mg/100 ml. The cholesterol was 250 mg/100 ml, total bilirubin 0.35 mg/100 ml, thymol turbidity 2.1 units, alkaline phosphatase 7.3 units and acid phosphatase 1.2 units (repeat determination 0.8 units). The results of a cephalin flocculation test were negative and trace. SGOT was 18 units, bromsulfalein retention 2.5% and serum total protein 6.0 gm/100 ml, with albumin 3.2 and globulin 2.8 gm/100 ml. The C-reactive protein was negative, latex fixation nonreactive, zinc precipitable globulin 1.54 units, and deoxyribonucleic acid (DNA) antibodies negative. A repeat determination for serum total protein was 7.1 gm/100 ml with albumin 4.2 and globulin 2.9 gm/100 ml. Roentgenograms of the chest, skull, vertebral column and hips revealed no abnormalities. Abdominal roentgenograms were consistent with mild ileus. The electrocardiogram demonstrated borderline voltage criteria for left ventricular hypertrophy and the Q-T interval was prolonged. A biopsy specimen of sternal bone marrow was hypercellular with a slight increase in

plasma cells and normal lymphocytes. The patient refused liver biopsy.

The serum proteins were restudied with the following results. Gel formation no longer occurred with standing at room temperature. On electrophoretic analysis in starch gel the abnormal component was only a small portion of the total proteins. On immuno-electrophoresis normal gamma globulin was observed with only slight prominence of the beta 2M precipitin arc. Repeat ultracentrifugal analysis showed that the abnormal component was present in only trace amounts and that normal gamma globulin was the major component of $S_{20W}^{6.4}$. Repeat studies of the serum viscosity revealed a transit time of 85 seconds and a relative viscosity of 1.9.

Renal function studies were repeated on June 8, 1962, with the following results: C_{IN}^{112} ml/minute/1.73 m^2 ; C_{PAH} 538 ml/minute/1.73 m^2 ; U_{MAX} 731 mOsm/kg; serum osmolality 286 mOsm/kg; U:P osmolality 256 $T^C_{mH_2O}$ 5.4 ml/minute.

The patient's clinical course following the second admission was unremarkable. The back pain responded to symptomatic therapy. He was asymptomatic except for lethargy and mental dullness and was discharged to a medical clinic on September 11, 1962. Re-examination on February 12, 1963, revealed no abnormalities and protein studies were completely normal.

SUPPLEMENTAL REFERENCES DISORDERS OF PLASMA PROTEIN METABOLISM

Remission of Macroglobulinemia Coincident with Hepatitis

WOLF RE; RIEDEL LO; LEVIN WC RITZMANN SE
Archives of Internal Medicine 120: 1972; 392-395

Alpha-Heavy Chain Disease: Report of a Case with Spontaneous Regression

SALA P; TONUTTI E; MAZZOLINI S; ANTONUTTO G;
BRAMEZZA M
Scandinavian Journal of Haematology 31: 1983; 149-154

HISTIOCYTOSIS

Spontaneous Resolution of Histiocytosis X

Report of a Case

MEENAN FO; CAHALANE SF

Archives of Dermatology 96: Nov 1967; 532-535

Extracted Summary

A case of histiocytosis X with spontaneous remission is described. The patient presented is an infant of six months, with cutaneous and bony lesions. No specific treatment was given, but the child was free of signs and symptoms two years later. The histological findings of eosinophils and fibrosis are probably of good prognostic import.

SELECTED CASE REPORT

A 6-month-old female infant was admitted to the skin department of the Children's Hospital, on September 26, 1964, with a history of a skin eruption that had been present for two months. She was a firstborn child and there was nothing relevant in the parents' history.

General Examination: This revealed a very pale child, who was not too sick, of normal weight and development for her age. She presented a scaling follicular papular rash which was extensive on the back and the occipital area of the scalp. It was sparse on the front of the trunk, and the limbs were clear. No other physical abnormality was detected except for some slight swelling in the left parietal bone. There was no enlargement of the spleen, liver, or lymph nodes. The following laboratory results were obtained: hemoglobin, 10.5 gm/100 ml; hematocrit, 32%; white blood cells (WBC), 7,000/mm³ with a normal differential count; platelets, 246,000/mm³; erythrocyte sedimentation rate, 48 mm after one hour (Westergren); urinalysis protein, ++, small amount of pus; urine culture yielded *Bacillus proteus*. Blood sugar, serum cholesterol, electrophoresis of serum proteins, and coagulation studies were all normal. The Wassermann reaction was negative. Biopsy of iliac crest marrow showed a very cellular marrow with normal proportionate development of all three major lines. There was evidence of slight megakaryoblastic erythropoiesis, a finding which was regarded as physiological at this age. There were no atypical cells.

Histopathology: Biopsies were taken from cutaneous lesions on the back and from an area of softening in the left parietal bone. Immediate preparations by the imprint technique were examined and the material was fixed in formalin. Examination of May Grunwald Giemsa imprint preparations and hematoxylin and eosin histological preparations showed a similar cell picture in all cases. In the skin there was a cellular infiltrate in the upper

dermis consisting of a small and large mononuclear cells and eosinophilic polymorphonuclears. The sections of the bony lesion showed a diffuse cellular infiltrate composed of histiocytes, small round cell, and eosinophilic polymorphonuclears. Fibrosis was evident in some areas. The cytological details were particularly well seen in the imprint preparations. Vacuoles of lipid appearance occurred within the cytoplasm of many of the histiocytes.

X-ray Examination: X-rays were taken of the skull and skeletal system. A large rounded defect was seen in the anterior part of the left parietal bone, and less well defined defects were situated more posteriorly within the same bone. The edges of the damaged defect were dense and well defined. No abnormalities were seen in x-rays of the chest and long bones. Radiological bone age was normal.

Course: In the hospital, the child's condition continued to be satisfactory and the anemia improved. The skin eruption began to involute. The urinary infection was difficult to clear up, but finally yielded to ampicillin. As the child seemed to be in good condition it was decided to withhold all treatment, and send her home for a period of six months. She was readmitted in May 1965. She had continued to develop normally over the previous six months. The skin eruption had completely disappeared leaving some slight depressed scars at the site of the lesions. Blood biochemical values were normal. Hemoglobin was 12.2 gm/100 ml; WBC, 5,600 with a normal differential. X-rays of the skull showed no change in the bony lesions. The child was again discharged on no treatment, and readmitted in May 1966. She was well and healthy, and her growth and development had continued normally. There were no abnormal laboratory findings. The skin had remained soundly healed. X-rays of the skull showed that the bony lesions had completely cleared up.

Histiocytosis X: Natural History and Management in Childhood

PRITCHARD J

Clinical and Experimental Dermatology 4: 1979; 421-433

Extracted Summary

Multi-system histiocytosis X is still a potentially fatal disorder. Death occurs from pulmonary, hepatic, small bowel or bone marrow failure often with severe intercurrent infection as the terminal illness. Chemotherapy has had some impact on mortality but morbidity in survivors is still a real problem. Around 50% of survivors will have a significant handicap. Complete response can be achieved with a variety of chemotherapeutic agents but the introduction of combination therapy has led to unacceptable toxicity especially in the very young. There is preliminary evidence that treatment with calf 'thymic humoral factor' may benefit a proportion of patients. This recent work supports the notion that histiocytosis X is not a true malignancy, but rather a subtle form of immune deficiency possibly involving a soluble thymic or T-lymphocyte product.

SELECTED CASE REPORT

The mother of a 6-month-old child sought medical advice after noting the child's reluctance to move his leg for 1 month. There were no other abnormal clinical signs and the remainder of a skeletal survey and

a bone marrow were normal. Biopsy revealed histiocytosis X. Since the baby was not walking, an expectant policy was followed. The femur healed spontaneously, and 1 1/2 years later there had been no recurrence.

Spontaneous Regression of Congenital Cutaneous Histiocytosis X

Report of a Case with Discussion of Nosology and Pathogenesis

DEHNER LP; BAMFORD JT; McDONALD EC
Pediatric Pathology 1(1): Jan-March 1983; 99-106

Extracted Summary

Spontaneous regression of histiocytosis X is a rare biologic event as judged by the extensive recorded experience in the literature. We present a case of congenital cutaneous histiocytosis X that resolved without specific therapy in the first week of life. Histologic and ultrastructural studies confirmed the interpretation. This child is an example of so-called pure cutaneous histiocytosis, which, like the other unisystem forms of the disorders, has an excellent prognosis.

SELECTED CASE REPORT

The patient, a 2,570 gram female infant, was the product of a pregnancy complicated by Rh incompatibility in gravida 2, para 2, ABO mother. During her first pregnancy, immunotherapy was apparently unavailable. Rh titers during the second pregnancy ranged from a low of 1:256 to 1:1,800. A diagnostic amniocentesis in the last trimester revealed optical densities in zones I and II. With evidence of pulmonary maturation, labor was induced uneventfully. The Apgar scores at 1 and 5 minutes were 7 and 8, respectively. At the time of delivery, there were eight discrete oval cutaneous lesions measuring 0.5 centimeters in greatest diameter. The anatomic distribution was the following: face (2), right axilla (1), left shoulder (1), left scapula (1), right arm (1), left arm (1) and right gastrocnemius region (1). These lesions were slightly raised, intensely erythematous, and hemorrhagic. Vesicles were noted on the flattened surface. Three new lesions developed in the first 24 hours of life. Neither petechiae nor purpura

was evident. It was thought that the cutaneous lesions represented extramedullary hematopoiesis. The liver was palpable 2 centimeters below the right costal margin and the spleen 0.5 centimeters below the left costal margin. Pertinent laboratory studies yielded the following results: hemoglobin, 12.5 gm/dl; hematocrit, 36.2%; mean corpuscular volume (MCV), 102; mean corpuscular hemoglobin (MCH), 34.7; mean corpuscular hemoglobin concentration (MCHC), 34.6; white cell count, 13,500/mm³; Coombs' test, 4+ positive; and total bilirubin, 8.6 mg/dl (direct 1.3 mg/dl) to a high of 14.4 mg/dl. Because of the hyperbilirubinemia, an exchange transfusion was performed and phototherapy was instituted. A skin biopsy was also performed. During the next 3 days, the icterus diminished and there was a rapid resolution of the skin lesions. The patient is doing well at 1 year of age. There are no residual skin changes and extracutaneous manifestations of histiocytosis X are not evident by physical examination or skeletal survey.

Spontaneous Remission of Multi-System Histiocytosis X

BROADBENT V; PRITCHARD J; DAVIES EG; LEVINSKY RJ; HEAF D; ATHERTON DJ;
PINCOTT JR; TUCKER S
Lancet 1(8371): Feb 4 1984; 253-254

Extracted Summary

Two infants presented with biopsy-proven histiocytosis X affecting multiple sites. Since neither showed evidence of organ failure or of constitutional upset, no specific therapy was given. In each case there was long-lasting spontaneous regression of disease. Analysis of blood mononu-

clear cells revealed a raised T₄:T₈ (helper:suppressor T lymphocyte) ratio at diagnosis but a normal ratio during remission. These observations support the argument that multi-system histiocytosis X, even in infants (Letterer-Siwe disease), is not a malignancy and that an 'expectant' treatment policy may be indicated in selected patients.

SELECTED CASE REPORTS

Case 1: A first baby was born to healthy unrelated parents, each with healthy children by a previous marriage. A rash appeared on the baby's cheeks within 24 hours of birth. At age 5 days the rash spread to the groins and buttocks and later, with fluctuating severity, to the trunk and proximal limbs. The diagnosis of HX was made by skin biopsy, and the baby was referred to the Hospital for Sick Children.

Examination revealed several hundred discrete 1-2 millimeter reddish-brown papules more or less confined to the skin of the neck and trunk and particularly numerous in the folds of the groins, where there were superficial erosions. His parents pointed out that depigmented areas among the papules represented scars of lesions that had healed spontaneously. The baby was tachypnoeic (30-40 /minute at rest) and had some rib recession. There was no anaemia, lymphadenopathy, or hepatosplenomegaly; the baby was not distressed, and his nutrition was excellent. Blood count and bone marrow aspirate and trephine biopsy were normal. Skeletal survey showed no lytic lesions, and liver function tests, including serum albumin, were normal. Chest x-ray showed an increase in interstitial shadowing and some hyperinflation lung volume was reduced (thoracic gas volume at functional residual capacity [TGV] was 86 milliliters; normal for body length 122-186 milliliters) with decreased lung compliance (4-6 ml/centimeter H₂O; normal for body length 5.5-11.5 ml/centimeter H₂O). Direct immunofluorescence testing of throat washings revealed no evidence of infection with cytomegalovirus (CMV), respiratory syncytial virus (RSV), *Pneumocystis carinii*, or other respiratory pathogen. Immunological testing showed normal serum immunoglobulin levels and yeast opsonisation. Lymphocytes showed a normal proliferative response to phytohaemagglutinin (PHA) stimulation. The number of circulating T(E-rosette-forming) cells was within normal limits but the T₄:T₈ lymphocyte ratio was very high at 5.4:1 (normal for age 2:1) owing to a deficiency of T₈ positive cells.

As there was no constitutional upset, and because many of the skin lesions appeared to have healed spontaneously, an expectant approach to treatment was adopted.

Two months later the baby developed biopsy-confirmed gingival involvement, treated with curettage, and the T₄:T₈ ratio had risen to 6.8:1.

By age 5 months the skin had cleared, the mouth had healed, and both chest x-ray and lung function had returned to normal (TGV 140 milliliters [normal for body length 128-194 milliliters]; compliance 6.1 ml/centimeter H₂O [normal for body length 6-12 ml/centimeter H₂O]). At age 8 months the T₄:T₈ ratio was normal (1.5:1). At age 2 years the child was well and chest x-ray was normal. All the earlier skin lesions had disappeared apart from minor intertrigo deep in the folds of the groins.

Case 2: A 3-month-old girl, born to healthy unrelated Pakistani parents, presented with gastroenteritis and required hospital admission for intravenous fluid therapy. A rash had been present for 2 weeks. A generalised brown-red papular eruption over the trunk and scaly erythema of the scalp resembling "cradle-cap" were noted, but there was no lymphadenopathy, hepatosplenomegaly, or respiratory difficulty. The diagnosis of HX was established by skin biopsy. Chest x-ray showed fine diffuse mottling of both lung fields, and both lung volumes (TGV 111 milliliters; normal for body length 152-227 milliliters) and lung compliance (6.2 ml/centimeter H₂O; normal for body length 7-14.5 ml/centimeter H₂O) were reduced. There was no serological evidence of infection with CMV, RSV, *P. carinii*, or other respiratory pathogens. Blood count, bone-marrow aspirate, trephine biopsy, liver function tests, and skeletal survey were all normal. Immunological studies showed normal serum immunoglobulins, yeast opsonisation, and PHA response. Analysis of blood mononuclear cells showed a raised T₄:T₈ ratio of 3:1.

After recovering rapidly from gastroenteritis, the baby thrived. In view of her excellent general condition, no specific therapy was given. Over the next 5 months the disease underwent spontaneous and complete remission. At age 2 years clinical examination, chest x-ray, and the T₄:T₈ ratio (1:1) were normal, and the child continued to make good general progress.

A Solitary Variant of Congenital Self-Healing Reticulohistiocytosis: Solitary Hashimoto-Pritzker Disease

BERGER TG; LANE AT; HEADINGTON JT; HARTMANN K; BURRISH G; LEVIN MW;
DISANTAGNESE PA; SCHWARTZ JL; LAMBERT JS
Pediatric Dermatology 3(3): June 1986; 230-236

Extracted Summary

Four neonates had solitary, congenital, rapidly growing, spontaneously ulcerating tumors of the face, trunk, and extremities. No extracutaneous involvement was found, and all lesions spontaneously involuted. Mononuclear cells of the cutaneous infiltrate were Langerhans' cells. These findings expand the spectrum of congenital self-healing reticulohistiocytosis.

SELECTED CASE REPORTS

A female child (Patient 1) was the product of an uncomplicated pregnancy in a 31-year-old Hispanic woman, gravida 7, para 5, abortus 2. At birth she had a solitary 1 centimeter brown nodule on the right temple. During the first week of life the lesion spontaneously ulcerated and crusted. Over the next six weeks the lesion grew to 2 centimeters in diameter and maintained a large central ulcer, despite several courses of oral antibiotics. At age 7 weeks, physical examination revealed a 2-x 2 centimeter, crusted, right temporal ulcer with raised borders. Results of a complete blood cell count, urinalysis, liver-spleen scan, bone scan, skeletal survey, chest and skull films, and examination of bone marrow aspirate were normal. Results of routine serum chemical determinations, including cholesterol and triglycerides, also were normal. By 12 weeks the skin lesion had reached a diameter of 2.5 centimeters. By 18 weeks it had involuted completely, leaving an atrophic scar.

A 3,510 gram male child (Patient 2) was born to a 19-year-old, black, gravida 2, para 2 woman whose pregnancy was significant only for recurrent urinary tract infections treated successfully with Keflex. In the delivery room, initial physical examination of the newborn showed a 1 centimeter, dry, crateriform nodule with central necrotic ulceration on the dorsum of the right foot.

Physical examination was otherwise normal. The skin lesion crusted and involuted at 2 weeks, and by 9 weeks consisted only of a small, flat, hyperpigmented 1 centimeter scar. The child's growth and development have been normal.

A 2-day-old male infant (Patient 3) was seen by a consulting dermatologist for an ulcerated nodule on the hypothenar eminence of the right hand, present at birth. Results of all clinical and laboratory studies after a biopsy diagnosis of Langerhans' cell tumor were negative. The lesion spontaneously cleared, leaving a small scar. The child is alive and well at five years of age.

A black male child (Patient 4), the product of an uncomplicated pregnancy and delivery, at birth had an erythematous, left inguinal cutaneous nodule measuring 1 x 2 centimeters. On day 2, superficial ulceration was noted, which rapidly progressed to central necrosis. The remainder of the physical examination and results of routine laboratory studies (complete blood count, urinalysis, and chest radiograph) were unremarkable. The lesion involuted during the next 10 weeks and was undetectable on follow-up examination at age 1 year.

Spontaneous Healing of Langerhans Cell Histiocytosis (Histiocytosis-X)

CORBEEL L; EGGERMONT E; DESMYTER J; SURMONT I; DE VOS R; DE WOLF-PEETERS C;
COBBAERT C; EYKENS A
European Journal of Pediatrics 148(1): Oct 1988; 32-33

Extracted Summary

A three month old male infant presented with pallor, hepatomegaly (4.5 centimeters), splenomegaly (1.5 centimeters), anaemia (Hb 6 gm/dl) and thrombocytopenia ($16 \times 10^9/l$). A liver biopsy was diagnostic for Langerhans cell histiocytosis (histiocytosis X). The patient's lymphocytes, co-cultured with neonatal lymphocytes, were positive for virus-like particles without

reverse transcriptase activity. The hepatomegaly diminished after 6 months and a second liver biopsy showed decreased histiocytic infiltration. No treatment was given. A second viral blood culture remained negative. After 14 months, the hepatomegaly had disappeared completely and there were no more abnormal haematological or clinical findings.

SELECTED CASE REPORT

A 3-month-old male infant, D. B., without past history was first seen on account of pallor and vomiting. Anaemia, hepatomegaly (4.5 centimeters) and splenomegaly (1 centimeter under the costal margin) were recorded. A transfusion was given but recurrence of pallor prompted referral to our department. Upon admission, the infant's nutritional condition was excellent; there was no fever, but a few purpuric spots were noticed on both feet.

Haematological examination showed a haemoglobin content of 6 gm/dl, a red cell count of $2.3 \times 10^9/l$, a white cell count of $10.5 \times 10^9/l$ with 47% neutrophils, 16×10^9 thrombocytes/l, and reticulocytes 9%-20%. Bone marrow studies ruled out leukaemia and neoplastic processes. There was an erythroblastic reaction with good differentiation of the myeloid line and many megacaryocytes.

Liver function tests, coagulation factors, catecholamine excretion, and blood and bone marrow karyotype were normal. However, plasma triglycerides were increased to 285 mg/dl and blood cholesterol was 129 mg/dl. Echography of the abdominal cavity did not reveal a tumour, but a few hypodense zones were seen in the enlarged liver. X-ray films of the chest and skull and bone technetium isotopic scintigraphy were normal. A surgical liver biopsy was performed under the protection of platelet infusion.

The general architecture of the liver was preserved, but histiocytic infiltration was evident in the portal areas and in the sinusoids. Some of these histiocytes were characterized by an indented nucleus and a moderate amount of cytoplasm: the others showed a normal to small nucleus and an abundant amount of cytoplasm with remnants of phagocytic activity (pigmented granules, lipid vacuoles and erythrocytes). The hepatocytes were swollen and in many of them steatosis was visible. Ultrastructural studies confirmed the presence of phagocytic histiocytes; moreover, macrophages with Birbeck granules, i.e., Langerhans histiocytes, were observed. The histological diagnosis was histiocytosis X.

Immunohistochemistry demonstrated the presence of phagocytic histiocytes (with positive reactions for OKM5, neuroprotein S100 and α_1 antichymotrypsin) as well as the presence of Langerhans cells (positive for S100 and OKT6), confirming the ultrastructural diagnosis.

The increased plasma triglyceride level and the hepatic steatosis prompted a further exploration of lipid metabolism. A lipidogram demonstrated almost complete absence of lipoprotein A. The amount of esterified chol-

esterol was low (13% of the normal value). LCAT (lecithin cholesterol acyltransferase) activity was less than 10% of normal, but the concentration of the enzyme, measured by radioimmunoassay, was 50% of normal, and therefore suggestive of a heterozygous state. This was confirmed by determination of the enzyme activity in the family members. As the clinical findings were quite different from those found in homozygotes for LCAT deficiency, it was considered that the disturbances of lipid metabolism were secondary.

Bacteriological studies in this afebrile patient were negative. Serial serology for common viruses was unremarkable and did not show increases in antibody titres. Attempts at virus isolation from nasopharyngeal aspirate, saliva, stools, urine and liver and bone marrow biopsies, performed on primary monkey kidney, human diploid fibroblast, HeLa and RD cell monolayers, were negative. However, when the patient's lymphocytes were co-cultured with neonatal lymphocytes, as in the isolation procedure for HIV, the culture was destroyed within a few days; this effect was serially transmissible with fresh lymphocytes, but so far this has not been possible either with lymphocyte cell lines or the above monolayers. There was no evidence for a retrovirus, since HIV Ag and reverse transcriptase activity were not detected in the cultures; HIV serology has remained negative. After negative staining, pellets of the supernatant of lymphocyte cultures with cytopathic effect, as well as ruptured lymphocytes, showed sparse round particles, 60-80 nanometers in diameter, somewhat polymorphous and without clear internal structure or membrane. These "virus-like" objects were not seen in control cultures. Indirect immunofluorescence on "infected" lymphocytes showed that antibody against the presumptive virus is common in humans. So far, the agent has not been identified as a known virus.

No treatment was instituted. The child did well, the hepatomegaly regressed and a new liver biopsy performed 6 months later showed a decrease in cellular infiltration but little change in the ratio of free versus esterified cholesterol. A blood virus culture was repeated but was negative. The child was seen again 14 months later, when the hepatomegaly had disappeared completely, and the haematological findings and erythrocyte sedimentation rate were normal. Plasma esterified cholesterol amounted to 60%, as expected in heterozygotes, and the LCAT activity was again in the heterozygote range. Fluorescent antibodies were observed in the blood against the virus isolated during the first admission. T₄/T₈ ratio, which was 4 at the beginning of the disease, had decreased to 2.1.

Congenital Self-healing Reticulohistiocytosis

Report of a Patient with a Strikingly Large Tumor Mass

TIMPATANAPONG P; ROCHANAWUTANON M; SIRIPOONYA P; NITIDANDHAPRABHAS P

Pediatric Dermatology 6(1): Mar 1989; 28-32

Extracted Summary

A newborn male Thai infant had numerous brownish red nodules of various sizes scattered over both palms and soles, left thigh, abdomen, chin, and left upper eyelid. An extremely large tumor mass was present on the right sole. Many lesions showed spontaneous ulceration. No extracutaneous involvement was found. All lesions involuted spontaneously within two to three months, some with scar formation. Histology showed large numbers of mononucleated and multinucleated histiocytic cell infiltrations, 10% of which contained Birbeck's granules. Areas of necrosis and calcification were also seen in the largest tumor. No recurrence was observed after follow-up for three years.

SELECTED CASE REPORT

A male Thai infant was born at full-term in September 1985 to a healthy primigravida. He was delivered by cesarean section because of fetal distress and meconium staining. His birth weight was 2,850 grams, and Apgar scores were 9, 10, and 10 at 1, 2, and 5 minutes, respectively.

At the time of birth the infant exhibited numerous brownish red to bluish red, firm, papulonodular lesions on the abdomen, left thigh, chin, left upper eyelid, and both palms and soles. Some lesions were covered by hemorrhagic crusts and some by intact normal skin. The nodules were most numerous over both soles. The largest lesion on the right sole was about 8 centimeters. It looked almost like a large, red, applelike tumor mass attached to his heel. The mucous membranes were unaffected. No hepatosplenomegaly or lymph node enlargement was found. The patient's general condition was satisfactory.

A few days after birth, the largest mass on the right sole became eroded and showed surface necrosis. The size of this tumor mass strikingly decreased within one week to almost half its original size.

Results of a complete blood cell count, urinalysis, and serum biochemical determination were normal. Examination of bone marrow aspirate was also normal. Bone survey demonstrated a shadow of a large soft tissue mass at the proximal part of the right foot with small, scattered, calcified spots throughout the mass. No lytic bone lesion was observed.

Two biopsy specimens were obtained one week apart from two different lesions. The first was taken from a small nodule for light microscopic examination one day after birth. The hematoxylin eosin stained section showed dense cellular infiltrates occupying the entire thickness of the dermis with epidermal invasion. The infiltrates consisted mainly of large histiocyte-like cells with polymorphic, vesicular nuclei and eosinophilic, nonfoamy cytoplasm admixed with eosinophils, lymphocytes, and

extravasated erythrocytes. No erythroleukophagocytosis was observed. The small dermal vessels were dilated and showed swollen endothelium.

From the clinical appearance of vascularlike tumor and the histologic findings of increased cellularity and vascularity, the differential diagnosis at this time included histiocytic disorders and cellular angioma of infancy. The second biopsy was taken from the large, thick tumor mass one week after birth for light and electron microscopic examination. The histopathologic findings showed heavy cellular infiltrates throughout the dermis as well as the subcutaneous tissue. The infiltrations consisted of large, mononucleated and multinucleated histiocytes, eosinophils, and lymphocytes. Extravasated erythrocytes and foci of necrosis with deposits of calcium were scattered throughout the dermal infiltrate. Many giant cells contained tissue debris and calcium within abundant, pale-staining, foamy cytoplasm. Reticulum stain showed moderately increased reticulum fibers surrounding groups of cells and occasionally surrounding individual cells. Periodic acid-Schiff (PAS) staining on the sections revealed PAS positive, diastase-resistant granules in most of the histiocytes.

Electron microscopic examination of material from the second biopsy showed approximately 10% of the tumor cells to contain Langerhans' granules. A few concentrically laminated bodies were observed.

The ulcerated, large tumor mass on the right sole regressed rapidly without therapy to less than half its original size within one month. It regressed completely and healed with a large hyperpigmented scar in three months. All other small lesions also involuted spontaneously in the same period and left either hyperpigmented macules or small atrophic scars. Some disappeared without a trace. No recurrence was observed after an interval of three years, and the large scar on the right sole also became less conspicuous.

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American Journal of Dermatopathology 12(4): Aug 1990; 396-401

AMYLOIDOSIS

Spontaneous Regression of Diffuse Tracheobronchial Amyloidosis

HOF DG; RASP FL
Chest 76(2): Aug 1979; 237-239

Extracted Summary

Diffuse tracheobronchial amyloidosis which underwent an extensive spontaneous regression is described in a 39-year-old man. This regression was documented by serial roentgenograms of the chest, studies of pulmonary function, and bronchoscopic procedures with mucosal biopsies. The clinical implications of this spontaneous change are discussed.

SELECTED CASE REPORT

A 69-year-old white man presented with hemoptysis. This episode had begun three weeks prior to his being seen. He first noted only streaking of blood in the sputum associated with a minimal cough, but the hemoptysis increased in frequency and amount. He denied any fever, chills, or shortness of breath. The patient had a ten-pack-year history of smoking cigarettes but had stopped eight years previously. His only other respiratory complaint was chronic allergic rhinitis. This was exacerbated by grain dust, to which the patient was exposed at his work in a feed store. He had no other occupational exposure. The patient denied any history of asthmatic wheezing, or previous pneumonia. He had no known exposure to tuberculosis, and his Mantoux test with intermediate-strength tuberculin had been negative twice in the past. In 1974 and 1975, the patient had experienced transient episodes of hemoptysis, each with normal chest roentgenograms and with resolution coincident with oral antibiotic therapy.

On physical examination the patient was a well-developed white man in no acute distress. His blood pressure was 140/90 mmHg, the pulse rate was 72 beats/minute, the respiration rate was 14/minute, and the temperature was 37°C. (98.6°F.). Examination of the chest revealed occasional rhonchi over both bases but no wheezing or rales. The findings from the remainder of the examination were normal. The hematocrit reading was 43%, and the leukocyte count was 11,000/mm³, with a normal differential cell count. The chest roentgenogram showed a lingular infiltrate with loss of volume (new radiographic findings since 1975). The patient was begun on therapy with ampicillin (500 milligrams four times daily) and was referred to the chest clinic.

Five days later, the patient's status was unchanged. Therefore, he was admitted to the hospital for bronchoscopic examination and further work-up. Additional laboratory evaluation revealed a platelet count of 340,000/mm³ and normal results on studies of blood clotting. Serum electrolytes, blood urea nitrogen, creatinine, and hepatic enzymes, as well as thyroid function and urinary sediment were normal. The findings from serum protein electrophoresis were also normal without evidence of a monoclonal spike. The electrocardiogram was normal.

Subsequent to bronchoscopic examination, biopsy of the bone marrow and rectal mucosa were done and gave normal results.

Fiberoptic bronchoscopic examination performed with local anesthesia revealed normal vocal cords, trachea, and carina; however, just below the level of the carina, a diffuse infiltrative process involving both main-stem bronchi was found. This process produced narrowing and partial obstruction of every segmental orifice. Although the obstructive tissue appeared friable, lobar segmental orifices could not be penetrated by the bronchoscope. At a distance the subsegmental bronchi did not appear to be involved. Representative specimens for biopsy revealed submucosal, eosinophilic, amorphous hyaline material that showed birefringence when stained with Congo red and was enhanced when stained with crystal violet. The diagnosis of amyloid was further confirmed with electron-microscopic examination, which demonstrated the characteristic fibrillar matrix of the material.

No therapy was instituted at this time; however, the patient was advised to remain off work indefinitely and to avoid exposure to grain dust or cigarette smoke. Over the next month the patient's hemoptysis and respiratory complaints resolved, and the productive cough decreased. Repeat studies of pulmonary function revealed no changes in the previous spirometric data, volumes, or arterial blood gas levels; however, there was a marked improvement in the peak flows. Repeat bronchoscopic examination performed five weeks after the initial diagnosis revealed a remarkable resolution of the diffuse process which had been observed earlier. Nearly all segments were open, easily examined, and free of mucosal involvement. Specimens from biopsy of these areas were now normal, failing to show the presence of amyloid. Only minimal involvement of the right middle lobar orifice and left secondary carina persisted. Radiographic findings also showed improvement in the previous area of volume loss. Since the spontaneous improvement, the patient has continued to do well over a nine-month period.

SUPPLEMENTAL REFERENCE AMYLOIDOSIS

Nephrotic Syndrome in Amyloidosis. Spontaneous Regression After Re-establishing Nutrition (letter) (Syndrome Néphrotique de l'Amylose. Régression Spontanée après Renutrition)

LEJONC JL; BROCHARD P; GEORGE C; SCHAEFFER A; PORTOS JL

La Presse Medicale 9(18): Apr 19 1980; 1308-1310

Deficiencies of Humoral Immunity

Spontaneous Recovery of Selective IgA Deficiency

Additional Case Reports and A Review

BLUM PM; HONG R; STIEHM ER
Clinical Pediatrics 21(2): Feb 1982; 77-80

Extracted Summary

Selective IgA deficiency, a common primary immunodeficiency, occasionally may undergo spontaneous recovery. In this paper we present three additional children whose IgA levels spontaneously returned to normal. All three presented with gastrointestinal symptoms, and one child also had frequent upper respiratory infections. We review other cases of spontaneous IgA deficiency, and the role of exogenous function in its etiology, and possible mechanisms of recovery.

SELECTED CASE REPORTS

Case 1: This 2-year-old white boy was referred because of frequent sore throats and upper respiratory infections. Because of milk intolerance, he had been fed soy formula. The family history was unremarkable and physical examination was normal. The initial IgA level was 4 mg/dl, while IgG and IgM were normal. Immunoglobulins of the mother, father, and an 18-month old sister were normal. Anti-IgA antibodies were absent. Repeat immunoglobulins 2 years later were IgG, 885 mg/dl; IgM, 93 mg/dl; and IgA, 0. Two additional years later, the IgG was 1,203 mg/dl, IgM 140mg/dl, and IgA 135 mg/dl (repeated once). He was symptom free at that time.

Case 2: This 1-year-old white girl was admitted to UCLA Hospital because of diarrhea and failure to thrive. Extensive laboratory evaluation revealed no abnormalities except for an IgA of 10 mg/dl. Anti-IgA

antibodies were absent. The child's diarrhea abated somewhat on soy formula feedings, which were continued until age 4. Both parents' immunoglobulins were normal. A brother had also experienced chronic diarrhea and failure to thrive. He recovered gradually after age 10. Two years later the patient's IgA level was 26 mg/dl, and 4 years later it was 47 mg/dl. Her most recent value at age 9 was 132 mg/dl. Following recovery of IgA level, the immune system was further characterized. Her T cells were 70% by E rosetting, and PHA stimulation was normal. B cells, including IgA-staining B cells, were present in normal distribution. In vitro immunoglobulin production following PWM stimulation was normal for IgG, IgM, and IgA. However, her chronic diarrhea did not abate until age 8, 6 years after the IgA levels began to increase. She now can tolerate milk.

SUPPLEMENTAL REFERENCES DEFICIENCIES OF HUMORAL IMMUNITY

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The Evolving Clinical Course of Patients with Insulin Receptor Autoantibodies: Spontaneous Remission or Receptor Proliferation with Hypoglycemia
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