Simultaneous Occurrence of Spherocytosis and Polydactyly in a Brazilian Family

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Polydactyly, the presence of extra-fingers at hands or feet, is a rare anomaly usually inherited through a dominant gene. Another condition which remembers ulnar hexadactyly is the formation of small finger-like excrescences in the ulnar part of the hand known as *pedunculated postminimi* (review in Gates, 1946).

Spherocytosis is still another rare condition: the erythrocytes appear with an almost spherical shape differing from the usual biconcave form and show diminished resistance to hemolysis by hypotonic saline solutions. Persons with this disease present many other clinical characteristics, such as anemia of a hemolytic type, jaundice, splenomegaly, leg ulcers and cholelithiasis. Usually the condition is also inherited by means of a dominant gene.

Many investigators have reported several neurologic disturbances as well as osseous and developmental anomalies which use to occur simultaneously with spherocytosis. Among these polydactyly is frequently mentioned. Is this association fortuitous or is there a causal relation between this last condition and spherocytosis? The occurrence of both anomalies in one person prompted the following study which aims at clarifying the relation between the two.

Material and Methods

The family was discovered through information given by one of their affected members (III-2) who at the time was a patient of the 38th Infirmary of " Santa Casa de Misericordia de Pôrto Alegre ", a hospital for needy people. This person suffered from a strong anemia of the hemolytic type, clinical and laboratory examinations revealing a diagnosis of spherocytosis. The patient presented a small finger-like excrescence in the medial face of his first phalanx at the 5th digit of the left hand which remembered polydactyly (fig. 1) and knew of other relatives with the same

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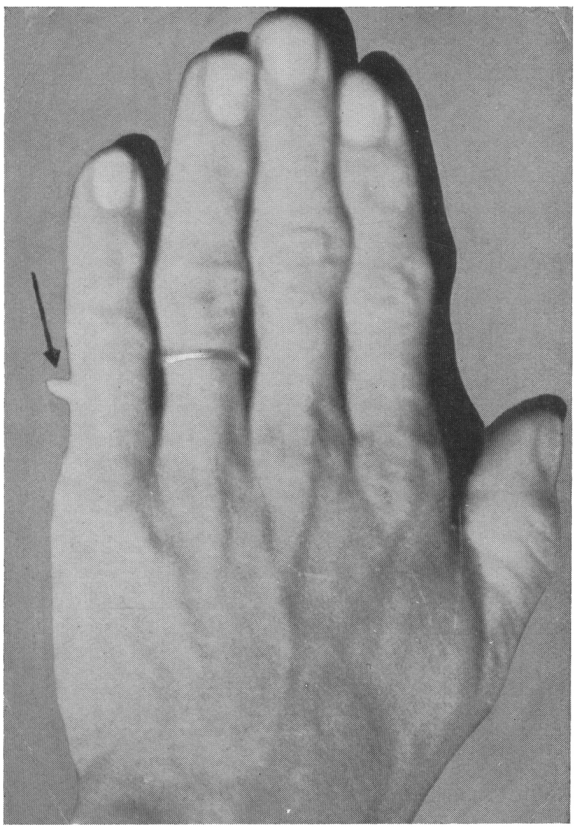

Fig. 1. The pedunculated postminimi found in one of the affected members of the family

anomaly. Thereupon all other available members of his family were examined by the authors in their homes. The majority of them live in a place called Rincão dos Mello in the 5th district of General Camara, at a distance of approximately 159 km from Pôrto Alegre, the Capital of the State of Rio Grande do Sul.

Questions were asked to the persons studied about the occurrence of the anomaly among their relatives and if they had suffered from asthenia, jaundice, leg ulcers and biliary colics.

Physical examinations were subsequently performed considering: 1) skin (searching for leg ulcers and jaundice); 2) visible mucosa (searching for jaundice and anemia); 3) liver (looking for hepatomegaly and sensibility in the cystic point); 4) spleen (looking for splenomegaly through palpation).

The neurological signs tested were: psyche, voluntary motility, pupillary reflexes (of accommodation and photo-motor), deep reflexes (in the upper limbs, bicipital and stylo-radial; in the lower limbs, patellar and Achilles tendon reflex), superficial reflex (only the plantar). In addition, a search was made for extra-fingers in the hands or feet.

Blood samples were collected by venepuncture for laboratory examinations which consisted of the following items: 1) reticulocytes (stained by the blue brilliant Cresil method); 2) spherocytes (stained by the May Gruenwald-Giemsa method); 3) corpuscular fragility (according to the technic described by Dacie, 1954); 4) bilirubin (modified Malloy Evelyn method of Ducci Watson).

Also blood group determinations were conducted for linkage studies between the genes conditioning these characteristics, as well as electrophoresis of serum proteins, the results of which will be the subject of a separate publication.

Description of the Family

The information gathered involves five generations totaling 117 related individuals (fig. 2). 78 were examined by the authors, 17 out of which proved to be spherocytics, 7 polydactylics and 3 spherocytic-polydactylics. II-6 and II-11, already deceased, were carriers of the gene for spherocytosis. II-4 presented polydactyly according to the information of his relatives.

The following summary will reproduce the results of the anamnesis, physical and laboratory examinations of the afflicted persons, as well as additional data about persons reportedly affected. (Roman numerals indicate the generation, arabic the situation of the individual in this generation).

II-1 — F. J. S., 78 years, male, white, married, farmer.

Anamnesis. Informs that was always slightly jaundiced, having at the age of 25 years a crisis of intense exacerbation of the symptom. Denies asthenia, leg ulcers and biliary colics. During his youth he accidentally amputated the pedunculated finger of the left hand.

Physical Examination. Presents a questionable jaundice. His conjunctiva is moderately anemiated. Absence of leg ulcers and hepatomegaly. Does not feel pain at the cystic point. Spleen palpable to an extension of 4 cm., perpendicular to the left costal border, painless, smooth surface and regular margin. Normal cutaneous plantar reflex. Hyporeflexia of the inferior limbs. Concerning pupillary reflexes he presents normal accommodation to light and distance. Vestigial pedunculated finger at the 5th finger of the left hand; all other extremities are normal.

Laboratory Examinations. Reticulocytes — 15 per cent; Spherocytes — present; Corpuscular fragility — 0.85 to 0.55 gm of NaCl in 100 ml. Bilirubin — total: 0.80 mg per cent, direct immediate: 0.07 mg per cent.

II-4 — F. S., female, unmarried, deceased at approximately 25 years of age during a crisis of variola. According to members of the family she did not show signs of icterus but presented an extra finger at the right hand with nail.

II-6 — B. A. S., female, married, deceased with 54 years from a disease whose symptomatology remembers the clinical picture of meningitis. Presented icterus.

II-10 — J. S., 67 years, male, white, married, farmer.

Anamnesis. Jaundiced since he was 12 years old. Asthenia present during all of his life. Cholecystalgia for the last 10 years and a large leg ulcer which appeared at the same time in both inferior limbs.

Physical Examination. The ulcer mentioned above measures 15 cm of diameter and is situated in the anterior middle part of the left leg. Jaundiced. Conjunctiva moderately

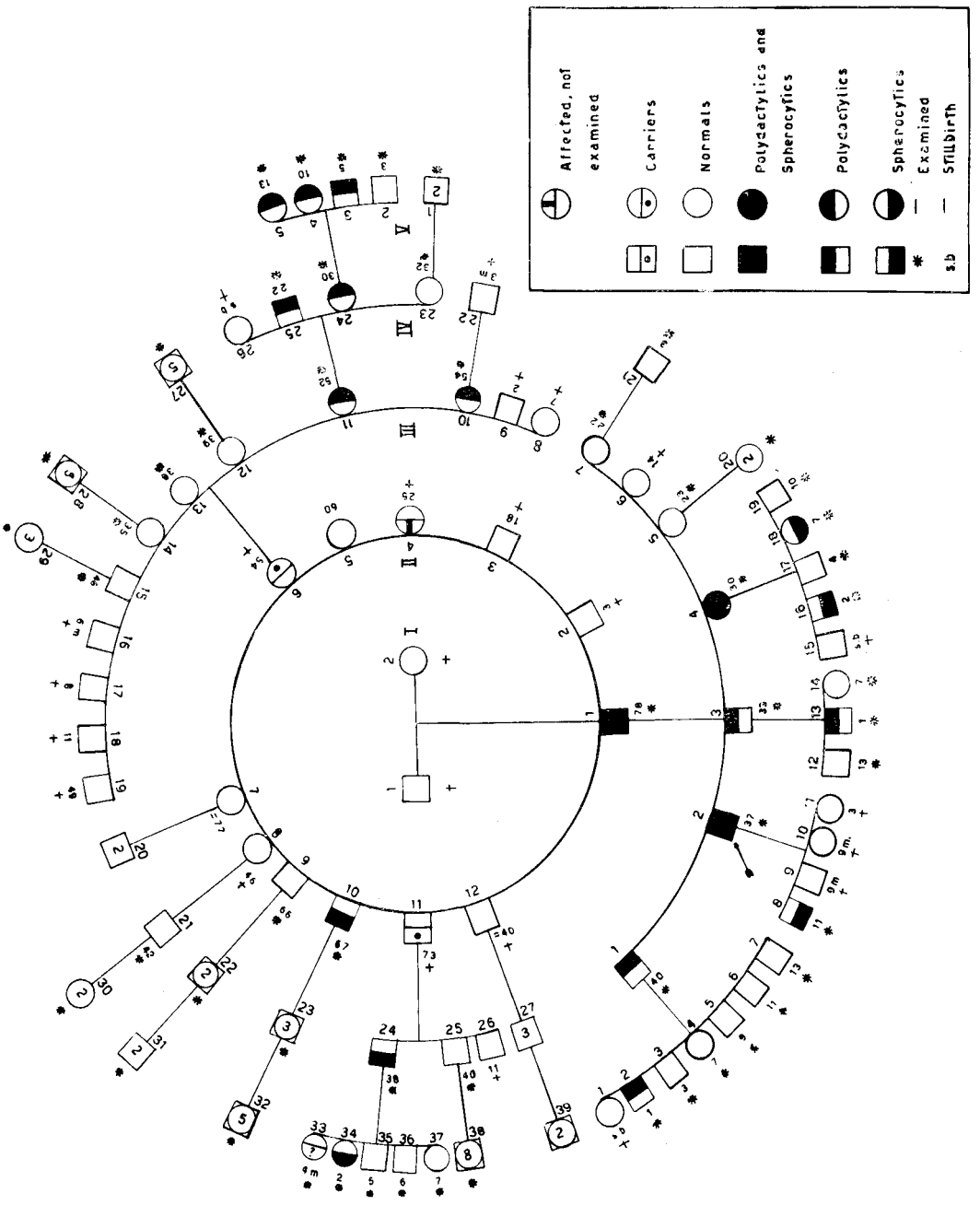

Fig. 2. Pedigree of the family studied

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anemiated. The inferior limit of the liver goes 3 cm beyond the right costal border. The cystic point is slightly painful under palpation. Spleen palpable at an extension of 12 cm perpendicular to the left costal border, painless, smooth surface, and regular margin. Nervous system without particularities. Absence of extra-fingers.

Laboratory Examinations. Reticulocytes — 20 per cent; Spherocytes — present; Corpuscular fragility — 0.85 to 0.55 gm of NaCl in 100 ml.

II-11 — T. J. S., male, married, deceased at the age of 73. Jaundiced since he was 8 years old. Biliary colics were very frequent, and forced him to seek medical assistance several times. Complaints at the time before his death suggest intestinal malignant neoplasia.

III-1 — L. J. S., 40 years, male, white, married, farmer.

Anamnesis. He was always healthy. Denies jaundice, asthenia, leg ulcers and biliary tract disease.

Physical Examination. Skin, visible mucosa, liver, spleen and nervous system, without particularities. Presence of extra-finger at the 5th finger of both hands, these being quite conspicuous at the right and vestigial at the left. The inferior limbs are normal.

Laboratory Examinations. Reticulocytes — normal; Spherocytes — absent; Corpuscular fragility — normal; Bilirubin — total: 1.0 mg per cent, direct immediate: 0.3 mg per cent.

III-2 — A. J. S., the propositus, 37 years, male, white, married, farmer.

Anamnesis. The patient arrived at the hospital complaining about intense asthenia, a tumor in the left hypochondrium and tachycardia after some physical effort. He feels asthenia and indisposition since he was 15 years old. Jaundice, abdominal pain, palpitations and prostration came when he was 22 years. Since then a tumor has appeared in the left hypochondrium and he shows symptoms of varying intensity. During the last two years he was practically unfit for work. Denies biliary colics and leg ulcers. Informs that when he was born he presented an extra-finger at both hands, the one of the right hand having disappeared due to early surgical exeresis, while the extra-finger of the left hand is still visible.

Physical Examination. The patient presents at both hands at the ulnar border areas without pigment contrasting with the coloring of the dorsal parts. Visible mucosa are intensely discolored. Conjunctiva moderately icteric. Absence of leg ulcers. Liver: relative limit of the right hemiclavicular line: superior in the 6th intercostal and inferior in the costal border level. Spleen: palpable at an extension of 10 cm, perpendicular to the left costal border, painless, smooth surface and regular margin. The cutaneous plantar reflex is normal at the left. Babinski sign inconstant at the right. Hyporeflexia generalized in the inferior limbs; asymmetry is stronger in the reflexes of the left. Normal pupillary reflexes. Moderate anisocoria with mydriasis in the left. Vestigial pedunculated finger in the 5th finger of the right hand and more developed in the left hand. Radiography does not show any bone formation in the extra-finger. Finger-prints are also absent.

Laboratory Examinations. Reticulocytes — 15 per cent; Spherocytes — present; Corpuscular fragility — 0.85 to 0.55 gm of NaCl in 100 ml; Serum iron — 215 μgm by 100 ml; Bilirubin — total: 3.3 mg per cent — direct immediate: 0.12 mg per cent. Urinary uro-

bilinogen: dilution until 1: 50. Tests of hepatic function and histopathological observation through hepatic puncture gave normal results. A cholecystographic examination disclosed mixed calculus.

This patient had a splenectomy during his hospitalization, followed by a remarkable improvement in symptoms and signs.

III-3 — O. S., 33 years, male, white, married, farmer.

Anamnesis. Does not recall asthenia, jaundice, biliary colics or leg ulcers.

Physical Examination. Skin, visible mucosa, liver, spleen and nervous system without particularities. Presents at the left hand a traumatic deformity. Vestigial pedunculated finger is found at the right hand and both feet.

Laboratory Examinations. Reticulocytes — normal; Spherocytes — absent; Corpuscular fragility — normal; Bilirubin — not determined.

III-4 — S. S. C., 30 years, female, white, married, housewife.

Anamnesis. Suffered from jaundice since infancy. Denies asthenia and leg ulcers. At the age of 18 years a tumor appeared in her left hypochondrium. Presents a report compatible with repeated cholecystalgia. Suffered five spontaneous abortions of approximately five months each one.

Physical Examination. Moderate jaundice. Without leg ulcers. The inferior limit of the liver exceeds the right costal border by 1.5 cm. Cystic point is painful under palpation. Spleen palpable at an extension of 13 cm perpendicular to the left costal border, painless, smooth surface and regular margin. The Babinski sign is positive at the left and doubtful at the right. All other reflexes are normal. The extra-finger is more developed in the right hand and vestigial in the left.

Laboratory Examinations. Reticulocytes — 25 per cent; Spherocytes — present; Corpuscular fragility — 0.85 to 0.50 gm of NaCl in 100 ml; Bilirubin — total: 4.5 mg per cent, direct immediate: 1.2 mg per cent.

III-10 — F. A. A. S., 54 years, female, white, married, housewife.

Anamnesis. She recalls being always jaundiced and asthenic. Denies biliary colics. Had leg ulcers during 10 years being cured 1 year ago. Suffered one spontaneous abortion delivering a fetus of four months.

Physical Examination. Skin without particularities. Jaundice. Conjunctiva slightly anemiated. The inferior limit of the liver exceeds the right costal border by 3 cm. The cystic point is painless. Spleen palpable at an extension of 8 cm perpendicular to the left costal border, painless, smooth surface and regular margin. Nervous system without particularities. Absence of extra-fingers.

Laboratory Examinations. Reticulocytes — 12 per cent; Spherocytes — present; Corpuscular fragility — 0.85 to 0.55 gm of NaCl in 100 ml.

III-11 — J. A. V., 52 years, female, white, married, housewife.

Anamnesis. She suffered from jaundice, biliary colics and asthenia since infancy. Hospitalized twice because of biliary colics, the first time when she was 8 years old, the second at the age of 40; she refused to be operated. Presented leg ulcers from 35 to 51 years, when she was submitted to saphenectomy. Had in the past several crisis of exacerbation of her symptoms with prostration and intense cephalea.

Physical Examination. Skin without particularities. Jaundice. Conjunctiva slightly anemiated. The inferior limit of the liver exceeds the right costal border by 3 cm. The cystic point is painless. Spleen palpable at an extension of 13 cm perpendicular to the left costal border, painless, smooth surface and regular margin. Nervous system without particularities. Absence of extra-fingers.

Laboratory Examinations. Reticulocytes — 16 per cent; Spherocytes — present; Corpuscular fragility — 0.85 to 0.55 gm of NaCl in 100 ml.

III-24 — A. O. S., 38 years, male, white, married, farmer.

Anamnesis. He was always icteric having a permanent moderate asthenia. Suffers from occasional pains in the right hypochondrium. Denies leg ulcers.

Physical Examination. Moderate jaundice. Conjunctiva slightly anemiated. The liver presents no particularities. The cystic point is painless. Spleen: palpable at an extension of 8 cm perpendicular to the left costal border, painless, smooth surface and regular margin. The Babinski sign is indistinct at the right. Absence of deep reflexes in the inferior limbs. Difficult pupillary accommodation for distance. Absence of pedunculated finger.

Laboratory Examinations. Reticulocytes — 14 per cent; Spherocytes — present; Corpuscular fragility — 0.85 to 0.55 gm of NaCl in 100 ml; Bilirubin — total: 0.96 mg per cent, direct immediate: 0.32 mg per cent.

IV-2 — E. D. S., 1 year, male, white.

Anamnesis. The mother says that until now the child has not presented any asthenia, biliary colics, jaundice or leg ulcers.

Physical Examination. Skin, visible mucosa, liver, spleen and nervous system without particularities. He presents an extra-finger only at the 5th finger of the left hand, all other extremities being normal.

Laboratory Examinations. Reticulocytes — normal; Spherocytes — absent.

IV-8 — A. M. S., 11 years, male, white, student.

Anamnesis. Denies suffering from asthenia, biliary colics and leg ulcers. Said that as far as he can remember, he was always jaundiced.

Physical Examination. Does not present leg ulcers. Icteric. Conjunctiva moderately anemiated. The liver is normal. Cystic point painless. Spleen: palpable in an extension of 6 cm perpendicular to the left costal border, painless, smooth surface and regular margin. Nervous system without particularities. Absence of pedunculated extra-fingers.

Laboratory Examinations. Reticulocytes — 22 per cent; Spherocytes — present; Corpuscular fragility — 0.75 to 0.40 gm of NaCl in 100 ml; Bilirubin — total: 3.33 mg per cent, direct immediate: 0.29 mg per cent.

IV-13 — O. J. S., 1 year, male, white.

Anamnesis. The parents of the child say that until now he has not presented jaundice, asthenia, biliary colics or leg ulcers.

Physical Examination. Skin, visible mucosa, liver, spleen and nervous system without particularities. He presents at both hands vestigial pedunculated extra-fingers.

Laboratory Examinations. Reticulocytes — normal; Spherocytes — absent; Corpuscular fragility — normal.

IV-16 — D. D. S., 2 years, male, white.

Anamnesis. His parents say that until now he has not presented jaundice, asthenia, biliary colics or leg ulcers.

Physical Examination. Skin, visible mucosa, liver, spleen and nervous system without particularities. Absence of extra-fingers at hands and feet.

Laboratory Examinations. Reticulocytes — 9 per cent; Spherocytes — present; Corpuscular fragility — 0.65 to 0.50 gm of NaCl in 100 ml; Bilirubin — total: 0.08 mg per cent, direct immediate — 0.06 mg per cent.

IV-18 — I. S. S., 7 years, female, white.

Anamnesis. The parents of the child say that until now she has not presented jaundice, asthenia, biliary colics or leg ulcers.

Physical Examination. Skin, visible mucosa, liver, spleen and nervous system without particularities. Absence of extra-fingers at hands and feet.

Laboratory Examinations. Reticulocytes — 16 per cent; Spherocytes — present; Corpuscular fragility — 0.85 to 0.45 gm of NaCl in 100 ml; Bilirubin — total: 0.80 mg per cent, direct immediate: 0.06 mg per cent.

IV-24 — M. J. V. F., 30 years, female, white, married, housewife.

Anamnesis. She suffered from intense astenia and slight jaundice since infancy. She recalls pains and colics in the right iliac fossa since she was 5 years old, as well as generalized osteocopic pains. Denies leg ulcers.

Physical Examination. Skin and conjunctiva jaundiced. The inferior limit of the liver exceeds the right costal border by 5 cm. The cystic point is painless. Spleen palpable at an extension of 7 cm perpendicular to the left costal border, painless, smooth surface and regular margin. Nervous system examination without particularities. Absence of extra-fingers.

Laboratory Examinations. Reticulocytes — 14 per cent; Spherocytes — present; Corpuscular fragility — 0.85 to 0.50 gm of NaCl in 100 ml.

IV-25 — A. J. V., 22 years, male, white, unmarried, farmer.

Anamnesis. Informed that he was never icteric, but refers a permanent slight asthenia. Denies biliary colics and leg ulcers.

Physical Examination. Skin without particularities. Conjunctiva slightly jaundiced. The inferior limit of the liver exceeds the right costal border by 3 cm. Cystic point painless. Spleen palpable at an extension of 2 cm perpendicular to the left costal border, painless, smooth surface and regular margin. Nervous system without particularities. Absence of extra-fingers.

Laboratory Examinations. Reticulocytes — 5 per cent; Spherocytes — present; Corpuscular fragility- 0.75 to 0.50 gm of NaCl in 100 ml.

IV-33 — L. E. M. S., 4 months, female, white.

Anamnesis. The parents of the child affirm that until now she has not presented jaundice, asthenia, biliary colics or leg ulcers.

Physical Examination. Skin, visible mucosa, liver, spleen and nervous system without particularities. Absence of extra-fingers at hands or feet.

Laboratory Examinations. Because of the child's early age only a small amount of blood, obtained by finger prick, was available. The slide smears suggest the presence of spherocytes.

IV-34 — M. L. M. S., 2 years, female, white.

Anamnesis. The parents of the child report that until now she has not presented jaundice, asthenia, biliary colics or leg ulcers.

Physical Examination. Skin without particularities. Visible mucosa anemiated but not icteric. Liver, spleen and nervous system without particularities. Absence of extra-fingers.

Laboratory Examinations. Like IV-33, due to his early age only finger prick blood was available for slide smears. They clearly accused the presence of spherocytes.

V-3 — E. H. V. F., 5 years, male, white.

Anamnesis. His parents mentioned a moderate asthenia, but denied biliary colics, jaundice and leg ulcers.

Physical Examination. Skin without particularities. Conjunctiva slightly jaundiced. Liver, spleen and nervous system withouth particularities. Absence of pedunculated fingers.

Laboratory Examinations. Reticulocytes — 13 per cent; Spherocytes — present; Corpuscular fragility 0.75 to 0.45 gm of NaCl in 100 ml.

V-4 — Z. B. V. F., 10 years, female, white, student.

Anamnesis. She recalls marked asthenia for several years. Two years ago she had a period of jaundice. Denies biliary colics and leg ulcers.

Table 1. Summary of the data of anamnesis and physical examination

Reference	Name	Polydactyly	Spherocytosis	Anamnesis				Physical Examination				
				Asthenia	Biliary colics	Jaundice	Leg ulcers	Jaundice	Hepatomegaly	Sensibility in the cystic point	Splenomegaly	Neurological findings
II-1	F. J. S.	Yes	Yes	No	No	Yes	No	Doubtful	No	No	4 cm	Hyporeflexia in the inferior limbs
II-10	J. S.	No	Yes	Yes	Yes	Yes	Yes	Yes	3 cm	Yes	12 cm	Without particularities
III-1	L. J. S.	Yes	No	No	No	No	No	No	No	No	No	Without particularities
III-2	A. J. S.	Yes	Yes	Yes	No	Yes	No	Yes	No	No	10 cm	Babinski sign is inconstantly positive at the right Hyporeflexia generalized in the inferior limbs. Moderate anisocoria.
III-3	O. S.	Yes	No	No	No	No	No	No	No	No	No	Without particularities
III-4	S. S. C.	Yes	Yes	No	Yes	Yes	No	Yes	1.5 cm	Yes	13 cm	Babinski sign is positive at the left and doubtful at the right
III-10	F. A. A. S.	No	Yes	Yes	No	Yes	Yes	Yes	3 cm	No	8 cm	Without particularities
III-11	J. A. V.	No	Yes	Yes	Yes	Yes	Yes	Yes	3 cm	No	13 cm	Without particularities
III-24	A. O. S.	No	Yes	Yes	No	Yes	No	Yes	No	No	8 cm	Babinski sign is doubtful at the right. Absence of deep reflexes in the inferior limbs. Difficult pupillary accommodation for distance
IV-2	E. D. S.	Yes	No	No	No	No	No	No	No	No	No	Without particularities
IV-8	A. M. S.	No	Yes	No	No	Yes	No	Yes	No	No	6 cm	Without particularities
IV-13	O. J. S.	Yes	No	No	No	No	No	No	No	No	No	Without particularities
IV-16	D. S. S.	No	Yes	No	No	No	No	No	No	No	No	Without particularities
IV-18	I. S. S.	No	Yes	No	No	No	No	No	No	No	No	Without particularities
IV-24	M. J. V. F.	No	Yes	Yes	No	Yes	No	Yes	5 cm	No	7 cm	Without particularities
IV-25	A. J. V.	No	Yes	Yes	No	No	No	Yes	3 cm	No	2 cm	Without particularities
IV-33	L. E. M. S	No	Yes	No	No	No	No	No	No	No	No	Without particularities
IV-34	M. L. M. S.	No	Yes	No	No	No	No	No	No	No	No	Without particularities
V-3	E. H. V. F.	No	Yes	Yes	No	No	No	Yes	No	No	No	Without particularites
V-4	Z. B. V. F.	No	Yes	Yes	No	Yes	No	Yes	No	No	2.5 cm	Without particularities
V-5	M. Z. V. F.	No	Yes	No	No	No	No	Yes	2 cm	No	No	Without particularities

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Table 2. Summary of the laboratory findings

Reference	Name	Polydactyly	Spherocytosis	Reticulocytes	Spherocytes	Corpuscular fragility	Bilirubin
II-1	F. J. S.	Yes	Yes	15%	Present	0.85 to 0.55	Total–0.80 mg% D. I. –0.07 mg%
II-10	J. S	No	Yes	20%	Present	0.85 to 0.55	. . . . .
III-1	L. J. S.	Yes	No	Normal	Absent	Normal	Total–1.0 mg% D. I. –0.3 mg%
III-2	A. J. S.	Yes	Yes	15%	Present	0.85 to 0.55	Total–3.3 mg% D. I. –0.12 mg%
III-3	O. S.	Yes	No	Normal	Absent	Normal	. . . . .
III-4	S. S. C.	Yes	Yes	25%	Present	0.85 to 0.50	Total–4.5 mg% D. I. –1.2 mg%
III-10	F. A. A. S.	No	Yes	12%	Present	0.85 to 0.55	. . . . .
III-11	J. A. V.	No	Yes	16%	Present	0.85 to 0.55	. . . . .
III-24	A. O. S.	No	Yes	14%	Present	0.85 to 0.55	Total–0.96 mg% D. I. –0.32 mg%
IV-2	E. D. S.	Yes	No	Normal	Absent	. . . .	. . . . .
IV-8	A. M. S.	No	Yes	22%	Present	0.75 to 0.40	Total–3.33 mg% D. I. –0.29 mg%
IV-13	O. J. S.	Yes	No	Normal	Absent	Normal	. . . . .
IV-16	D. S. S.	No	Yes	9%	Present	0.65 to 0.50	Total–0.08 mg% D. I. –0.06 mg%
IV-18	I. S. S.	No	Yes	16%	Present	0.85 to 0.45	Total–0.80 mg% D. I. –0.06 mg%
IV-24	M. J. V. F.	No	Yes	14%	Present	0.85 to 0.50	. . . . .
IV-25	A. J. V.	No	Yes	5%	Present	0.75 to 0.50	. . . . .
V-3	E. H. V. F.	No	Yes	13%	Present	0.75 to 0.45	. . . . .
V-4	Z. B. V. F.	No	Yes	7%	Present	0.75 to 0.50	. . . . .
V-5	M. Z. V. F.	No	Yes	8%	Present	0.75 to 0.50	. . . . .

Physical Examination. Skin without particularities. Conjunctiva slightly jaundiced. Liver without particularities. Spleen palpable at an estension of 2.5 cm perpendicular to the left costal border, painless, smooth surface and regular margin. Nervous system without particularities. Absence of extra-fingers.

Laboratory Examinations. Reticulocytes — 7 per cent; Spherocytes — present; Corpuscular fragility — 0.75 to 0.50 gm of NaCl in 100 ml.

V-5 — M. Z. V. F., 13 years, female, white, student.

Anamnesis. Denies leg ulcers, jaundice, asthenia and biliary colics.

Physical Examination. Skin without particularities. Conjunctiva slightly icteric. The inferior limit of the liver exceeds the right costal border by 2 cm. Spleen and nervous system without particularities. Absence of extra-fingers.

Laboratory Examinations. Reticulocytes — 8 per cent; Spherocytes — present; Corpuscular fragility — 0.75 to 0.50 gm of NaCl in 100 ml.

Analysis of the Clinical and Laboratory Data

As was mentioned in the description of the family thorough clinical and laboratory examinations were made of the propositus which resulted beyond doubt in affirming the occurrence of spherocytosis. With regard to all other persons related in this paper as being affected by the disease the presence of spherocytes plus an increased number of reticulocytes and corpuscular fragility were the most important symptoms to lead to this diagnosis. Other findings could be considered as being confirmatory only. The clinical data were obtained in the patients' homes under precarious conditions and their primary purpose was to corroborate the diagnosis given by the laboratory examinations for the establishment of a good genetic analysis.

Among the 17 persons diagnosed as spherocytics (table 1) it was verified that a history of asthenia was present in 9 of them; biliary colics occurred in 3, probable jaundice in 10 and leg ulcers in 3. Physical examinations indicated jaundice in 12 patients, hepatomegaly in 7, sensibility in the cystic point in 2, splenomegaly in 11 and neurological findings in 4. As far as the laboratory data are concerned (table 2), increased rates of reticulocytes and corpuscular fragility were found in all individuals with spherocytes.

Genetic Analysis and the Problem of Causal Relationship

Many text-books of hematology (for instance, Wintrobe, 1956 and Varela, 1958) mention polydactyly as a developmental anomaly frequently found in association with spherocytosis. At the outset we should therefore ask if this association is causal, that is, if polydactyly is merely a consequence of spherocytosis. This proposition does, however, not agree with the results obtained in the family studied by us, since II-1 (affected by polydactyly and spherocytosis) originated III-1 and III-3, who presen-

ted polydactyly only. The isolated occurrence of the two affections inherited through different generations speaks strongly in favor of the simultaneous occurrence of *two* hereditary abnormalities in this family.

It is known that spherocytosis, as well as polydactyly, is inherited by means of dominant genes; thus, the isolated segregation of each would be expected to be 1: 1. Indeed concerning spherocytosis the ratio in our case was 17 spherocytics: 17 normals, which happens to be in exact agreement with our expectation. In relation to polydactyly, however, if one considers the results according to the information given by relatives of the affected persons, a total of 8 polydactylics: 21 normals would be obtained with a significant lack of polydactylics ($X^2 = 5.82$; d. f. = 1; $P < 0.02$). On the other hand, if only individuals examined by the authors are considered, the ratio of 7 polydactylics: 11 normals will be found, a result which does not depart in a significant way from theoretical expectation. We conclude that due to the trivial nature of the anomaly it may have passed unnoticed in some individuals.

Are the two reported genes then located in the same chromosome or in different chromosomes?

Only the descendents of II-1, III-2 and III-4 who present both anomalies at the same time, furnish data about this question. We might suppose at the beginning that the two genes are in linkage and coupled (PS/ps x ps/ps). The existence of III-1 and III-3 who present polydactyly only, however, eliminates the possibility of complete linkage. If partial linkage exists one would expect to find a larger frequency of individuals with both anomalies (PS/ps) or with none of them (ps/ps); they would constitute the classes without recombination. In generation III four individuals of this category exist, against two who might result from recombination (III-1 and III-3). In generation IV, however, more individuals should result from recombination (IV-8; IV-16 and IV-18) than those originated from classes without recombination (IV-17 and IV-19). Thus it seems that such hypothesis does not apply to the observed data.

In the same way if one expects the genes to be in complete linkage but in repulsion (Ps/pS × ps/ps), no individual with both anomalies at the same time would appear in the next generation. The occurrence of individuals III-2 and III-4, who are polydactylics *and* spherocytics, is then against this hypothesis. If partial linkage exists a larger frequency of individuals would present only one of the anomalies; they would constitute the classes without recombination (Ps/ps or pS/ps). However, already in generation III four individuals carrying both anomalies or none of them (III-2; III-4; III-5 and III-7) appear against only two (III-1 and III-3), who might represent the classes without recombination.

It is concluded that at least in this family there exists no indication that the two genes under study are located on the same chromosome.

Table 3. Results of the blood group tests

No.	Parents	Sex	Sphero-cytosis (S)	Poly-dactyly (P)	Blood Groups		
					ABO	MN	Rh
II-1	I-1,2	♂	+	+	O	MN	CCDdee
II-9	I-1,2	♂	—	—	O	MN	CCDE
II-10	I-1,2	♂	+	—	O	MN	ccDE
III-1	II-1	♂	—	+	A	MN	CcDdee
III-2	II-1	♂	+	+	A	MN	CcDee
III-4	II-1	♀	+	+	A	MN	Ccddee
III-7	II-1	♀	—	—	A	N	CcDEe
III-10	II-6	♀	+	—	O	N	ccDE
III-11	II-6	♀	+	—	O	N	ccDee
III-12	II-6	♀	—	—	O	MN	ccDee
III-13	II-6	♀	—	—	O	MN	ccDE
III-14	II-6	♀	—	—	O	N	ccddee
III-15	II-6	♂	—	—	O	MN	ccDE
III-24	II-11	♂	+	—	O	MN	CCDee
III-25	II-11	♂	—	—	O	M	CCDee
IV-3	III-1	♂	—	—	O	M	CcDee
IV-4	III-1	♀	—	—	A	M	CCDee
IV-5	III-1	♂	—	—	A	M	ccddee
IV-6	III-1	♂	—	—	A	M	CcDee
IV-7	III-1	♂	—	—	O	MN	CcDee
IV-12	III-3	♂	—	—	A	MN	ccddee
IV-16	III-4	♂	+	—	A	MN	CcDdee
IV-18	III-4	♀	+	—	A	MN	CcDdee
IV-19	III-4	♂	—	—	A	M	CCDdee
IV-23	III-11	♀	—	—	A	MN	ccDee
IV-24	III-11	♀	+	—	A	MN	CcDee
IV-25	III-11	♂	+	—	A	MN	CcDee
IV-35	III-24	♂	—	—	O	MN	CCDee
IV-36	III-24	♂	—	—	A	M	CCDee
IV-37	III-24	♀	—	—	O	MN	CCDee
V-3	IV-24	♂	+	—	A	MN	CCDee
V-5	IV-24	♀	+	—	O	M	ccDee

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Linkage with Blood Groups

Blood groups of the majority of individuals under consideration were determined for linkage studies between the genes of spherocytosis, polydactyly and those responsible for the ABO, MN and Rh (tests with 4 sera) systems. The results can be observed in table 3. The application of the sib-pair method of Penrose to the data concerning spherocytosis and the above-mentioned blood groups did not show any indication of linkage. Data regarding polydactyly are too few for any conclusion to be reached.

Summary

A description is made of a large Brazilian family of white ancestry in which some individuals presented polydactyly, other spherocytosis, and some both anomalies together. The information obtained involves five generations totaling 117 related members. Seventy eight of them were examined by the authors through clinical and laboratory methods. Both anomalies were found to be inherited by means of autosomic dominant genes; their joint occurrence seems to be casual. No genetic linkage was apparent between the genes which conditioned spherocytosis and those responsible for the ABO, MN and Rh blood group systems.

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RIASSUNTO

In questo lavoro si fa una descrizione di una numerosa famiglia brasiliana, di antenati bianchi, in cui alcuni individui presentano polidattilia, altri sferocitosi e alcuni ambedue le anomalie. Le informazioni ottenute si estendono a cinque generazioni per un totale di 117 individui apparentati. 78 di essi sino stati esaminati dagli autori con metodi clinici e di laboratorio. Le anomalie sono ereditate attraverso i geni autosomici dominanti; il loro apparire simultaneo sembra essere casuale. Non venne riscontrata nessuna relazione genetica tra i geni che condizionano la sferocitosi e quelli responsabili dei sistemi di gruppi sanguigni ABO, MN, Rh.

RÉSUMÉ

Ce travail nous présente des études faites dans une famille brésilienne nombreuse, d'ascendance blanche, dans laquelle quelques individus présentent la polydactylie, d'autres la sphérocytose et quelques-uns les deux anomalies réunies. Les renseignements obtenus couvrent cinq générations avec un total de 117 individus apparentés; 78 d'entre eux ont été examinés par les auteurs avec des méthodes cliniques et des méthodes de laboratoire. Les deux anomalies sont transmises par l'intermédiaire de gènes autosomiques dominants. Leur apparition simultanée paraît être fortuite. On n'a trouvé aucune liaison génétique entre les gènes qui déterminent la sphérocytose et ceux desquels dépendent les systèmes de groupes sanguins ABO, MN et Rh.

ZUSAMMENFASSUNG

Die vorliegende Arbeit enthält Mitteilungen über eine mehrköpfige brasilianische Familie weisser Rasse. Einige Individuen zeigten Polidaktylie, andere Kugelzellenkrankheit (Sphärozythämie) und andere beide Krankheiten zusammen.

Die Angaben beziehen sich auf fünf Generationen mit der Gesamtzahl von 117 Individuen, 78 davon wurden von den Verfassern mit klinischen und laboratoriellen Methoden untersucht.

Beide Regelwidrigkeiten vererben sich durch autosome, dominante Gene; ihr gemeinsames Auftreten scheint zufällig zu sein.

Es wurde kein erblicher Zusammenhang zwischen den Genen welche die Sphärozythämie verursachen und denjenigen, die für die Blutgruppen ABO, MN und Rh verantwortlich sind, gefunden.