Secretin

Note: Secretin is not approved by the FDA for the treatment of Autism. True, a physician may use this "off label" at his or her own discretion. However without proper antibody testing first this "wonder drug" might become more than just a little problem for many. There are "theoretical" concerns re that even if one screens for antibodies appropriately, repeated infusions could trigger a child's immune system to "attack" their own Secretin (or its receptors) creating major medical problems. Also, many are concerned re "other" hormone effects / interactions over time on a child's young body. Researchers remain very concerned re allergic reactions (possibly fatal when given IV), and the unknown transmission of virus, retro-viruses, or other unknown "vectors" (i.e. priom organism, "mad-cow" type organisms, etc.) in the IV preparation for sure, ?? the oral (still trying to obtain further information).
In addition, as some time is passing, while the "jury is still out," just as with IVGG, after a few "wonder" stories, I am not hearing of any significant long term changes / success (beyond some GI help). Of 10 or 11 patients of mine who have tried Secretin (back East), only 1 has any success, 1 has had a complete disaster for about 2 months, and the others see no significant changes good or bad. Unless this agent had a significantly higher "cognitive" success rate, it is very likely the risks currently appear to be outweighing the gains by a long margin. Please review the precautions outlined from the PDR. Remember these are your children. Appropriate FDA trials are necessary to assure safety and determine any real efficacy.
Secretin has hit the US mass media , you may retrieve the stories here:
ABC's Good Morning America carried a story 6 October 1998 NBC's Dateline ran a story 7 October 1998 **The Abstracts that started it all…**
Improved social and language skills after secretin administration in patients with autistic spectrum disorders. Horvath K; Stefanatos G; Sokolski KN; Wachtel R; Nabors L; Tildon JT
Department of Pediatrics, University of Maryland School of Medicine, Maryland, USA. J Assoc Acad Minor Phys, 1998, 9:1, 9-15

Abstract: We report three children with *autistic spectrum disorders* (ed. this does not mean Autism DSMIV 299) who underwent upper gastrointestinal endoscopy and intravenous administration of secretin to stimulate pancreaticobiliary secretion. All three had an increased pancreaticobiliary secretory response when compared with nonautistic patients (7.5 to 10 mL/min versus 1 to 2 mL/min). Within 5 weeks of the secretin infusion, a significant amelioration of the children's gastrointestinal symptoms was observed, as was a dramatic improvement in their behavior, manifested by improved eye contact, alertness, and expansion of expressive language. These clinical observations suggest an association between gastrointestinal and brain function in patients with autistic behavior. (ed. known in research circles for many years is the gut-brain-immune system "triad")
Oral famotidine: a potential treatment for children with autism. Linday LA
College of Physicians and Surgeons, St Luke's-Roosevelt Hospital Center, New York, NY 10019, USA. Med Hypotheses, 1997 May, 48:5, 381-6

Abstract: Famotidine (Pepcid, a histamine-2 receptor blocker, is marketed for the treatment of peptic ulcer disease, gastroesophageal reflux, and the treatment of pathological hypersecretory conditions, including the Zollinger-Ellison syndrome. Recent reports indicate that it is also effective in relieving the deficit (or withdrawal) symptoms of adults with schizophrenia. Autism, a neuropsychiatric disorder which presents within the first few years of life, is defined by deficient social interaction, communication, language, play, and a markedly restricted repertoire of activities and interests. Similarities between the deficit symptoms of schizophrenia and the social deficit symptoms of autism suggest the hypothesis that famotidine may be useful in treating children with autism. Histamine serves as a neurotransmitter and neuromodulator in the brain. H2-receptors in the brain predominantly transmit inhibitory signals; when these receptors are stimulated in animals, spontaneous activity and exploratory behavior decrease; blockade of H2-receptors would therefore be expected to reverse this inhibition.

From the PDR

SECRETIN-FERRING (FERRING LABORATORIES, INC.)

DESCRIPTION:

FOR DIAGNOSTIC USE IN PANCREATIC DYSFUNCTION

Secretin is a gastrointestinal peptide hormone that was first extracted from porcine duodenum by Jorpes & Mutt (1961). The heptacosa-peptide was subsequently sequenced and synthesized by Mutt, Bodansky and their co-workers at the Karolinska Institute. Secretin-Ferring is a highly purified naturally occurring porcine hormone with a potency of not less than 3000 clinical units (CU) per mg peptide. Secretin is chemically defined as follows:

Mol.Wt. 3055.5

Empirical Formula: $C_{130}H_{220}N_{44}O_{41}$

Structural Formula: H-His-Ser-Asp-Gly-Thr-Phe-Thr-Ser-
Glu-Leu-Ser-Arg-Leu-Arg-Asp-Ser-Ala-Arg-Leu-Gln-Arg-
Leu-Leu-Gln-Gly-Leu-Val-NH_2

Secretin-Ferring contains 75 CU of lyophilized, sterile purified secretin, 1 mg of L-cysteine hydrochloride, and 20 mg of mannitol per vial. When reconstituted in 7.5 mL of Sodium Chloride Injection USP, each mL of solution contains 10 CU secretin for intravenous use. The pH of the reconstituted solution has a range of 2.5-5.0.

ACTIONS/CLINICAL PHARMACOLOGY:

The primary action of secretin is to increase the volume and bicarbonate content of secreted pancreatic juices. The standard unit of activity used for Secretin- Ferring is the clinical unit defined by Jorpes & Mutt in 1966. In a study of 6 healthy subjects the t(1/2) for secretin approximated 4 minutes with a clearance rate of 540 mL/min (Kolts and McGuigan, 1977). Normal ranges for pancreatic secretory response to intravenous secretin in patients with defined pancreatic diseases have been shown to vary. The variation is related to the secretin product used as well as inter-investigator differences in operative technique. However, it has been demonstrated that properly performed tests with secretin will identify pancreatic disease (Gutierrez and Baron, 1972, Lagerlof et al., 1967).

The pancreatic secretory responses to secretin in normal subjects and patients with well-documented pancreatitis are shown in Table 1 (Gutierrez and Baron, 1972).

Table 1

	Normal male subjects (10)(a)	Chronic Pancreatitis (5)
Volume secreted (mL/kg/hr)	3.6+/-0.8(b)	1.1+/-0.6
HCO_3 content (mEq/L)	114+/-20	71+/-33
HCO_3 output (mEq/kg/hr)	0.436+/-0.141	0.105+/-0.093

(a)number of subjects.

(b)-/X +/-S.D. The values obtained for Table 1 are derived from a single study by investigators skilled in performing the secretin test and are to be taken only as guidelines. These results should not be generalized to results of secretin testing conducted in other laboratories. However, a volume response of less than 2.0 mL/kg/hr, bicarbonate concentration of less than 90 mEq/liter and bicarbonate output of less than 0.2 mEq/kg/hr are consistent with impaired pancreatic function. A physician or institution planning to perform secretin testing for diagnosis of pancreatic disease should begin by assessing enough normal subjects (>/=5) to develop proficiency in proper technique and to generate normal response ranges for the three commonly assessed parameters of pancreatic exocrine response to Secretin-Ferring.

Proper technique for carrying out the secretin test of pancreatic function is described in DOSAGE AND ADMINISTRATION.

Secretin-Ferring administered intravenously stimulates gastrin release in patients with gastrinoma (Zollinger-Ellison syndrome), whereas no or only small changes in serum gastrin concentrations occur in normal subjects. Secretin- Ferring may produce a small decrease in serum gastrin levels in patients with duodenal ulcer disease. This gastrin response is the basis for the use of Secretin-Ferring as a provocative test in the evaluation of patients in whom gastrinoma is a diagnostic consideration. Accepted technique for carrying out the secretin provocation test is detailed in DOSAGE AND ADMINISTRATION.

INDICATIONS AND USAGE:

Secretin-Ferring (secretin) is indicated for:

(1) Diagnosis of pancreatic exocrine disease.

(2) As an adjunct in obtaining desquamated pancreatic cells for cytopathologic examination.

(3) Diagnosis of gastrinoma (Zollinger-Ellison syndrome).

CONTRAINDICATIONS:

Patients suffering from acute pancreatitis should not receive Secretin-Ferring until the attack has subsided.

WARNINGS:

Because of a potential allergic reaction to secretin, patients should receive an initial intravenous test dose of 0.1-1.0 CU. If no allergic reaction is noted after one minute the recommended dose may be injected slowly over 1 minute. A test dose is especially important in patients with a history of atopic allergy and/or asthma. Appropriate measures for the treatment of acute hypersensitivity reactions should be immediately available.

PRECAUTIONS:

GENERAL: Patients who have undergone vagotomy, or are receiving anticholinergics at the time of secretin testing, or who have inflammatory bowel disease may be hyporesponsive to secretin stimulation. This response does not indicate pancreatic disease. A greater than normal volume response to secretin stimulation, which can mask coexisting pancreatic disease, is occasionally encountered in patients with alcoholic or other liver disease.

DRUG/LABORATORY TEST INTERACTION: The concomitant use of anticholinergic agents may make patients hyporesponsive (false positive).

CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY: Long-term studies in animals have not been performed to evaluate the carcinogenic, mutagenic potential or possible impairment of fertility effects of secretin.

PREGNANCY (CATEGORY C): Animal reproduction studies have not been conducted with Secretin-Ferring. It is also not known whether Secretin-Ferring can cause fetal harm when administered to a pregnant woman or can affect reproductive capacity. Secretin-Ferring should be given to a pregnant woman for diagnosis of gastrinoma (Zollinger-Ellison syndrome) only if clearly needed. Insofar as fluoroscopic guidance is usually necessary to position the double-lumen tube used in the pancreatic function test, this test should be postponed until after delivery.

NURSING MOTHERS: It is not known whether secretin is excreted in human milk. Because many drugs are excreted in human milk, caution is advised when Secretin-Ferring is administered to a nursing woman. Further, normal values for pancreatic secretory response to Secretin-Ferring and for serum gastrin response have not been established for nursing women.

PEDIATRIC USE: Safety and effectiveness in children have not been established.

DRUG INTERACTIONS:

SEE PRECAUTIONS

ADVERSE REACTIONS:

No adverse reactions to Secretin-Ferring have been reported. ***(Ed: No repeat infusion studies have ever been done, as is being proposed for the children)***

DOSAGE AND ADMINISTRATION:

Secretin-Ferring should be prepared immediately prior to use. The contents of a vial are dissolved in 7.5 mL of Sodium Chloride Injection USP, to yield a concentration of 10 CU per mL. Avoid vigorous shaking. Discard any unused portion after reconstitution.

The reconstituted drug product should be inspected visually prior to administration. If particulate matter or discoloration are seen, the product should be discarded.

DOSAGE:

PANCREATIC FUNCTION TESTING AND PROCEDURE FOR OBTAINING DESQUAMATED PANCREATIC CELLS FOR CYTOPATHOLOGY: 1 CU per kg body weight by slow intravenous injection over 1 minute.

DIAGNOSIS OF GASTRINOMA (Zollinger-Ellison syndrome): 2 CU per kg body weight by slow intravenous injection over 1 minute.

ADMINISTRATION

1. PANCREATIC FUNCTION TESTING: A Dreiling type, radiopaque, double-lumen tube is passed through the mouth following a 12-15 hour fast. The proximal lumen of the tube is placed in the gastric antrum and the distal lumen just beyond the papilla of Vater with the aid of fluoroscopic guidance. The positioning of the tube must be confirmed and the tube secured prior to secretin testing. A negative pressure of 25-40 mm Hg is applied to both lumens and maintained throughout the test. Interruption of suction at 1 minute intervals improves the reliability of fluid collections. When uncontaminated duodenal contents are obtained--i.e., when these secretions are clear, although possibly bile stained, and have a pH of >/=6.0--a baseline sample of duodenal fluids is collected for 2 consecutive 10 minute periods. Subsequent to the baseline collections, Secretin-Ferring at a dose of 1 CU/kg of body weight is injected intravenously in approximately 1 minute. Duodenal fluid is then collected for 60 minutes after secretin administration. The aspirate is fractioned into four collection periods, the first two at 10 minute intervals, and the last two at 20 minute intervals. The duodenal lumen of the tube is cleared with an injection of air after collection of each fraction. Wide variations in volume of the aspirate will be indicative of incomplete aspiration or contamination. Each fraction of duodenal fluid is to be chilled and subsequently analyzed for volume and bicarbonate concentration.

2. PROCEDURE FOR OBTAINING DESQUAMATED PANCREATIC CELLS FOR CYTOPATHOLOGY: A duodenal aspirate obtained as under Pancreatic Function Testing is submitted for cytopathological examination.

3. SECRETIN TESTING FOR GASTRINOMA (Zollinger-Ellison syndrome). The patient should have fasted for at least 12 hours prior to beginning the test. Prior to injection of Secretin-Ferring, two blood samples are drawn for determination of fasting serum gastrin levels (baseline values). Subsequently, 2 CU of Secretin- Ferring per kg of body weight are administered intravenously over 1 minute; post-injection blood samples are collected after 1,2,5,10 and 30 minutes for determination of serum gastrin concentrations.

Gastrinoma is strongly indicated in patients with elevated fasting serum gastrin concentrations in the 120-500 pg/mL range (determined by RIA using an antibody to gastrin similar to that prepared by Rehfeld) and in patients who show an increase in serum gastrin concentration of more than 110 pg per mL over basal level.

HOW SUPPLIED:

Secretin-Ferring is supplied as a lyophilized sterile powder in 10 mL vials (NDC 55566-1075-1) containing 75 CU. The unreconstituted product should be stored at -20° C (freezer). However, the biological activity of Secretin-Ferring will not be significantly decreased by storage at temperatures up to 25° C for up to 3 weeks. Expiration date is marked on the label.

Caution: Federal (USA) law prohibits dispensing without prescription.

Manufactured for
Ferring Pharmaceuticals, Inc.
120 White Plains Rd., Suite 400
Tarrytown, NY 10591

By:
Ferring AB
Malmo, Sweden
DC-120: Rev. 06/88
Revision date May '92

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