THE TURKISH JOURNAL OF PEDIATRICS

VOLUME: 33 NUMBER: 4 OCTOBER-DECEMBER 1991

HONORARY EDITOR
İhsan DOĞRAMACI

EDITORS
Keriman TINAZTEPE
Erol KINIK

ASSOCIATE EDITORS
Özden SANAL
Turgay COŞKUN
Phyllis Lepon ERDOĞAN

MANAGING EDITOR
Kızılgül MORALI

EDITORIAL BOARD
İzzet BERKEL, Ankara
Nihat BİLGİNTURAN, Ankara
Talat GÖĞÜŞ, Ankara
Eunice G. JOHN, Chicago
Oğuz KAYAALP, Ankara
Olcay NEYZİ, İstanbul
İmran ÖZALP, Ankara
Tunç Alp ÖZGEN, Ankara
Sabiha ÖZGÜR, İzmir
Şinasi ÖZSOYLU, Ankara
Yavuz RENDA, Ankara
Burhan SAY, Tulsa
Kutay TAYŞİ, St. Louis
Behçet TINAZTEPE, Ankara
J. D. WARNER, London
Murat YURDAKÖK, Ankara

A joint publication of the Turkish National Pediatric Society and the Turkish and International Children's Center

ADDRESS FOR SUBSCRIPTIONS AND CORRESPONDENCE

The Turkish Journal of Pediatrics
P.K. 66, 06240 Samanpazarı, Ankara, Turkey

Telephone : (4) 311 22 53 - 324 23 26 - 324 49 90
Telex : 42999 tcsm tr
Fax : (4) 311 22 53

This Journal is listed in *Current Contents, Index Medicus, Abstracts on Hygiene and Communicable Diseases, Tropical Diseases Bulletin,* the *CAB Abstracts* database and the *Excerpta Medica* database *EMBASE.*

CONTENTS

ORIGINAL ARTICLES

Twenty-year Follow-up of 160 Patients With Ataxia-telangiectasia 205
F. Ersoy, A.İ. Berkel, Ö. Sanal, H. Oktay

Elimination of Maternal Antibodies Against Measles (Is the Policy of Vaccinating Children Younger than Nine Months of Age Suitable for Turkey?) 217
G. Kanra, M. Ceyhan

Diagnosis and Treatment of Intraspinal Lipomas 221
F. Dinçer, H.Z. Gökalp, C. Dinçer, A. Zorlutuna

Sodium and Potassium Levels in Colostrum 231
M. Yurdakök, O. Oran, G. Tekinalp

Diuretic Renography in Children: A Non-invasive Method For the Assessment of Upper Urinary Tract Pathologies 235
H. Durak, İ. Bernay, G. Erbengi, N. Ulutuncel

CASE REPORTS

Hydatid Disease Presenting as an Intrascrotal Mass in a Child 245
F. Kızılcan, F.C. Tanyel, N. Büyükpamukçu, A. Hiçsönmez

Oculocerebral Hypopigmentation Syndrome (Cross Syndrome) 247
H. Özkan, E. Ünsal, G. Köse

INVITED TOPIC

Failure to Breathe At Birth: Causes and Assessment 253
N.R.C. Roberton

ANNOUNCEMENTS 267
AUTHOR INDEX TO VOLUME 33 268
ARTICLE INDEX TO VOLUME 33 269
KEY WORD INDEX TO VOLUME 33 270

Owner: Turkish and International Children's Center
Administrator: Erol Kınık
Chief, Documentation and Publications: Phyllis Lepon Erdoğan

The Turkish Journal of Pediatrics 33:205-215, 1991

TWENTY-YEAR FOLLOW-UP OF 160 PATIENTS WITH ATAXIA-TELANGIECTASIA*

*Fügen Ersoy MD***, *A. İzzet Berkel MD****, *Özden Sanal MD*****
*Hamiyet Oktay MD******

SUMMARY: Ersoy F, Berkel AI, Sanal Ö, Oktay H. (Immunology Unit, Hacettepe University Institute of Child Health, Ankara, Turkey). Twenty-year follow-up of 160 patients with ataxia-telangiectasia. Turk J Pediatr 33: 205-215, 1991.

The clinical and immunological findings of 160 patients diagnosed over a period of twenty years as having ataxia-telangiectasia (AT) are presented. The study group composed of 68 females and 92 males were members of 117 families. The rate of parental consanguinity was 65 percent. The incidence of AT in 117 families was 36.6 percent. All patients had the characteristic facial and postural features of AT. The mean duration of follow-up of 160 patients was 6.35 years. Fifty patients had died during the follow-up (36 of pulmonary infections, 14 of malignancies). Somatic growth retardation was a prominent feature. Recurrent sinopulmonary infections were detected in 66 percent of patients. Two patients had hypothyroidism, one had diabetes mellitus, and one had both conditions. The incidence of malignancies was found to be 2.3 percent in the immediate relatives of the patients.

The total lymphocyte count was low in 57 percent, and skin tests to PHA, candida, PPD and SK-SD were negative in 17.7%, 72.6%, 43.6%, and 78.2% of patients, respectively. In vitro blastogenic response to PHA was low in 61 percent of patients. The mean value of E-rosette formation was significantly lower than control values. Six patients had low serum IgG levels. The serum IgM level was high in 26.6 percent of patients and the IgA level was low or absent in 51.3 percent. There was no correlation between immune disturbance and duration of illness. *Key words: ataxia-telangiectasia, cellular immunity, humoral immunity, clinical features, malignancy.*

Ataxia-telangiectasia (AT) is an autosomal recessive disorder of childhood characterized by progressive cerebellar ataxia, oculocutaneous telangiectasia, recurrent sinopulmonary infections, reduced cell-mediated immunity, absent or reduced serum IgA, reduced serum IgE, low or undetectable IgG2, premature aging and various endocrine disorders[1-12]. An increased incidence of cancer in patients and their relatives, elevated serum alpha fetoprotein levels, chromosomal abnormalities, and hypersensitivity of fibroblasts and lymphocytes to ionizing radiation are among the other findings in patients with AT[11,13-16]. Over a period of twenty years, we have evaluated and followed-up 160 patients with AT in 117 families. This communication describes the clinical and immunological findings and the outcome of these patients.

* From the Hacettepe University Institute of Child Health, Ankara.

** Professor of Pediatrics and Pediatric Immunologist, Hacettepe University Institute of Child Health.

*** Professor of Pediatrics and Pediatric Immunologist, State University of New York Health Science Center, USA.

**** Professor of Pediatrics and Pediatric Immunologist, Hacettepe University Faculty of Medicine.

***** Pediatrician, Ministry of Education Center, Beşevler, Ankara.

Material and Methods

One hundred and sixty patients with AT, ranging in age from three to 32 years seen at the Immunology Unit of Hacettepe University Children's Hospital over a twenty-year period were reevaluated in 1988 in respect to clinical and immunological findings. They were diagnosed as having AT by the presence of progressive cerebellar ataxia and eye movements simulating ophthalmoplegia and oculocutaneous telangiectasia.

In addition to the history and physical examination, chest and sinus X-rays were obtained and routine blood counts (hemoglobin, WBC, peripheral blood smear, total lymphocyte counts) were taken. Intradermal skin tests were performed with *Candida albicans* extract, PPD, phytohemagglutinin (PHA) and streptokinase-streptodornase (SK-SD) with doses previously reported[8]. Induration of five mm or more after 48 hours was considered a positive skin test. In vitro blastogenic response was measured using a previously described method[17]. E-rosette forming cells were determined by the method of Jondal et al[18]. Serum immunoglobulins (IgG, IgM, IgA) were measured by radial immunodiffusion (Behring-Werke immunodiffusion plates). For statistical analysis the chi-square and the paired chi-square test were used[19].

Results

Of a total 160 patients with AT, 68 (42.5%) were females and 92 (57.5%) were males. The male/female ratio was 1.3/1. Ninety-two patients were alive (mean age 12.7 ± 5.8 years) and fifty patients had died. The remaining 18 patients were lost-to-follow-up (Table I). The mean death age of 50 patients was 14.8 ± 6.4 years. Of 50 patients, thirty-six had died of pulmonary infections and 14 of malignancies. The mean duration of follow-up of all patients was 6.35 years. Parental consanguinity was noted in 76 out of 117 AT families (65%). There were 440 children in 117 AT families and 160 (36.3%) children had ataxia-telangiectasia. Of 117 families, 80 families had one, 28 families had two, and nine families had three affected children. There was no relationship between consanguinity and the number of affected children in the families.

TABLE I: The Outcome of Ataxia-Telangiectasia Patients (n = 160)

Sex	Male : 92 (57.5%)	Female : 68 (42.5%)
Outcome of patients	Living : 92	(mean age: 12.7 ± 5.8 years)
	Deceased : 50	(mean age: 14.8 ± 6.4 years)
	Unknown : 18	
Mean duration of follow-up	: 6.35 years	

The clinical findings of our patients and the comparison with Boder's 101 cases[11] are shown in Table II. Ataxia, which was the first symptom noticed by the parents, was recognized between the ages of six months and six years in 140 patients (mean age 2.5 years). In 20 patients, the parents could not remember the age of onset of ataxia. Conjunctival telangiectasia was the second major clinical manifestation of the disease. Telangiectasia was noticed by parents in 57 children whose ages ranged from one year to eight years (mean age 3.7 years).

TABLE II: Clinical Features of Patients With Ataxia-Telangiectasia

Feature	Cases with Data Available (No.)	Cases with Clinical Feature No. (%)	Boder's[11] Findings (%)
Cerebellar ataxia	160	160 (100%)	100
Oculocutaneous telangiectasia	160	160 (100%)	100
Characteristic facies and postural attitudes	160	160 (100%)	100
Dysarthric speech	160	160 (100%)	100
Progeric changes of hair and skin	160	150 (93.8%)	88
Diminished deep tendon reflexes	160	114 (71%)	78
Choreoathetosis	160	114 (71%)	91
Negative Romberg sign	160	114 (71%)	78
Oculomotor signs			
Apraxia of eye movements	84	68 (81%)	84
Nystagmus	84	66 (79%)	83
Strabismus	84	43 (51%)	47
Frequent sinopulmonary infections	160	106 (66%)	83
Retardation of somatic growth	160	100 (63%)	72
Parental consanguinity	117 (families)	76 (65%)	–

All patients had the characteristic facies and postural features due to cerebellar hypotonia and ataxia. Progeric changes of hair and skin with some gray hair, atrophic facial skin resembling scleroderma, inelastic ears, pigmentary changes and chronic seborrheic blepharitis were detected in 93.8 percent of patients (150/160). Deep tendon reflexes (DTR) were diminished in 71 percent (114/160) of patients. Choreoathetosis was a prominent extrapyramidal feature and the Romberg sign was negative in 71 percent (114/160) of patients.

Of 84 AT patients, 68 patients (81%) had oculomotor apraxia, 66 patients (79%) had nystagmus and 43 patients (51%) had strabismus.

Retardation of somatic growth was a prominent feature and the respective heights and weights of 100 patients (63%) were below the tenth percentile, with 75 of these patients being below the third percentile.

Recurrent sinopulmonary infections were detected in 106 patients (66%) with 43 patients having atelectasis and/or bronchiectasis. The growth of 66 of 106 patients with recurrent infections (62.2%) and 20 of 48 patients without infections (41.6%) were below the third percentile. The difference between these two groups was significant with respect to the presence of growth retardation ($P < 0.05$).

Three patients had hypothyroidism and one of them developed diabetes mellitus at 15 years of age. Another patient was also diagnosed as having diabetes at the age of 22 years.

Fifteen patients (9.4%) developed malignant neoplasms (Table III). Of these 15 patients, seven had acute lymphoblastic leukemia (ALL), two had Hodgkin's

TABLE III: Type and Outcome of Malignancy in Ataxia-Telangiectasia Patients

Patient	Sex	Age at Onset of Malignancy (yrs)	Type of Malignancy	Outcome
1. ZT	F	15	Non-Hodgkin's lymphoma	Living
2. YA	M	31	Chronic myeloid leukemia	Ex (35 yrs)
3. ŞB	F	7	Pons glioma	Ex (7 yrs)
4. ÖK	M	17	Acute lymphoblastic leukemia	Ex (18 yrs)
5. ÖD	M	5	Acute lymphoblastic leukemia	Ex (?)
6. ÖA	M	11	Acute lymphoblastic leukemia	Ex (11 yrs)
7. OA	M	10	Non-Hodgkin's lymphoma	Ex (10 yrs)
8. ŞA	M	7	Acute lymphoblastic leukemia	Ex (9 yrs)
9. SA	M	7	Hodgkin's lymphoma	?
10. AA	M	8	Acute lymphoblastic leukemia	Ex (8 yrs)
11. SA	M	10	Burkitt's lymphoma	Ex (?)
12. İS	F	12	Hodgkin's lymphoma	Ex (12 yrs)
13. MY	F	17	Lung Ca (?)	Ex (17 yrs)
14. AA	F	11	Acute lymphoblastic leukemia	Ex (11 yrs)
15. AY	M	15	Acute lymphoblastic leukemia	Ex (15 yrs)

* Exitus

lymphoma and two had non-Hodgkin's lymphoma. The incidence of malignancies was found to be 2.3 percent (14/600) in the immediate relatives of AT patients (Table IV).

Immunological findings of AT patients are shown in Table V. The total lymphocyte count was less than 2000/mm^3 in 57 percent (78/136) of patients when first seen. Decreased lymphocyte counts were detected in another eight patients during

TABLE IV: Type of Malignancy in Relatives of Ataxia-Telangiectasia Patients

Families	Relative with Malignancy	Type of Malignancy
1	Brother	Acute lymphoblastic leukemia
2	Brother	Acute lymphoblastic leukemia
3	Grandfather	Larynx carcinoma
4	Mother	Breast carcinoma
	Grandmother	Breast carcinoma
5	Grandmother	Lung carcinoma
6	Grandfather	?
7	Grandmother	Lung carcinoma
8	Great grandfather	Rectum carcinoma
9	Great grandfather	?
10	Grandfather	Stomach carcinoma
11	Uncle	Larynx carcinoma
	Grandfather	Larynx carcinoma
12	Uncle	Larynx carcinoma

TABLE V: Immunological Findings in Ataxia-Telangiectasia Patients

Lymphopenia		78/136 patients	57 %
Negative skin tests	PHA	22/124 patients	17.7%
	Candida	90/124 patients	72.6%
	SK-SD	54/123 patients	43.6%
	PPD	93/119 patients	78.2%
Decreased E-rosettes		35/110 patients*	31.8%
Reduced in vitro PHA response		47/77 patients	61 %
IgA deficiency		79/154 patients	51.3%
High serum IgM level		41/154 patients	26.6%

* Two SD below normal values. Mean value of E-rosettes of AT patients was significantly lower than control values ($P < 0.001$).

follow-up and increases were observed in ten patients whose initial counts were low.

The phytohemagglutinin skin test was negative in 17.7 percent (22/124), the candida skin test in 72.6 percent (90/124), SK-SD in 43.6 percent (54/124) and PPD in 78.2 percent (93/119) of patients.

Of 110 patients tested, E-rosette formation was low in 35. The mean value (54.8 ± 11.6) of E-rosette formation was significantly lower than control values (69.2 ± 8) ($P < 0.05$). No significant change was observed in the percentage of E-rosette formation during the follow-up period.

In six patients, serum IgG levels were two standard deviations below normal, one (61%). No significant change was detected in PHA response in AT patients during their follow-up except for three patients who had showed transient increases (one patient was treated with transfer factor and two with levamisole).

In six patients serum IgG levels were two standard deviations below normal, one of them had very low IgG (120 mg/dl). Although the patient was given standard gammaglobulin monthly, he died of pulmonary infection. Of 154 patients, serum IgM levels were found to be increased in 41 (26.6%). IgA levels were low in 57.5 percent (61/106) of patients with recurrent sinopulmonary infections and in 37.5 percent (18/46) of patients without infection. The difference between these two groups was significant with respect to presence of recurrent sinopulmonary infections ($P < 0.001$). Serum IgA levels were low in all 41 patients with high IgM. Immunoglobulin determinations were repeated in 47 patients and no significant change was observed.

Discussion

Ataxia-telangiectasia is a complex multisystemic disorder. It can be easily diagnosed on purely phenotypic characteristics of progressive cerebellar ataxia, oculocutaneous telangiectasia and proneness to progressive sinopulmonary disease. The first cases from Turkey were published by Kıran et al[20]. Another study on clinical and immunological aspects of 31 patients was reported by our group in the same year[8]. Including these 31 patients, we were able to evaluate and follow-up 160 patients in 117 families (68 females and 92 males) between the ages of three and 32 years. The incidence of AT was found to be 36.6 percent in these families, supporting an autosomal recessive inheritance. This figure was reported to vary between 25-36 percent in previously reported series[8,21,22].

In our series, the parental consanguinity rate was recorded as 65 percent. This high rate is attributed to the common practice in Turkey of marrying relatives. In fact, the incidence of such marriages has been reported to be 20.9 percent[23].

Typical AT can be easily diagnosed on the basis of clinical characteristics. In the series presented, ataxia was noticed by parents in children ranging in age from six months to six years while telangiectasia was recognized by parents when the children ranged in age between one year to eight years. All patients had the characteristic facies of AT, dysarthric speech and diminished DTR, compatible with previous reports[3,4,7,8,11]. Oculomotor signs are almost uniformly present in AT and are diagnostically important, particularly since they may be present before

the appearance of the ocular telangiectasis. Since the oculomotor signs are subtle, they can easily be overlooked in the early stage while in the advanced stage they are severe and can simulate ophthalmoplegia[1,11,24-27]. In our series the rates of oculomotor apraxia, nystagmus and strabismus were compatible with those reported in previous studies[11,26].

Progeric changes involving the hair and skin are cardinal features of AT[4,11]. Some gray hair is usually found even in young children. Diffuse graying of the hair may continue throughout adolescence but it progresses normally thereafter[11]. Subcutaneous baby fat is lost early. In the early stages of the disease, facial skin tends to become atrophic and the ears inelastic. Such progeric findings and pigmentary changes of the skin were detected in 93 percent of our patients.

Somatic growth retardation is a prominent feature of AT and is found in most patients[4,11]. The respective heights and weights of children between four and seven years of age are typically at the tenth percentile and fall below the third percentile in adolescence. The cause of growth retardation is not clearly understood. It has been suggested that it is influenced by chronic sinopulmonary disease but it also occurs in its absence[11]. In our series, 62.5 percent of AT patients were below the tenth percentile and 47 percent of patients were below the third percentile. Growth retardation was observed more frequently in patients with recurrent sinopulmonary infections.

In our series, severe recurrent sinopulmonary infection was the main cause of death. In previous studies, the presence of sinopulmonary infections was found to be between 50-85 percent of AT patients, and it was noted as being the third major component of the syndrome and also the most frequent cause of death[3,8,11].

AT patients are prone to develop malignant neoplasms similar to patients with other immunodeficiency diseases. The incidence of malignant neoplasms among AT patients has been estimated to be 10-15 percent[28]. Although lymphoreticular malignacies occur most commonly, other neoplasms such as basal cell carcinoma, adenocarcinoma of stomach, ovarian dysgerminoma, medulloblastoma and glial tumor of brain may develop in these patients[11,13-15,28]. In our series, 15 patients developed malignancies, and of these, 12 had lymphoid neoplasms. The incidence of malignancies was found to be 9.4 percent which is compatible with previous reports[11,13,28]. Two explanations have been suggested for the high incidence of lymphoid cancer in AT patients[29]. T-cell immunodeficiency may be caused by inefficient joining of T-cell receptor genes which results in inversions and translocations and this type of immunodeficiency then fosters oncogenesis. A second possibility is that the translocations and inversions involve nearby oncogenes.

The incidence of malignancies has also been found to be increased in the immediate relatives of AT patients. Swift and co-workers[13] have estimated the risk of death from a malignant neoplasm as being five-fold greater in close relatives of AT patients than in the general population. The incidence of leukemia, lymphoma, ovarian, and gastric and biliary system carcinomas is increased in AT families. Furthermore, heterozygous females are at risk of breast cancer[30]. In our series, malignant neoplasms were detected in 14 immediate relatives (2.3%) of our patients. Of the 14 relatives, two had breast cancer, two had ALL, four had cancer of the larynx and two had lung cancer. While it has been reported that breast cancer and gastric cancer are the more common malignancies in AT heterozygotes[13,30], in our series, respiratory tract malignancies (larynx and lung Ca) were seen mainly in close relatives.

Various endocrine abnormalities including ovarian dysgenesis and insulin-resistant diabetes have been reported in AT patients[31,32]. In our series, three patients had hypothyroidism with clinical symptoms and one of them had developed type-I diabetes mellitus at 15 years of age. Another patient had also been diagnosed as having diabetes at the age of 22 years. To our knowledge, no reports of hypothyroidism associated with ataxia-telangiectasia have been published in the literature. In a previous study, normal thyroid functions and increased growth hormone levels following L-dopa stimulation were detected in 12 of our AT patients studied[33]. Of 12 patients, four showed an abnormal glucose tolerance test and increased production of insulin during the test.

Immunological evaluation of 160 AT patients showed variable degrees of humoral and/or cellular immune dysfunction. The absolute lymphocyte count was low in 57 percent of patients, a result compatible with previous studies[6-9]. No significant change in lymphocyte counts was observed during the follow-up period.

Delayed hypersensitivity responses to common skin test antigens have been found to be negative in the majority of AT patients[6-9,20]. McFarlin et al[7] have found a higher percentage of positive reactions to dinitrochlorobenzene (DNCB) than that reported by other investigators[34,35]. In our series, delayed hypersensitivity reaction to PHA, *Candida*, SK-SD and PPD were negative in 17.7-78.2 percent of patients and there was no change in responses to repeated tests.

The percentage of E-rosette forming cells was low in 31 percent of our patients and the mean value was significantly lower than control values ($P < 0.05$). Although in some studies a normal percentage of E-rosettes has been reported, it has been found to be low in most reports[8,36,37]. No change was observed in the percentages of E-rosettes in the repeated tests. In vitro blastogenic responses to mitogens and common antigens have been found to be low in 50-60 percent of patients[7,8,21]. McFarlin and Oppenheim[38] have reported that the blastogenic response of lymphocytes may vary during the course of a patient's illness.

Furthermore, in some patients, reduced responses to PHA and Pokeweed mitogen (PWM) can be improved by increasing the concentration of stimulant. An inhibitory serum factor has been shown to decrease the response of normal lymphocytes to PHA. In our series, 61 percent of patients had a low blastogenic response to PHA, and only three patients showed a transient increase following transfer factor or levamisole therapy. In one of our previous studies, 11 out of 15 patients showed a normal response in mixed lymphocyte culture, even though their responses to PHA and antigens (*Candida*, SK-SD) had been low[8]. This finding was attributed to different T lymphocyte subpopulations responding to different antigens and allogeneic lymphocytes.

Some abnormalities in humoral immunity have been reported in AT patients, the most striking of which is IgA deficiency. It is found in about 70% of cases[5-8,31,34,35]. In this study, 51.3 percent of AT patients had IgA deficiency and the occurrence of frequent pulmonary infections was more common in patients with low serum IgA than in patients with normal IgA, a finding contrary to previous reports[8,11]. Serum IgG levels were low in six patients, and in one patient, it was especially low (120 mg/dl). This patient was given standard gammaglobulin but he died of pulmonary disease. Serum IgM levels were high in 26.6 percent of patients, all of whom had decreased IgA levels. The increase of the IgM level was attributed to frequent infections or compensation of the low IgA level in these patients.

We found no correlation between the disturbance of immune functions and the duration of illness. Our study showed that IgA deficiency is a factor responsible, at least in part, for sinopulmonary infections and that recurrent infections may be an additional factor influencing somatic growth in AT patients.

REFERENCES

1. Syllaba L, Henner K. Contribution à l'indépendance de l'athétose double idiopathique et congénitale. *Rev Neurol* 1:541, 1926.
2. Louis-Bar D. Sur un syndrome progressif comprenant des télangiectasies capillaires cutanées et conjonctivales symétriques, à disposition naevoïde et des troubles cérébelleux. *Confin Neurol* (Basel) 4:32, 1941.
3. Boder E, Sedgwick RP. Ataxia-telangiectasia: a familial syndrome of progressive cerebellar ataxia, oculocutaneous telangiectasia and frequent infection. A preliminary report on seven children, an autopsy and a case history. *USC Med Bull* 6:15, 1957.
4. Boder E, Sedgwick RP. Ataxia-telangiectasia: a familial syndrome of progressive cerebellar ataxia, oculocutaneous telangiectasia and frequent pulmonary infection. *Pediatrics* 21:526, 1958.
5. Young RR, Austen KF, Moser HW. Abnormalities of serum gamma 1A globulin and ataxia-telangiectasia. *Medicine* 43:423, 1964.
6. Elsen AH, Karpati G, Laszlo T, et al. Immunologic deficiency in ataxia-telangiectasia. *N Engl J Med* 272:18, 1965.

7. McFarlin DE, Strober W, Waldmann TA. Ataxia-telangiectasia. *Medicine* 51:281, 1972.
8. Ersoy F, Berkel AI. Clinical and immunological studies in twenty families with ataxia-telangiectasia. *Turk J Pediatr* 10:145, 1974.
9. Berkel AI, Ersoy F, Sanal Ö, et al. Immune dysfunctions in ataxia-telangiectasia. In Müftüoğlu A. (ed). *Proceedings 5th European Immunology Meeting,* Istanbul, Turkey, June 4-6, 1982. New York: Plenum Press, 1984, p. 173.
10. Oxelius VA, Berkel AI, Hanson LA. IgG2 deficiency in ataxia-telangiectasia. *N Engl J Med* 306:515, 1982.
11. Boder E. Ataxia-telangiectasia: an overview. In Gatti RA, Swift M (eds). *Ataxia-Telangiectasia: Genetics, Neuropathology, and Immunology of a Degenerative Disease of Childhood.* New York: Liss, 1985, pp. 1-63.
12. Fiorilli M, Antonelli A, Russo G, et al. Variant of ataxia-telangiectasia with low level radiosensitivity. *Hum Genet* 70:274, 1985.
13. Swift M, Sholman L, Perry M, et al. Malignant neoplasms in the families of patients with ataxia-telangiectasia. *Cancer Res* 36:209, 1976.
14. Berkel AI, Ersoy F. Ataxia-telangiectasia and malignancies. *Turk J Pediatr* 16:82, 1974.
15. Painter RB, Young BR. Radiosensitivity in ataxia-telangiectasia: a new explanation. *Proc Natl Acad Sci USA* 77:7315, 1980.
16. Waldmann TA, McIntire KR. Serum-alpha-fetoprotein levels in patients with ataxia-telangiectasia. *Lancet* 2:1112, 1972.
17. August CS, Berkel AI, Levy RH, et al. Establishment of immunological competence in a child with congenital thymic aplasia by a graft of fetal thymus. *Lancet* 1:1080, 1970.
18. Jondal M, Holm G, Wigzell H. Surface markers on human T and B lymphocytes. I. A large population of lymphocytes forming non-immune rosettes with sheep red blood cells. *J Exp Med* 136:207, 1972.
19. Sümbüloğlu K. Sağlık Bilimlerinde Araştırma Teknikleri ve İstatistik. Ankara: Matiş Yayınları, 1978, pp. 121-124.
20. Kıran Ö, Yalaz K, Tayşi K, et al. Immunological studies in ataxia-telangiectasia. *Clin Genet* 5:40, 1974.
21. Levin S, Perlov S. Ataxia-telangiectasia in Israel. With observations on its relationship to malignant disease. *Isr J Med Sci* 7:1535, 1971.
22. Tadjoedin MK, Fraser FC. Heredity of ataxia-telangiectasia (Louis-Bar syndrome). *Am J Dis Child* 110:64, 1965.
23. Ulusoy M, Tunçbilek E. Türkiye'de akraba evlilikleri ve çocuk ölümlerine etkisi. *Nüfus Bilim Dergisi* 9:7, 1987.
24. Smith JL, Cogan DG. Ataxia-telangiectasia. *AMA Arch Ophthalmol* 62:364, 1959.
25. Hyams SW, Reisner SH, Neumann E. The eye signs in ataxia-telangiectasia. *Am J Ophthalmol* 62:1118, 1966.
26. Thieffry S, Arthuis M, Alcardi J, Lyon G. L'ataxie-télangiectasia. *Rev Neurol* 105:390, 1961.
27. Baloh R, Yee RD, Boder E. Eye-movements in ataxia-telangiectasia. *Neurology* 28:1099-1978.
28. Gatti RA, Good RA. Occurrence of malignancy in immunodeficiency diseases. *Cancer* 28:89, 1971.
29. Davis MM, Gatti RA, Sparks RS. Neoplasia and chromosomal breakage in ataxia-telangiectasia: a 2: 14 translocation. In Gatti RA, Swift M (eds). *Genetics, Neuropathology and Immunology of a Degenerative Disease of Childhood.* New York: Liss, 1985, pp. 197-203.
30. Swift M, Reitnauer PJ, Morrell D, Chase CL. Breast and other cancers in families with ataxia-telangiectasia. *N Engl J Med* 316:1289, 1987.

31. Ammann AJ, Duquesnoy RJ, Good RA. Endocrinological studies in ataxia-telangiectasia and other immunological deficiency diseases. *Clin Exp Immunol* 6:587, 1970.

32. Schalch DS, McFarlin DE, Barlow MH. An unusual form of diabetes mellitus in ataxia-telangiectasia. *N Engl J Med* 202:1396, 1970.

33. Yordam N. Ataksi-telanjiektazi'de endokrin fonksiyonlarının incelenmesi. *Çocuk Sağlığı ve Hastalıkları Dergisi* 25:307, 1982.

34. Epstein W, Fudenberg HH, Reed WB, et al. Immunologic studies in ataxia-telangiectasia. *Int Arch Allergy* 30:15, 1966.

35. Peterson RD, Cooper MD, Good RA. Lymphoid tissue abnormalities associated with ataxia-telangiectasia. *Am J Med* 41:342, 1966.

36. Bach JF. Evaluation of T-cells and thymic serum factors in man using the rosette technique. *Transplant Rev* 16:196, 1973.

37. Gatti RA, Bick M, Tam CF, et al. Ataxia-telangiectasia: A multiparameter analysis of eight families. *Clin Immunol Immunopathol* 23:501, 1982.

38. McFarlin DE, Oppenheim JJ. Impaired lymphocyte transformation in ataxia-telangiectasia in part due to a plasma inhibitory factor. *J Immunol* 103:1212, 1969.

The Turkish Journal of Pediatrics 33:217-220, 1991

ELIMINATION OF MATERNAL ANTIBODIES AGAINST MEASLES

(Is the Policy of Vaccinating Children Younger than Nine Months of Age Suitable for Turkey?)*

*Güler Kanra MD***, Mehmet Ceyhan MD****

SUMMARY: Kanra G, Ceyhan M. (Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Elimination of maternal antibodies against measles (Is the policy of vaccinating children younger than nine months of age suitable for Turkey?). Turk J Pediatr 33: 217-220, 1991.

Maternal antibodies against measles in 223 healthy children aged 22 to 31 weeks were studied. The ratio of children with detectable antibodies declined from 61.4 percent at 22-23 weeks of age to 20 percent at 26-27 weeks of age. Since the minimum proportion of antibody-positive children (15.6% at 26-27 weeks of age) is still higher than the optimum proportion (5%), the Schwarz vaccine which is used mostly in measles immunization seems not to be effective to obtain a high seroconversion rate in our infants. We suggest that the Edmonston-Zagreb strain of measles vaccine be used for infants under 9 months of age in Turkey. *Key words: maternal antibodies against measles, measles vaccination.*

Despite the advent of the measles vaccine in 1959, the illness remains one of the most severe and important infectious diseases in the developing world. The virus is responsible for the death of millions of children and precipitates diarrhea, malnutrition and blindness in a substantial proportion of victims[1-4]. Measles is a serious public health problem especially in those areas where the disease mostly occurs during the latter part of the first year of life[2].

National public health recommendations for measles vaccination differ from country to country. The World Health Organization (WHO) recommends that immunization with a live attenuated measles vaccine should be carried out when the child is around the age of nine months, at which time the transplacentally acquired immunity is waning[5]. At this age, the administration of one standard dose of the Schwarz strain measles vaccine successfully immunizes at least 90 percent of the vaccinees. However, despite the vaccination, measles has become hyperendemic in many of the crowded, urban areas of developing countries, probably because of the high influx of susceptible children from the surrounding rural areas who have insufficient vaccination coverage[6]. As a consequence, many fatal cases have been observed before the age of nine months. Reports from The Gambia[7] and South Africa[8] indicate that 18 to 45 percent of all measles cases

* From the Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara.

** Professor of Pediatrics, Hacettepe University Faculty of Medicine.

*** Associate Professor of Pediatrics, Hacettepe University Faculty of Medicine.

occur in infants under the age of nine months. With the aim of decreasing the incidence of measles in this age group, many studies are being performed regarding the vaccination of infants aged between 4-6 months[9]. In that age group, unfortunately, the effectiveness of the measles vaccine is reduced to a great degree by the virus neutralizing activity of the transplacentally acquired maternal measles antibodies[10,11]. Therefore, the most important factor affecting the success of measles immunization is the disappearance of maternal anti-measles antibody. In order to determine the optimum age for measles vaccination, we studied the rate of disappearance of anti-measles antibodies in a group of children aged between 22 and 31 weeks.

Material and Methods

The study population consisted of 223 healthy infants who were 22 to 31 weeks of age. They were registered in the Hacettepe University Rural Hospital at Etimesgut, a district 16 km from Ankara, were they had received comprehensive medical care since birth. The age distribution was: 57 were 22 to 23 weeks, 29 were 24 to 25 weeks, 32 were 26 to 27 weeks, 65 were 28 to 29 weeks, and 40 were 30 to 31 weeks. The children had no history of measles nor signs of immunological deficiency.

Separated serum samples were stored at –20°C until titration could be performed in the laboratory. Measles specific antibodies were determined by an enzyme-linked immunosorbent assay (ELISA; Behring diagnostic kit)[12]. Titres were expressed as the last dilution yielding an optic density of 0.2. Seropositivity was defined as the appearance of a detectable level of antibodies (1:32).

Results

Seropositivity, which is the result of the presence of maternal anti-measles antibodies, was 73/223 (32.7%) in all children in the study. The proportion of children with detectable antibodies declined progressively with increasing age (Fig. 1). The distribution of maternal antibody levels in relation to age shows a progressive reduction with increasing age from 22 weeks to 27 weeks. Thus the proportion of antibody positive children declined from 61.4 percent at 22-23 weeks to 15.8 percent at 26-27 weeks. While an evident decrease occurred during those weeks, thereafter no decline was observed up to 31 weeks of age.

Discussion

Since measles occurs at earlier ages in developing countries, WHO has lowered the optimum age for measles vaccination in children to nine months or younger[5]. The usual vaccine is the Schwarz vaccine, a higly attenuated strain of a chick-cell adapted measles virus. At this age, seroconversion after vaccination is about 90

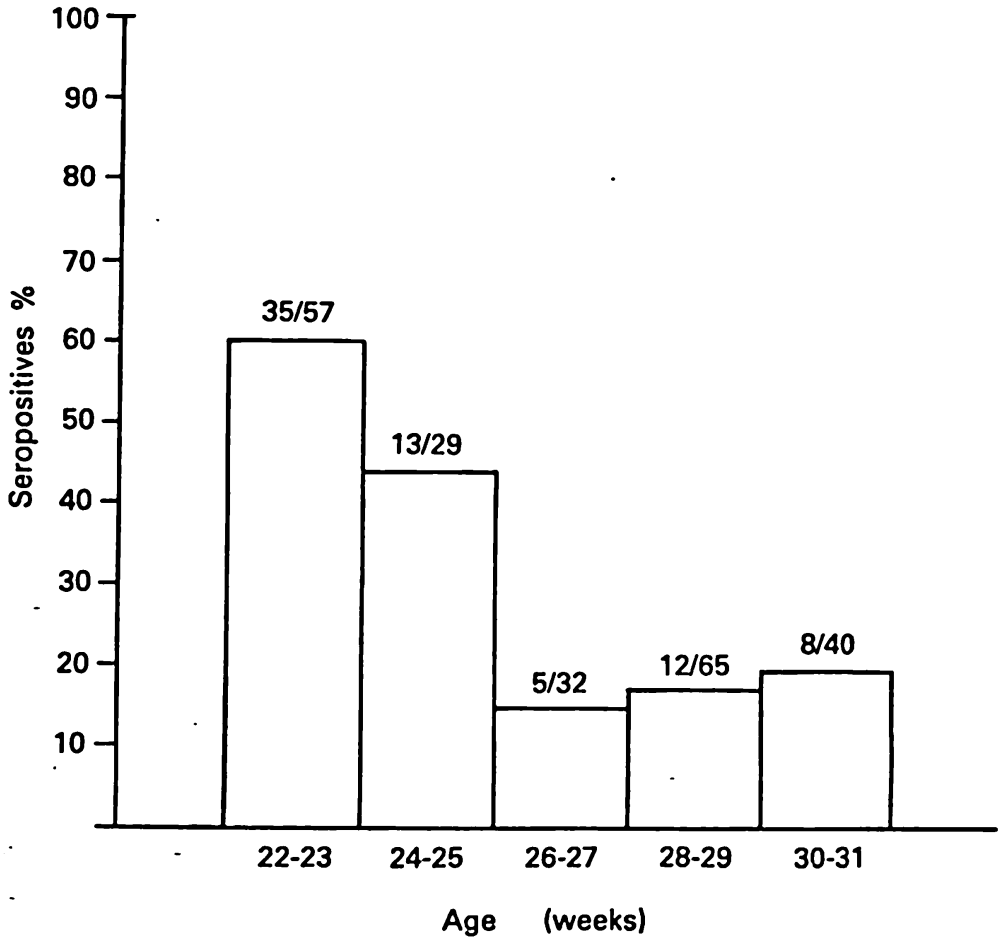

Fig. 1: Proportion of seropositive children according to age.

percent[9]. Although vaccination during the said period results in better protection than at 15 months of age, measles has still not been eradicated in the world. Recently, the median age of the onset of measles has dropped since the disease has become hyperendemic in developing countries, owing to the constant influx of susceptible children from poorly immunized rural areas[6]. The target of investigators studying measles immunization is to vaccinate infants aged between four and six months. However, if children are immunized at this age, the vaccine failure rate rises strikingly because maternal antibody, the level of which is inversely related to the age of the child, neutralizes the virus[9]. Thus the key point of measles vaccination is the level of maternal antibodies.

In our study, we found anti-measles antibody to be present in 15.6 to 61.4 percent of children aged 22 to 31 weeks. Since the maximum antibody positivity rate in children of a community must be lower than 5 percent innoculation to obtain optimal seroconversion after innoculation with the Schwarz vaccine[13], it is not possible to obtain sufficient protection in this age group.

The cause for the slow elimination of maternal antibodies against measles in Turkish children is unknown. However, this occurrence is also evidenced in

infants aged between 7-10 months in many other developing areas of the world[14]. The reason for this is unclear. Since our infants cannot be seroconverted at the age of 22 to 31 weeks with Schwarz vaccine, because of their maternal anti-measles antibodies, we must consider using a different strain of measles virus, called the Edmonston-Zagreb virus which has been used in many studies[15,16]. The results of these studies show the effectiveness of the Edmonston-Zagreb vaccine strain given to children under the age of nine months. Another study is being carried out to determine the efficacy of the Edmonston-Zagreb measles vaccine given to Turkish children under the age of nine months.

REFERENCES

1. Christie AB. *Infectious Diseases: Epidemiology and Clinical Practice.* Edinburgh: Churchill Livingstone, 1974, pp. 374-406.
2. Shahid NS, Clauquin P, Shaikh K, Zimicki S. Long-term complication of measles in rural Bangladesh. *J Trop Med Hyg* 86:77, 1983.
3. Krugman S, Ward R, Katz SL. *Infectious Diseases of Children* (6th ed). St. Louis: CV Mosby, 1977, p. 141.
4. Foster A, Sommer A. Childhood blindness from corneal ulceration in Africa: causes, prevention, and treatment. *Bull WHO* 64:619, 1986.
5. Hall AJ, Greenwood BM, Whittle H. Modern vaccines. Practice in developing countries. *Lancet* 335:774, 1990.
6. Preblud SR, Katz SL. Measles vaccine. In Plotkin SA, Mortimer EA Jr (eds). *Vaccines.* Philadelphia: WB Saunders, 1988, pp. 182-222.
7. Whittle HC, Rowland MG, Mann GF, et al. Immunization of 4-6 month old Gambian infants with Edmonston-Zagreb measles vaccine. *Lancet* 2:834, 1984.
8. Loening WE, Coovadia HM. Age-specific occurrence rates of measles in urban, peri-urban, and rural environments: implication for time of vaccination. *Lancet* 2:324, 1983.
9. Whittle HC, Mann G, Eccles M, et al. Effects of dose and strain of vaccine on success of measles vaccination of infants aged 4-5 months. *Lancet* 1:963, 1988.
10. McGraw TT. Reimmunization following early immunization with measles vaccine: a prospective study. *Pediatrics* 77:45, 1986.
11. Black FL, Berman LL, Libel M, et al. Inadequate immunity to measles in children vaccinated at an early age: effect of revaccination. *Bull WHO* 62:315, 1984.
12. Sabin AB, Flores Arechiga A, Fernandez de Castro J, et al. Successful immunization of children with and without maternal antibody by aerosolized measles vaccine. I. Different results with undiluted human diploid cell and chick embryo fibroblast vaccines. *JAMA* 249:2651, 1983.
13. Burgess W, Tomkins A, Garelick H, Mann G. Measles immunization trials in Mbeya, Tanzania. Unpublished data.
14. Linnemann CC Jr, Dine MS, Roselle GA, Askey PA. Measles immunity after revaccination: results in children vaccinated before 10 months of age. *Pediatrics* 69:332, 1982.
15. Ikić DM. Edmonston-Zagreb strain of measles vaccine: epidemiologic evaluation in Yugoslavia. *Rev Infect Dis* 5:558, 1983.
16. Markowitz LE, Bernier RH. Immunization of young infants with Edmonston-Zagreb measles vaccine. *Pediatr Infect Dis J* 6:809, 1987.

The Turkish Journal of Pediatrics 33:221-230, 1991

DIAGNOSIS AND TREATMENT OF INTRASPINAL LIPOMAS*

*Fitnat Dinçer MD***, Hamit Ziya Gökalp MD***, Cumhur Dinçer MD***
*Ahmet Zorlutuna MD*****

SUMMARY: Dinçer F, Gökalp HZ, Dinçer C, Zorlutuna A. (Department of Physical and Rehabilitative Medicine, Hacettepe University Faculty of Medicine, Ankara, and the Department of Neurosurgery, Ankara University Faculty of Medicine, Ankara, Turkey). Diagnosis and treatment of intraspinal lipomas. Turk J Pediatr 33: 221-230, 1991.

In this article a 32-case series of intraspinal lipoma localized to the lumbosacral region is presented. All of the patients underwent surgery. Recent reports in the literature indicate that although these lesions show advanced and progressive neurological deficits, very good results can be achieved with surgical treatment.

The advantages of computed tomography in diagnosis and the importance of early surgical intervention and postoperative rehabilitation are emphasized. *Key words: intraspinal lipoma, surgical intervention, rehabilitation.*

Intraspinal lipoma is a lesion localized to the lumbosacral region and characterized by progressive muscle weakness in the lower extremities and sphincter disturbances. This lesion may sometimes cause weakness only in the sphincter muscles[1]. There are some contrary opinions as to the timing of surgical intervention. It is a matter of discussion as to whether surgery should be performed before or after neurological deficits develop. Nowadays, it has become easier to make an accurate and differential diagnosis by means of computed tomography (CT). Detailed information concerning the spinal canal and the mass is very helpful in the timing of surgical intervention[2].

Material and Methods

The study population consisted of 32 patients, 15 males and 17 females with intraspinal lipoma who were examined in the Department of Neurosurgery of the Ankara University Faculty of Medicine between 1976 and 1989.

Fifteen patients (47%) were below two years of age; thirteen patients (40%) were between two-fifteen years of age, and the remaining four patients (13%) were between twelve to fifty-two years of age. All patients were categorized

* From the Department of Physical and Rehabilitative Medicine, Hacettepe University Faculty of Medicine, Ankara, and the Department of Neurosurgery, Ankara University Faculty of Medicine, Ankara.

** Associate Professor of Physical and Rehabilitative Medicine, Hacettepe University Faculty of Medicine.

*** Professor of Neurosurgery, Ankara University Faculty of Medicine.

**** Resident in Neurosurgery, Ankara University Faculty of Medicine.

according to age group, familial dysraphic conditions, symptomatology and clinical findings. A detailed physical examination of the neurological, dermatological and musculoskeletal systems was carried out to determine skin lesions and neurological deficits.

Neuroradiological investigations were performed using plain roentgenography, myelography and computed tomography.

Surgery was performed on all patients, those with progressive and mild neurological deficits and also those with stable neurological signs. Our aim was to decompress the neural structures and free them from the tethering position. Total excision of the intraspinal part of the lipoma was not attempted in every case. During the operation, we used electrostimulation to prevent possible additional neurological damage, and the non-functional neural elements were excised in order to remove the fixed structures.

An intensive physiotherapy program including active, passive, active-resistive and strengthening exercises and a gait training program was initiated.

Results

Familial dysraphic conditions associated with intraspinal lipoma were not detected in our patients, even though four patients (12%) were products of consanguineous unions.

Various types of skin lesions were present in ten patients (31%) (Table I) and complaints of neurological deficits were present in twenty-two patients (50%). Subcutaneous lipomas were detected in twenty-four patients (75%). Of the other skin lesions, the commonest were dimples (ten cases; 31%). There were no skin lesions in four patients (13%).

TABLE I: 32 Cases of Intraspinal Lipomas and Skin Lesions

	Cases	
Lesions	No. of Cases	Percentage
Subcutaneous mass	24	75
Dimples	10	31
Hemangioma	8	25
Hypertrichosis	3	9
Dermal sinus	3	9
Normal	4	12.1

Twelve patients (37.5%) complained of polyuria, dysuria or constipation. In fourteen patients (43.7%) neurological complaints were of a progressive nature. In the presence of congenital lesions in addition to intraspinal lipoma, patients may show progressive or stable neurological signs (Tables II and III). On examination (Table III) eighteen patients (56.2%) had a motor deficit defined as either weakness or a sphincter disturbance. The others had mild neurological deficits such as reflex changes. In four patients asymmetrical neurological signs were present.

TABLE II: 32 Cases of Intraspinal Lipomas and Associated Congenital Anomalies

Associated Anomaly	No. of Cases
Spina bifida	32
Radicular anomalies	10
Intraspinal cord lesions:	
– Terminal hydromyelia	3
– Teratoma	2
– Dermoid cyst	2
– Diastematomyelia	1
Extraspinal malformations:	
– Genital-anal malformations	2
– Urinary tract malformations	1
– Anal stenosis	1
– Arnold-Chiari (I)	1
– Extremity anomalies	4

TABLE III: Neurological Deficits in Intraspinal Lipomas

Neurological Deficits	No. of Cases
Motor-sphincter disturbance	18
Motor deficit	11
Sphincter disturbance	7
Abnormal reflex (Hypo or hyperactive)	20
Perineal sensorial impairment	14

In the adult group (12%) primary symptoms were related to the neurogenic bladder. If possible, electromyography of the lower extremities and perineum and urodynamic investigations should be added to the neurological evaluation.

Neuroradiological investigations included plain roentgenograms, myelography and CT. Spina bifida was detected in every patient on direct roentgenograms (Fig. 1). When myelography was used alone, only the expansile process within the

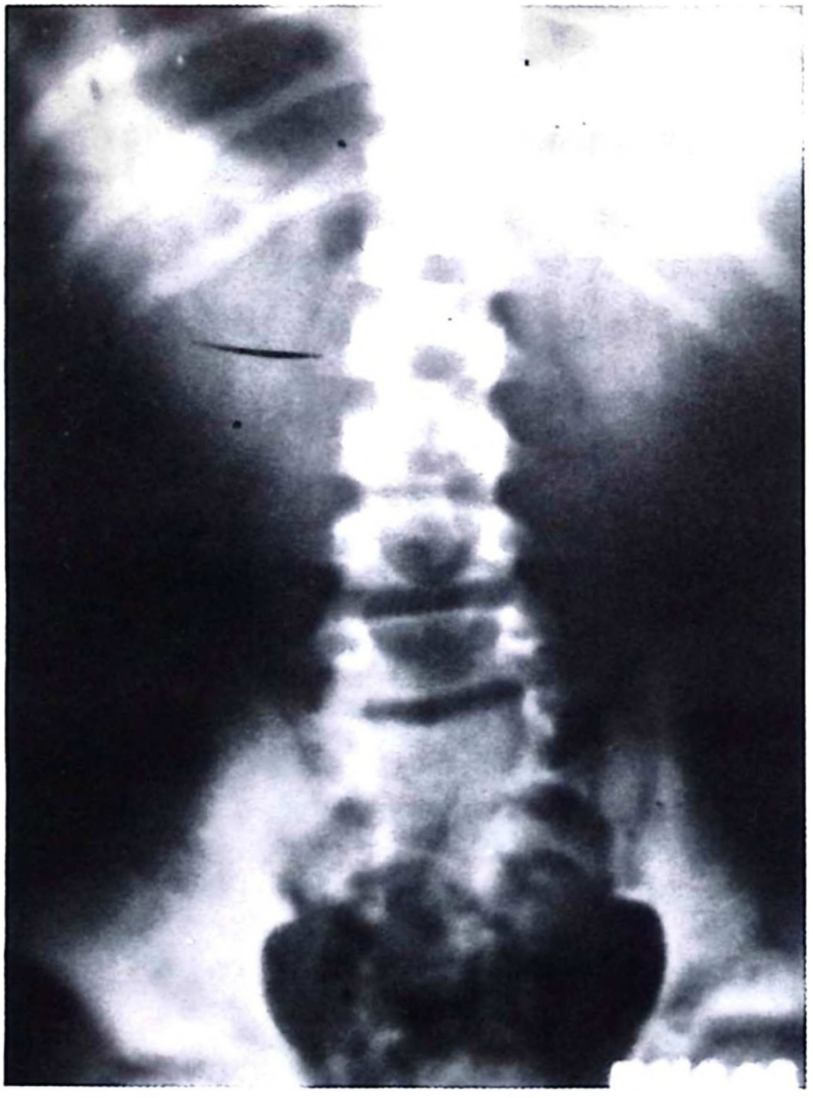

Fig. 1: Spina bifida; on direct roentgenogram of lumbosacral region.

widened spinal canal was identified. As a result of CT investigations, the nature and anatomopathologic position of the masses inside or outside the spinal canal were easily evaluated (Figs. 2-4).

In every patient in our series the conus medullaris was localized downwards and fixed to the lipoma and surrounding tissues with fibrous bands. These fixations

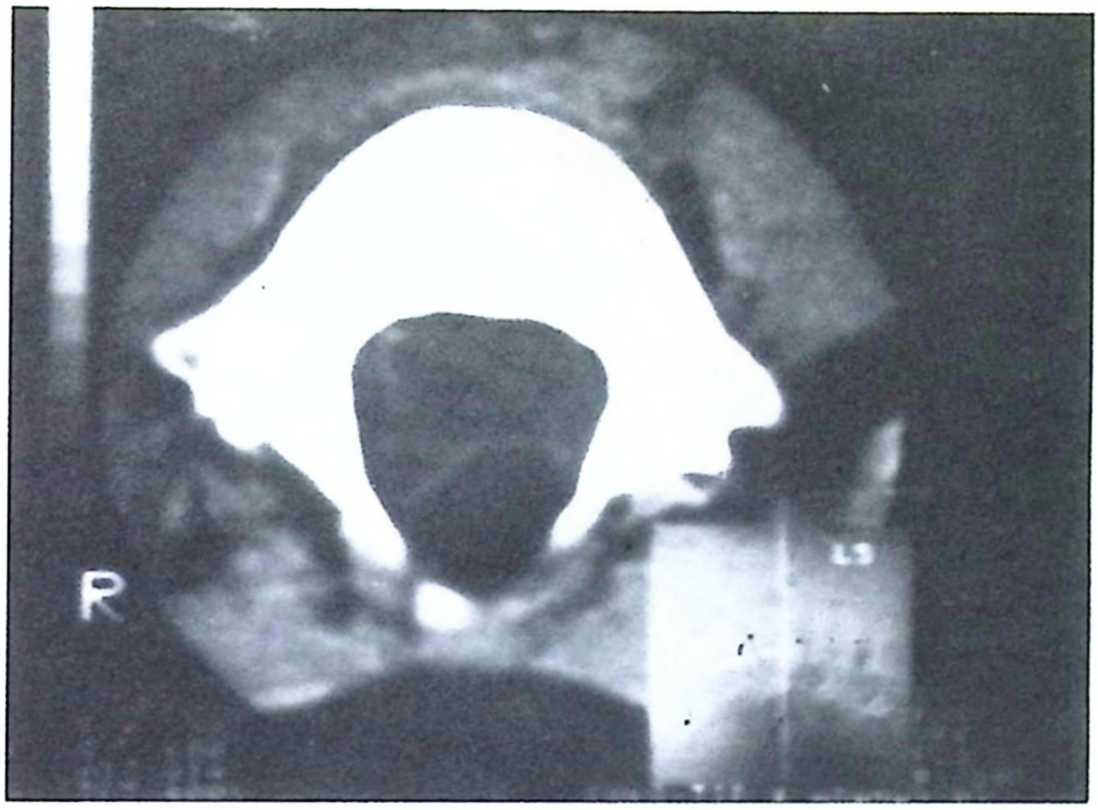

Fig. 2: Spina bifida and intracanalicular lipoma (hypodense) on computed tomography.

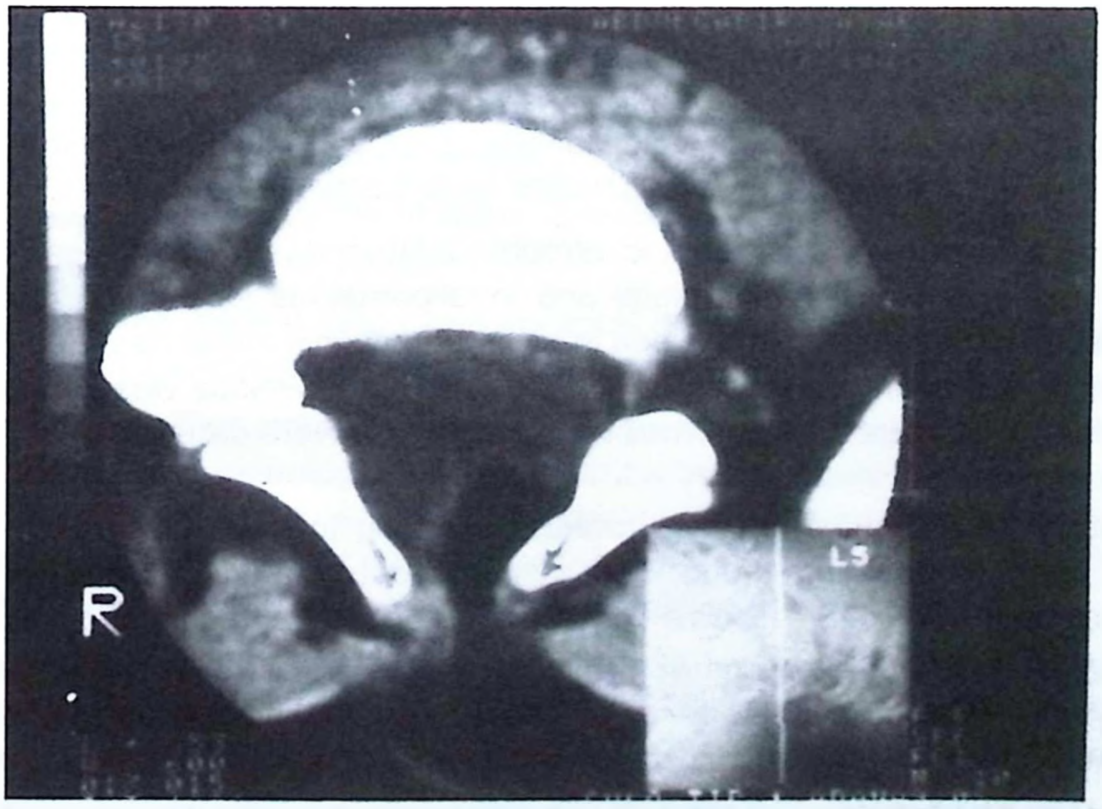

Fig. 3: Epidural lipoma, with extraspinal invasion, on computed tomography.

Fig. 4: Subdural lipoma; hypodense lesion spreading out to subcutaneous tissues in the presence of a wide canal defect, on computed tomography.

were detected essentially on the same side as the extremity with the neurological deficits. It was also observed that the neural elements were compressed or fixed. The fixations were detected either by myelography or CT or during surgery. During the operation, morphologic abnormalities and functional disturbances were frequently observed in the patients with congenital anomalies.

Roots were hypertrophic, dystrophic, atrophic, infiltrated with adipose and fibrous tissue and aberrant, with intradural and intralipomatous localization. Electrical stimulation is of help to the surgeon in saving functional structures. Sometimes the excision of neural elements mixed with fatty fibrous tissue was very difficult to perform and, therefore, abnormal neural elements were detected with fibrous tissue as well.

Lipomas were classified into two groups according to their relationship to the nerve roots. In the first group, comprising twenty patients, the roots were localized ventrally to the lipoma-cord surface and as a result of satisfactory excision, untethering (removal of fixation) was possible. In the second group, comprising twelve patients, (37.6%) the roots passed through the lipoma, preventing total excision.

There was no postoperative mortality. In eight patients, subcutaneous collection developed in the postoperative stage. In one of them, a dermal sinus was repaired

by surgical intervention. In the early postoperative stage, additional neurological deficits were detected in three patients (9%).

Preoperative neurological deficits subsided in seventeen patients (53%) and remained the same in twelve patients (37%).

The results were evaluated in the early postoperative stages. Improvements in neurological deficits such as motor and sphincter dysfunctions were observed. Complete improvement was detected after surgical intervention in two patients (6%) with progressive neurological deficits. However, in patients with non-progressive neurological deficits, we could not detect such improvement. There was improvement in the postoperative stage in ten (76%) out of seventeen patients with preoperative progressive neurological deficits and in seven (38%) out of eighteen patients with preoperative nonprogressive deficits. We are not able to give accurate numerical values regarding the future progress of twelve patients whose lipomas were subtotally excised, since they did not return for follow-up examinations.

Eighteen (56.25%) of the patients with motor weakness in the lower extremities also had a neurogenic bladder for which an appropriate rehabilitative approach was undertaken.

Discussion

Intraspinal lipomas are lesions which cause progressive neurological deficits such as paraplegia and incontinence. The risk of neurological disturbances is present in patients of all ages and progresses with the passage of time[3].

According to the literature, there is a higher rate of this tumor occurring in females than in males. In our study, there were 15 males (47%) and 17 females (53.1%), which complied with the above.

In our series, the highest ratio of neurological disturbances was reported as 67 percent which is indicative of spontaneous neurological disturbances.

Families seek medical attention for their children because of the presence of skin lesions rather than neurological deficits. In the adult population, however, the opposite is true. It is not very easy to evaluate the past neurological status of children but it should be kept in mind that they form the highest risk group[4,5]. The main reason for neurological disturbance is tethered cord[6].

These factors may explain the early or late progression of the findings or the sudden onset of disturbances after trauma. In non-traumatic conditions, compression is probably the most important reason for the sudden onset of disturbances.

As a result of biochemical research, it has been demonstrated that in lipomas, accumulation is faster and mobilization is slower when compared to normal

adipose tissue cells[7,8,9]. Therefore, it is found that the metabolism of intraspinal lipoma cells is similar to that of normal adipocytes and that a low-calorie diet may be quite helpful in preventing postoperative recurrences.

If intraspinal lipomas are evaluated neuroradiologically, it is observed that the results of plain roentgenograms and myelograms are not specific for these lesions; they can only enlighten us about the anomalies of bony structures and neural elements. Diastematomyelia and root anomalies are demonstrated by metrizamide myelogram. Computed tomography and magnetic resonance imaging (MRI), in addition to evaluating the type of the tumor, also reveal the presence of tethered cord, other bony anomalies and the extraspinal invasion of the tumour[10,11]. Intraspinal lipomas that appear with low density on CT, show high signal intensity and spike-like superior extension in the spinal canal on MRI[2]. Thus, it seems that CT and MRI are the most informative diagnostic tools. In addition, CT, which offers detailed information about lesions and malformations, substantiates the opinion of surgeons who prefer early surgical intervention.

There are two therapeutic approaches when dealing with spinal lipomas. The first entails a period of observation in which the surgeon monitors the lesion and then performs surgery when neurological deficits appear. This method is preferred by surgeons who wish to avoid postoperative complications and disturbances[5,12]. In our opinion, any delay will give rise to the formation of irreversible neurological deficits. However, neurosurgical intervention may result in a patient being deficit-free but will neither completely cure deformities of the musculoskeletal system, which have already developed, nor prevent their progress[1]. In our series, only two cases out of eighteen with neurological deficits became deficit-free after surgery.

The early postoperative stage has been accepted as being one month. The degree of success of surgical intervention depends on the number and duration of neurological deficits, congenital malformations and related nerve root anomalies. However, after the detection of intraspinal lipoma, the symptoms which may appear at any age may have an insidious onset. The condition of some patients may suddenly deteriorate, such as occurred in two of our patients. Recently, an increasing number of authors have preferred the second method of treatment. They recommend immediate surgical invention after diagnosis, even if the patient is without deficit[3,11,13,14] and emphasize the potential effect of lipomas. Other authors recommend that surgery be performed as early as possible in order to prevent the risk of sudden onset of disturbances in the infantile stages[1,15-17]. We kept these recommendations in mind, especially in regard to our cases in which paraplegia developed suddenly, and took the same decision.

A review of the literature reveals that the results achieved in these patients are much better than in patients that have not been subjected to surgery. Postoperative disturbances can be minimized by electrostimulation[18].

In deficit-free patients prophylactic surgical intervention should be contemplated. In our experience with these cases, we found postoperative neurological disturbances to be 9 percent, which is rather higher than that reported in the literature.

In nonoperated series, this ratio has been reported to be 56 percent[3,12,17].

According to McLone et al[2], the use of the CO_2 laser reduces the operation time and permits more extensive removal of the intramedullary component of these lesions.

Early application of a rehabilitation program in addition to surgical intervention in paraparetic, paraplegic patients are as important as early diagnosis and surgical intervention[9].

Eighteen of our patients with motor deficits also had a neurogenic bladder. The lesion level is very important for the success of a rehabilitation program (Table IV). According to Rusk[21], patients with a lesion level above T_{10} cannot be functional ambulatories, while those with a lesion level below T_{10} can after the implementation of a rehabilitation program. Our results were parallel with those reported by experts[19-21].

TABLE IV: The Lesion Level in Rehabilitated Patients

Lesion Level	No. of Patients
$T_{12}L_1$	2
$L_{1/2}$	2
$L_{2/3}$	2
$L_{3/4}$	4
$L_{4/5}$	5
L_5S_1	3

In our series, according to the results of surgical intervention, the ratio of additional neurological deficits was 9 percent. The development of spontaneous neurological deficits was 67 percent. When we compare these two figures, the importance of early surgical intervention and systematic therapy is clearly understood.

Additional information about the lesion, arrived at by using CT and MRI, is very helpful for surgical intervention.

In addition, electrostimulation and laser facilitate the surgical treatment[2]. The importance of rehabilitation cannot be underestimated or neglected in the treatment of these patients, and it should be remembered that laser, electrostimulation and post-operative rehabilitation encourage surgeons to operate as early as possible on patients with nonprogressive, mild neurological deficits.

REFERENCES

1. James CC, Lassman LP. *Spina Bifida Occulta.* New York: Grune, 1981, pp. 230.
2. McLone DG, Naidich TP. Laser resection of fifty spinal lipomas. *Neurosurgery* 18:611, 1986.
3. Petit H, Jomin M, Julliot JP, et al. Dysraphie lumbo-sacrée et "moelle longue" de révélation tardive (neuf observations). *Rev Neurol (Paris)* 135:427, 1979.
4. Thierry A, Archimbaud JP, Perrin J, et al. Aspects neurologiques et urologiques particuliers des tumeurs développées sur spina bifida occulta chez l'adulte et le grand enfaut. A propos de 2 cas de lipomes lombro-sacrés opérés. *Neurochirurgie* 14:809, 1968.
5. Boccon-Gibod L, Pierre Kahn A, Hurel JP. Dysraphies spinales occultes à révélation urologique chez l'adulte. Six observations. *Ann Urol (Paris)* 18:17, 1984.
6. Yamada S, Zinke DE, Sanders D. Pathophysiology of 'tethered cord syndrome'. *J Neurosurg* 54:494, 1981.
7. Giudicelli Y, Pecquery R, Agli B, et al. Lipoprotein lipase and hormone-sensitive lipase activities in human subcutaneous lipomas: comparison with normal subcutaneous adipose tissue. *Clin Sci Mol Med* 50:315, 1976.
8. Pecquery R, Malagrida L, Guidicelli Y. Adipocyte adenylate cyclase and alpha- and beta-adrenergic receptors in one case of multiple symmetric lipomatosis. *Biomedicine* 33:64, 1980.
9. Chapman PH, Davis KR. Surgical treatment of spinal lipomas in childhood. In Raimondi AJ (ed). *Concepts in Pediatric Neurosurgery,* No. 3. Basel: S Karger, 1983, pp. 178-190.
10. Kaplan JO, Quencer RM. The occult tethered conus syndrome in the adult. *Radiology* 137:387, 1980.
11. Pang D, Wilberger JE Jr. Tethered cord syndrome in adults. *J Neurosurg* 57:32, 1982.
12. Bruce DA, Schut L. Spinal lipomas in infancy and childhood. *Childs Brain* 5:192, 1979.
13. AL-Mefty O, Kandzari S, Fox JL. Neurogenic bladder and the tethered spinal cord syndrome. *J Urol* 122:112, 1979.
14. McLone DG, Mutluer S, Naidich TP. Lipomeningoceles of the conus medullares. In Raimondi AJ (ed). *Concepts in Pediatric Neurosurgery,* No. 3. Basel: S Karger, 1983, pp. 170-177.
15. Harris HW, Miller OF. Midline cutaneous and spinal defects. Midline cutaneous abnormalities associated with occult spinal disorders. *Arch Dermatol* 112:1724, 1976.
16. Kieck CF. De Villiers JC. Subcutaneous lumbosacral lipomas. *S Afr Med J* 49:1563, 1975.
17. Villarejo FJ, Blazquez MG, Gutierrez-Diaz JA. Intraspinal lipomas in children. *Childs Brain* 2:361, 1976.
18. Hoffman HJ, Taecholarn C, Hendrick EB, Humphreys RP. Management of lipomyelomeningoceles. Experience at the Hospital for Sick Children, Toronto. *J Neurosurg* 62:1, 1985.
19. Guttman L. *Spinal Cord Injuries: Comprehensive Management and Research.* Oxford: Blackwell Scl, 1973, pp. 101-123.
20. Goodgold J. *Rehabilitation Medicine.* St. Louis: Mosby, 1988, pp. 147-192.
21. Rusk HA (ed). *Rehabilitation Medicine.* St. Louis: Mosby, 1977, pp. 326-334.

The Turkish Journal of Pediatrics 33:231-234, 1991

SODIUM AND POTASSIUM LEVELS IN COLOSTRUM*

*Murat Yurdakök MD***, Olcay Oran MD***, Gülsevin Tekinalp MD****

SUMMARY: Yurdakök M, Oran O, Tekinalp G. (Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara, Turkey). Sodium and potassium levels in colostrum. Turk J Pediatr 33: 231-234, 1991.

The sodium and potassium concentrations of serum, urine and breast milk from 40 healthy, lactating mothers aged 18 to 35 years were measured. Nineteen women were primiparous and 26 were delivered prematurely for various reasons. No correlation was found between colostrum and urine sodium and potassium levels, and colostrum and serum potassium levels, however, there was a correlation found between colostrum and serum sodium levels (r: 0.311, $p<0.05$). *Key words: colostrum, sodium, potassium.*

When comparing the composition of colostrum with mature breast milk, the former is seen to be richer in mineral content[1,2].

Therefore, the present study was undertaken to investigate the sodium and potassium concentrations of colostrum, and their relation to serum and urine concentrations.

Material and Methods

The study population consisted of 40 healthy, lactating women aged between 18 to 35 years, 19 of whom were primiparous, and the remainder multiparous. Twenty-six of the mothers were delivered of pre-term babies for various reasons. They were on no medication other than vitamins, and were asked to continue with their usual diet.

Serum, urine and breast milk samples were obtained simultaneously from mothers at 9-10 a.m. during the first week of lactation. Sample collection time coincided with feeding time. Milk samples were collected in clean glass containers by emptying the right breast with a pump. After mixing, the fresh milk samples were analyzed. All mothers were requested to collect urine. Blood samples were taken from a peripheral vein. The sodium and potassium concentrations of blood, urine and milk were determined by flame photometry. The results were expressed as a mean ± SD and the Student's *t* test was used to compare the results.

---

* From the Department of Pediatrics, Hacettepe University Faculty of Medicine, Ankara.

** Associate Professor of Pediatrics, Hacettepe University Faculty of Medicine.

*** Professor of Pediatrics, Hacettepe University Faculty of Medicine.

Results

The results are summarized in Tables I and II. Gestational age, birth weight, maternal age and maternal body weight were found to have no effect on serum sodium and potassium levels.

There was no correlation found between colostrum and urine sodium and potassium levels, and also between colostrum and serum potassium levels. But colostrum sodium and serum sodium levels showed a correlation (r: 0.311, $p<0.05$).

TABLE I: Sodium and Potassium Levels in Colostrum

		Sodium (mEq / L)	Potassium (mEq / L)
Gestational age	32-34 w (n: 10)	33.65 ± 22.96	18.35 ± 6.76
	35-37 w (n: 16)	47.91 ± 29.50	15.27 ± 4.01
	38-41 w (n: 14)	42.84 ± 20.79 $p > 0.05$	15.62 ± 3.85 $p > 0.05$
Birth weight	< 2500 g (n: 21)	43.16 ± 25.99	16.19 ± 5.74
	⩾ 2500 g (n: 19)	41.92 ± 24.89 $p > 0.05$	16.13 ± 3.73 $p > 0.05$
Maternal age	⩽ 25 y (n: 19)	40.15 ± 29.74	15.97 ± 5.52
	> 25 y (n: 21)	44.74 ± 20.67 $p > 0.05$	16.00 ± 4.06 $p > 0.05$
Maternal relative weight*	⩾ 40 (n: 12)	40.33 ± 13.01	15.80 ± 4.17
	< 40 (n: 18)	43.44 ± 27.12 $p > 0.05$	16.63 ± 6.20 $p > 0.05$
Total	(n: 40)	42.57 ± 25.16	16.16 ± 4.83

* Maternal relative weight: Body weight X 100 / Height.

TABLE II: Sodium and Potassium Levels in Serum, Urine and Colostrum

	Sodium (mEq / L)	Potassium (mEq / L)
Serum (n: 40)	138.95 ± 4.79	4.72 ± 0.99
Urine (n: 40)	141.40 ± 78.19	45.60 ± 23.83
Colostrum (n: 40)	42.57 ± 25.16	16.16 ± 4.83

Serum Na^+ and colostrum Na^+ r: 0.311 ± 0.154, t: 2.025, $p < 0.05$
y: 136.43 ± 0.06 x, F: 0.927

In other groups there is no correlation.

Discussion

Colostrum compared with mature milk is more viscous and richer in protein. It is considerably richer in minerals but poorer in carbohydrates, fat, and certain vitamins[1,2]. Sodium and chloride are often found to be present in greater amounts by as much as 50-100 per cent in preterm milk during the first two weeks, as compared with term milk, which meets the estimated requirement of the preterm infant[3-12]. However, we could not find any difference in sodium and potassium concentrations of colostrum of mothers delivering preterm or full-term babies.

Maternal dietary sodium and chloride intake appears to have no significant effect on the milk sodium and chloride content. The concentrations of these electrolytes are not related to milk volume[12-14].

Since a correlation was found between urinary and milk potassium levels, but not for sodium levels, Keenan et al[12] suggested that dietary potassium may have an effect on milk. In our study, we could not find any correlation between colostrum and serum or urinary potassium, however, there was a slight correlation found between milk and serum sodium levels. This finding is inconsistent with a previous report[12], and may have been related to the analysis of colostrum in this study.

Diurnal variations in the composition of milk have been reported. Sodium and potassium concentrations are higher at night than in the morning[12]. We obtained milk samples from the mothers at the same hour, so as to exclude diurnal variations of the electrolyte content of the milk.

Variations in the concentration of milk components occur during a feeding, from foremilk to hindmilk. The first portion of milk obtained is called the "foremilk". It is rather watery and contains a lesser amount of electrolytes[1]. In this study, we

collected whole milk from the breast by using a pump. After mixing, we used this substance which contains foremilk and hindmilk to determine the sodium and potassium levels.

In some women, the composition of milk differs slightly from right breast to left breast, although the difference has not been found to be significant[15]. We excluded this possibility by taking milk samples from the right breast in all women.

Maternal age may also affect milk electrolyte concentrations. A study has recently shown that adolescent milk was consistently 50 percent lower in sodium when compared with adult milk[16]. However, in our study no difference was found in the sodium and potassium contents of the colostrum of women below or above the age of 25 years.

According to our findings, maternal age, infant birth weight and maternal body weight do not affect the sodium and potassium content of colostrum.

REFERENCES

1. Anderson GH. Human milk feeding. *Pediatr Clin North Am* 32:335, 1985.
2. De Filippi JP, Kaanders H, Hofman A. Sodium in diet and milk of breast-feeding women. *Acta Paediatr Scand* 70:417, 1981.
3. Atkinson SA, Radde IC, Chance GW, et al. Macro-mineral content of milk obtained during early lactation from mothers of premature infant. *Early Hum Dev* 4:5, 1980.
4. Anderson GH. The effect of prematurity on milk composition and its physiological basis. *Fed Proc* 43:2438, 1984.
5. Gross SJ, David RJ, Bauman L, Tomarelli RM. Nutritional composition of milk produced by mothers delivering preterm. *J Pediatr* 96:641, 1980.
6. Lemons JA, Moye L, Hall D. Simmons M. Differences in the composition of preterm and term human milk during early lactation. *Pediatr Res* 16:113, 1982.
7. Gross SJ. Growth and biochemical response of preterm infants fed human milk or modified infant formula. *N Engl J Med* 308:237, 1983.
8. Anderson GH, Atkinson SA, Bryan MH. Energy and macronutrient content of human milk during early lactation from mothers giving birth prematurely and at term. *Am J Clin Nutr* 34:258, 1981.
9. Chessex P, Reichman B, Verellen G, et al. Quality of growth in premature infants fed their own mothers' milk. *J Pediatr* 102:107, 1983.
10. Atkinson SA, Radde IC, Anderson GH. Macromineral balances in premature infants fed their own mothers' milk or formula. *J Pediatr* 102:99, 1983.
11. Anderson GH, Bryan MH. Is the premature infant's own mother's milk best? *J Pediatr Gastroenterol Nutr* 1:157, 1982.
12. Keenan BS, Buzek SW, Garza C, et al. Diurnal and longitudinal variations in human milk sodium and potassium: implication for nutrition and physiology. *Am J Clin Nutr* 35:527, 1982.
13. Lönnerdal B. Effects of maternal dietary intake on human milk composition. *J Nutr* 116:499, 1986.
14. Asnes RS, Wisotsky DH, Migel PF, et al. The dietary chloride deficiency syndrome occurring in a breast-fed infant. *J Pediatr* 100:923, 1982.
15. Neville MC, Keller RP, Seacat J, et al. Studies on human lactation. I. Within-feed and between-breast variation in selected components of human milk. *Am J Clin Nutr* 40:635, 1984.
16. Lipsman S, Dewey KG, Lönnerdal B. Breast-feeding among teenage mothers: milk composition, infant growth, and maternal dietary intake. *J Pediatr Gastroenterol Nutr* 4:426, 1985.

The Turkish Journal of Pediatrics 33:235-243, 1991

DIURETIC RENOGRAPHY IN CHILDREN: A NON-INVASIVE METHOD FOR THE ASSESSMENT OF UPPER URINARY TRACT PATHOLOGIES*

*Hatice Durak MD***, İrem Bernay MD***, Günaydın Erbengi MD**** Nergis Ulutuncel BS*****

SUMMARY: Durak H, Bernay İ, Erbengi G, Ulutuncel N. (Department of Nuclear Medicine, Hacettepe University Faculty of Medicine, Ankara, Turkey). Diuretic renography in children: a non-invasive method for the assessment of upper urinary tract pathologies. Turk J Pediatr 33: 235-243, 1991.

Thirty-eight kidneys from 20 children were studied with diuretic renography and the findings in 32 kidneys were compared with the results obtained using IVP. The diuretic renography findings were consistent with those of the IVP in 72 percent of the patients. The main disparity was the dilated nonobstructed pattern observed in the kidneys with normal IVP's, which is pointed out as being an asset of diuretic renography in revealing the functional status of kidneys.

The sensitivity in detecting true obstruction was found to be 67 percent (4/6), and the specificity 95 percent (20/21). The accuracy of the technique was 85 percent with a false (+) rate of 5 percent (1/21) and false (−) rate of 33 percent (2/6).

Diuretic renography is a simple, safe, non-invasive technique, easily applied to children with high specificity in excluding obstruction in a dilated renal pelvis. *Key words: radioisotope renography, radionuclide imaging.*

Retention of either tracer or contrast material within a renal pelvis is a common finding in the practice of pediatric radiology and nuclear medicine[1]. The diagnosis of obstruction as the cause of this type of retention is important because surgical intervention in obstructive hydronephrosis will spare renal function, whereas, a nonobstructed dilated collecting system does not require surgery[2].

Diuretic renography was first described by O'Reilly et al[3] in 1978, and subsequent reports confirmed its value as a useful technique in the assessment of dilated upper urinary tract to distinguish between true obstruction and nonobstructive dilatation[2,4-9]. Diuretic renography is a simple, safe, non-invasive technique, easily applied to children.

In the present study, diuretic renography was applied to 20 children with various urinary symptoms and the results were compared with intravenous pyelography (IVP).

* From the Department of Nuclear Medicine, Hacettepe University Faculty of Medicine, Ankara.

** Specialist in Nuclear Medicine, 9 Eylül University, İzmir.

*** Assistant Professor of Nuclear Medicine, 19 Mayıs University, Samsun.

**** Professor of Nuclear Medicine, Hacettepe University Faculty of Medicine.

***** Physics Engineer, Hacettepe University Faculty of Medicine.

Material and Methods

In this study thirty-eight kidneys from 20 children were investigated. Renograms were performed with ^{99m}Tc DTPA using an intravenous (i.v.) dose of 6 m Ci/1.7m^2. The patients were observed from the posterior view in the supine position with a Toshiba GCL-501 gamma camera and associated computer. All children were normally hydrated. Furosemide in a dose of 0.5 mg/kg was administered intravenously approximately 20 minutes after the radiopharmaceutical was injected. Observation resumed about 20 minutes after administration of the diuretic.

After data collection was complete, each kidney was analyzed by the computer. The kidney regions of interest including the pelvis and a background area adjacent to each kidney were drawn and background corrected time-activity curves were generated for each kidney. Split renal function estimates were derived from the one minute interval between the 80th and the 140th second of the curve. The shape of the time activity curve and the pattern of response to the diuretic were evaluated as described by O'Reilly et al[3] as:

Group I response : Normal renogram (Fig. 1).

Group II response : No excretion even after furosemide (obstructive pattern) (Fig. 2).

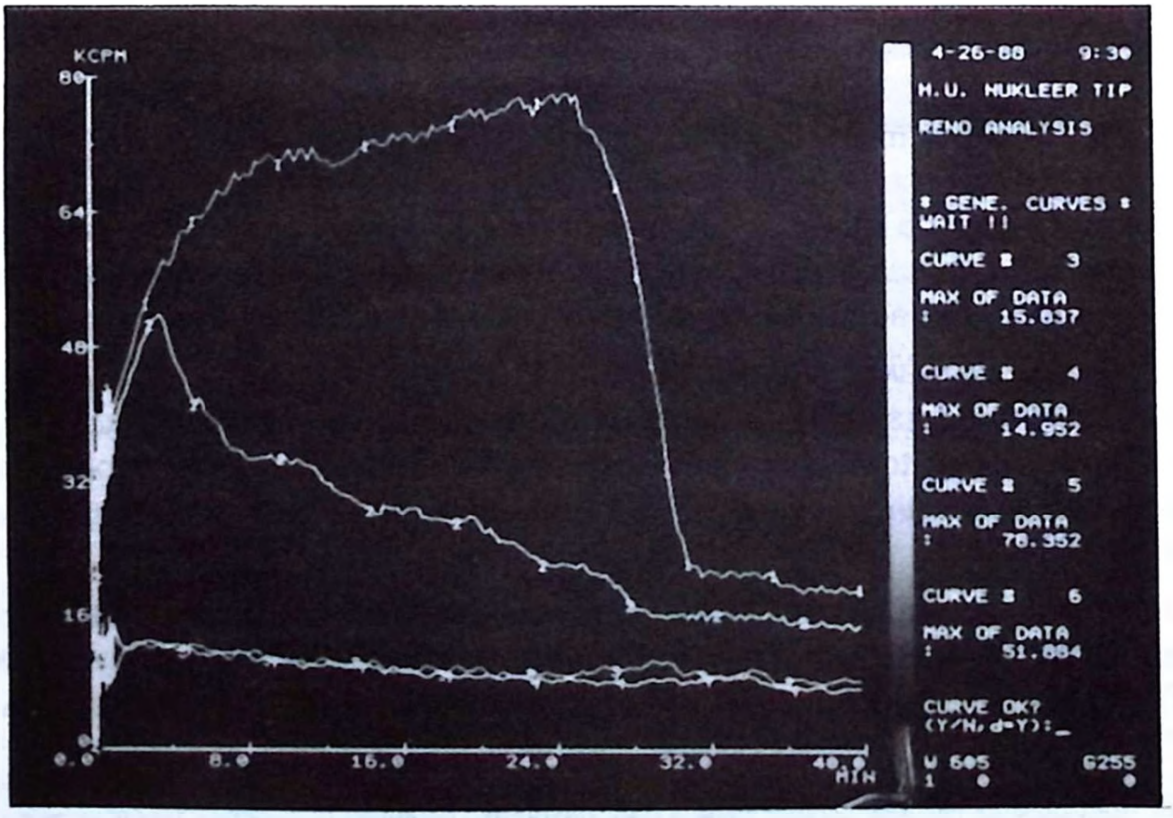

Fig. 1: Curve 2 is a normal renogram curve (Group I). Curve I reveals the dilated nonobstructive pattern of response with a rapid excretion after the diuretic administered at 20 min (Group IIIa).

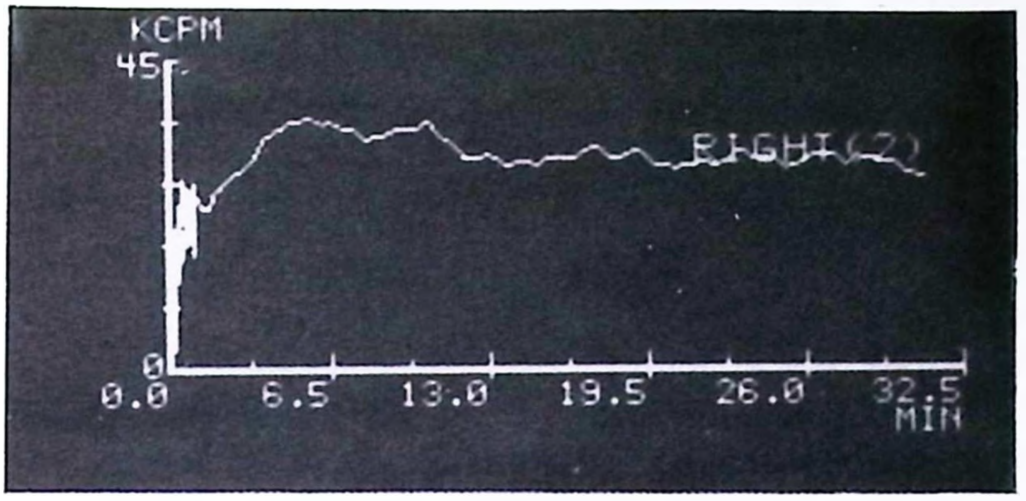

Fig. 2: Obstructive curve pattern with no response to the diuretic administered at 20 min (Group II).

Group III response : *IIIa* : Rapid excretion after furosemide (dilated nonobstructive pattern) (Fig. 1).

IIIb : Partial improvement after furosemide (equivocal) (Fig. 3).

Group IIIb which was accepted as a dilated nonobstructive pattern is discussed. Impairment of renal function is accepted as being less than 40 percent of relative function[9].

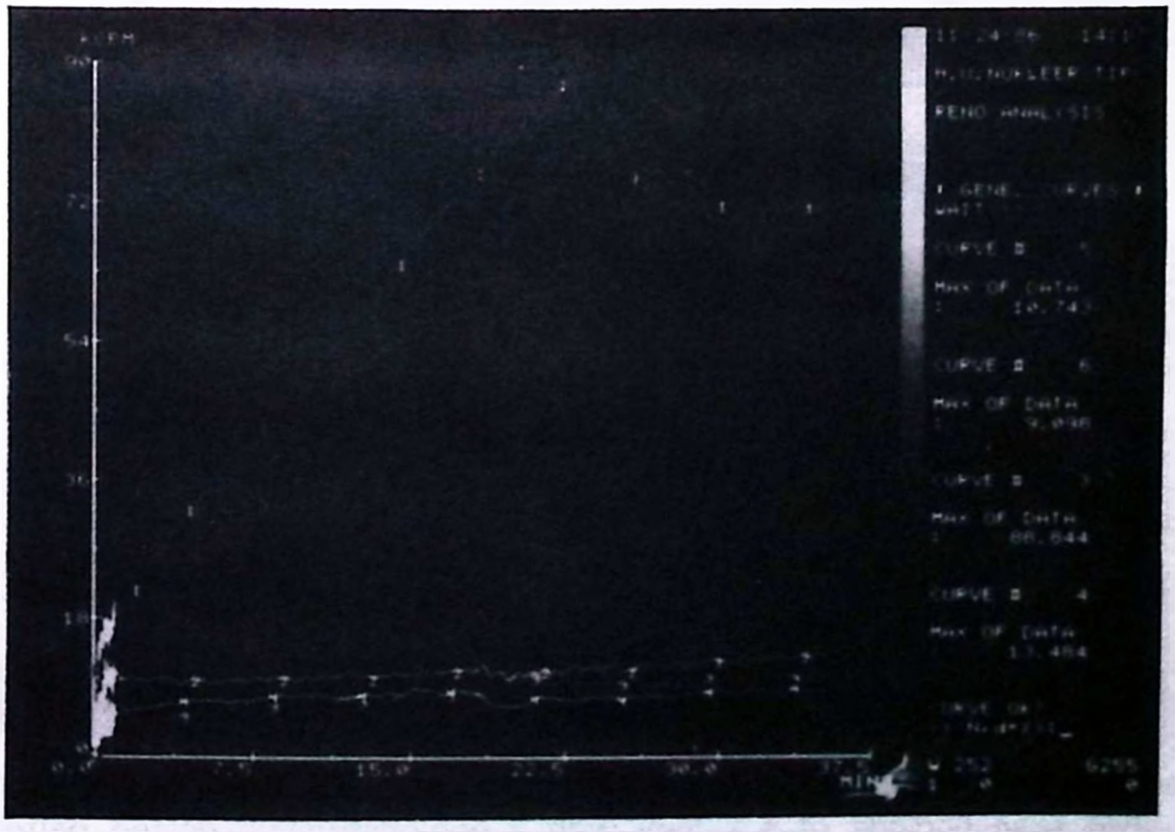

Fig. 3: Curve 1 reveals the IIIb response with partial improvement after the diuretic administered at 20 min.

Results

Diuretic renography was performed on 20 children with various urinary tract symptoms regardless of the presence of any suspected obstructions. Clinical diagnoses of the patients are summarized in Table I. Of the 38 individual kidneys examined, 32 kidneys had comparable IVP's. Ultrasonography was performed in ten patients but the results were not compared with those obtained from diuretic renography because of the small number of patients studied. There were eleven girls and nine boys, ranging in age from 4.5 months to 12 years (average five years) with six patients ≤ one year of age and 12 patients ≤ five years of age.

Diuretic Renography Results : Ten kidneys were in Group I, seven kidneys in Group II, nine kidneys in Group IIIa, and five kidneys in Group IIIb. Seven kidneys were evaluated as nonfunctioning according to split renal function estimates (Table II).

TABLE I: Clinical Diagnoses of the Patients

Clinical Diagnoses	Number of Patients
Hydronephrosis	7
Genitourinary system abnormality	5
Pelvic dilatation after pyeloplasty	3
Malignancy	2
VUR with atrophy	2
Hemolytic uremic syndrome	1
Total	**20**

TABLE II: Number of Kidneys in Groups I, II, IIIa, IIIb and Non-functioning Kidneys Demonstrated by Diuretic Renography

Group	Number of Patients
I	10
II	7
IIIa	9
IIIb	5
Non-functioning	7
Total	**38**

Scan findings of a kidney with an obstructive response (Group II) are shown in Fig. 4, while scan findings of a kidney with a non-obstructive dilated pattern of response (Group IIIa) are illustrated in Fig. 5.

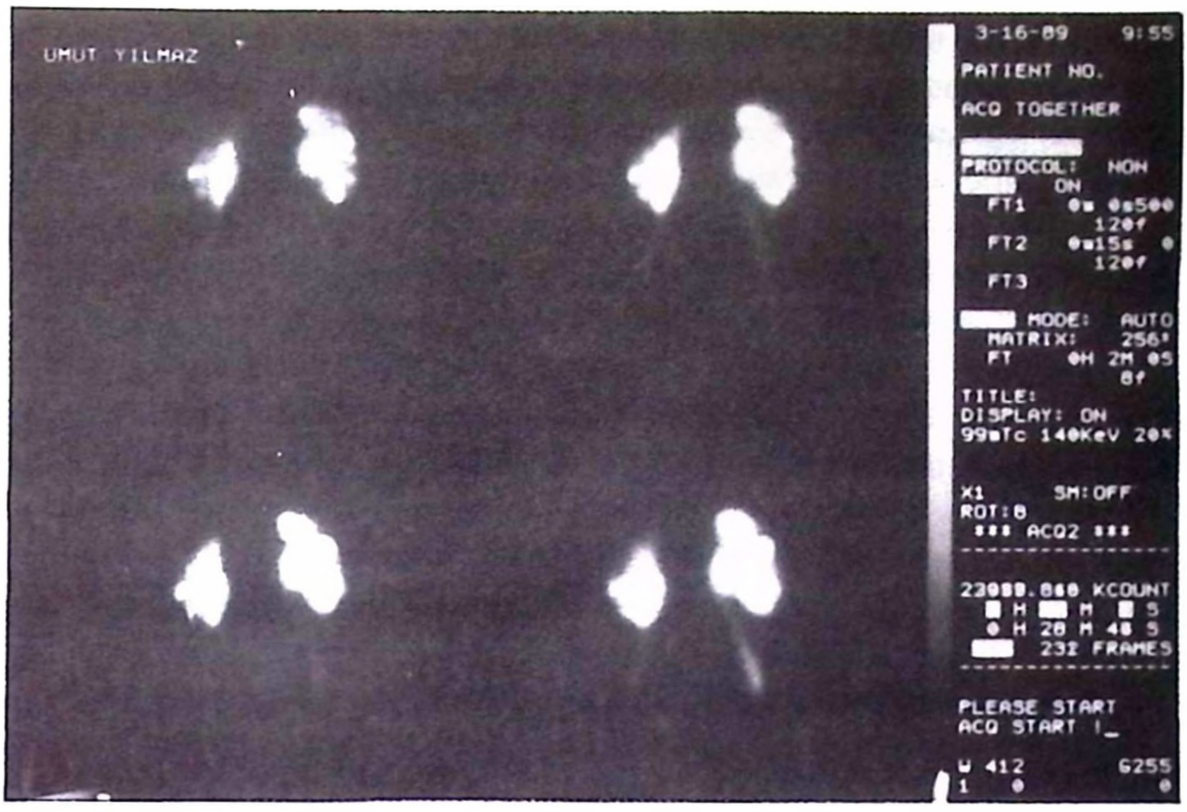

Fig. 4: Scan findings of an obstructive kidney. Upper left: 15 min., upper right: 20 min., lower left: 25 min. and lower right 30 min. image after the administration of radiopharmaceutical. Diuretic was given at 20 min. There is no washout observed from the pelvis after the administration of the diuretic.

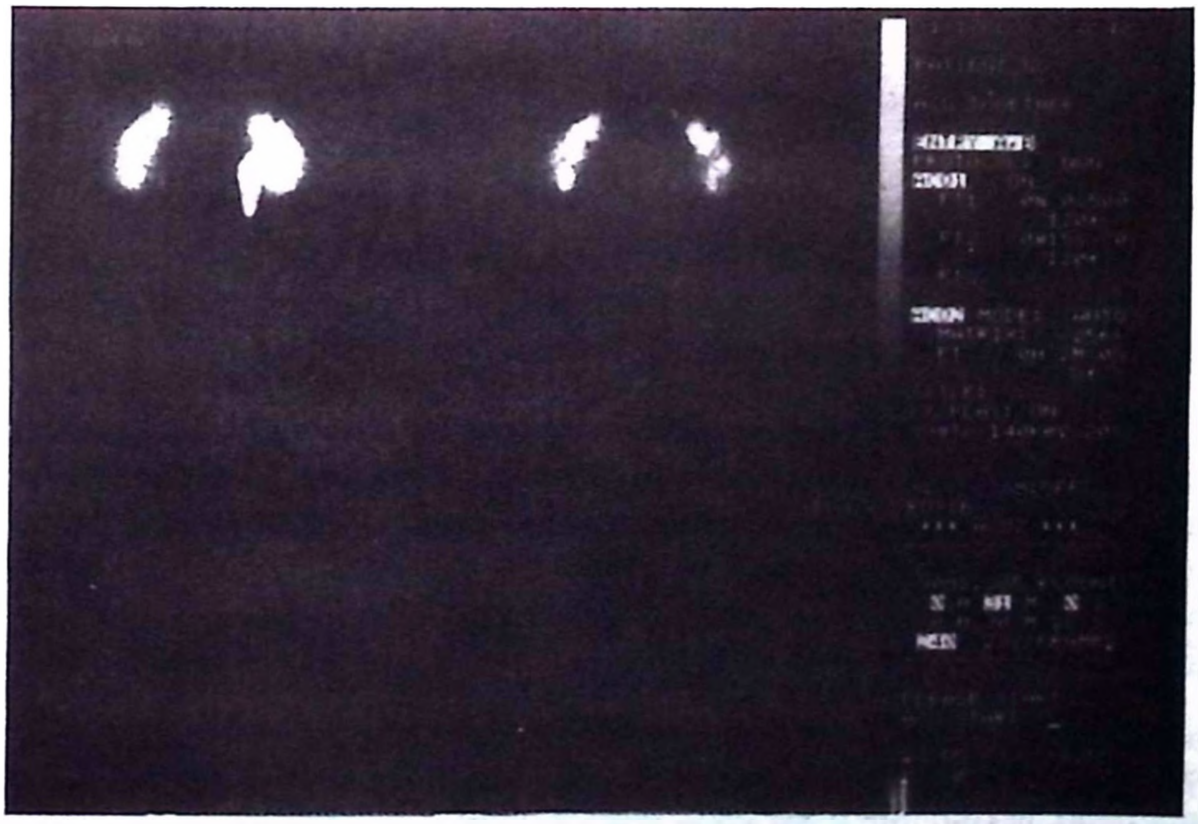

Fig. 5: Scan findings of a dilated nonobstructive kidney. Upper left: 15 min., upper right: 20 min., lower left: 25 min. and lower right 30 min. image after the administration of the radiopharmaceutical. Diuretic was given at 20 min. Washout from the pelvis is obvious after the administration of the diuretic.

The findings on the diuretic renograms were consistent with those obtained from the IVPs of 23 kidneys (72%) but differed in nine (28%). In seven kidneys, the disparity consisted of dilated nonobstructed renogram patterns observed on the normal IVPs. One kidney, which was evaluated as nonfunctioning by diuretic renography, was visualized by IVP, and seemed obstructed while one kidney, evaluated as normal by IVP, had normal excretion but a diminished renogram curve, suggesting hypofunction (Table III).

TABLE III: Diuretic Renography Findings Compared With IVP Findings of Patients

	Diuretic Renography					
IVP	I	II	IIIa	IIIb	Non-function	Total
Normal	7		5	2		14
Hydronephrosis		1	2	1		4
Ureteral ectasia	2		1			3
Obstructive (U-P)		3				3
No excretion		1		1	1	3
Calyceal clubbing	1					1
Non-functioning					4	4
Total	10	5	8	4	5	32

The diagnosis of obstruction or nonobstructive dilatation was confirmed by either surgery or clinical follow-up in 27 kidneys and, therefore, only these kidneys are included in sensitivity and specificity calculations.

The sensitivity of detecting true obstruction was 67 percent (4/6), specificity 95 percent (20/21), with a false (+) rate of 5 percent (1/21) and a false (−) rate of 33 percent (2/6). Two kidneys with confirmed obstruction were not visualized by diuretic renography and were interpreted as nonfunctioning. Thus 2/6 (33%) should be considered an indeterminate rate rather than a false (−) rate. The test was 89 percent accurate (24/27).

Group IIIb : There were five kidneys under study in Group IIIb. In two kidneys, the contralateral kidney had a ureteropelvic (U-P) obstruction. One kidney was part of a horseshoe kidney while the other had a U-P obstruction confirmed by surgery. The other two, were the kidneys of the same patient, one of which had a prior pyelolithotomy, and the other a second pyeloplasty for U-P obstruction.

Discussion

A diuretic renogram has two components: the histogram and the scan. The histogram is a time activity curve which graphically reveals the accumulation and washout of the radioisotope before and after the administration of furosemide. In the case of true obstruction, the radioactive tracer fails to washout after injection of furosemide and that occurrence is mainly determined from the histogram. The scan provides serial images which reveal the anatomic localization of the obstruction or the dilatation. The dose of radiation absorbed is considerably lower than that used in the IVP. The kidney receives 20 mrad/mCi, the whole body 6 mrad/mCi and the ovaries 4 mrad/mCi. The bladder is the critical organ, receiving 490 mrad/mCi[10]. In a standard study, it was reported that the IVP delivers 1200 mrads to the ovaries and 220 mrads to the bone marrow[11].

Diuretic renography may be used in evaluating ureteropelvic (U-P) junction obstruction[5], megaureter[5,7], urinary diversion (stomal stenosis), ureteroneocystostomy, Prune Belly syndrome, ureteral valves, ureteral injury (excluding obstruction in renal transplant rejection[5]) and in persistent dilatation after surgery[2,7].

Counts from an overdistended bladder may interfere with the counts from the lower urinary tract and pelvic kidneys. Bladder pressure can also be trasmitted to the renal pelvis even without reflux[3]. In high grade vesicoureteral reflux (VUR), radioactive urine from the bladder refluxes back to the pelvis, simulating an obstruction[5].

A poorly functioning kidney also simulates an obstructive pattern by not being able to respond to the diuretic[5,7,9,12].

In severe hydronephrosis, the collecting system becomes too large, so an increase in the flow of urine may not be able to overcome the "mixing chamber effect" described as the slow turnover of the radiolabeled urine in a large volume. This may result in insufficient emptying of the renal pelvis, simulating obstruction[2,7,9].

The only false (+) interpretation in our study was a poorly functioning kidney (19% of total function) with a fourth grade VUR. Two false (−) interpretations were very poorly functioning kidneys which were not visualized by diuretic renography.

Shore et al[2] and Senac et al[7] reported the sensitivity for detecting obstruction as 83 percent and the specificity as 94 and 86 percent, respectively. According to Senac and associates, the accuracy of the test was 85 percent. We found the degree of sensitivity to be less than that reported in the literature. The reason for our result was that two kidneys in the study had not been visualized during diuretic renography, however, during surgery they were found to be obstructed.

Disparity with IVP : In seven kidneys with normal IVP's, five kidneys had a Group IIIa and two kidneys had a Group IIIb response to the diuretic.

Healthy kidneys share the excretion of water and solutes equally in proportion to the renal mass and function. In the case of a unilateral obstruction, water and electrolyte excretion shifts to the unaffected kidney, increasing the water flow through it[13]. Every tract has its own individual maximum flow rate potential and may fail to compensate at higher flow rates[14]. Thus, we can speculate that it may even be difficult for a normally functioning kidney to handle total water and electrolyte excretion, resulting in delayed pelvic clearance and pelvic dilatation in the long run. Diuretic injection may overcome this problem by further elevating the pressure[14]. This type of loading of a kidney may be detected by diuretic renography before any significant anatomical changes occur, which may explain the disparity with IVP.

In some cases, the lesser affected kidney may have a masked obstruction in which the pressure rise may overcome the obstruction, demonstrating a Group IIIa or IIIb response[13]. Koff et al[5] accepted both Group IIIa and Group IIIb responses as a dilated nonobstructed pattern and found that only one child with a Group IIIb response had an obstruction. According to Koff's data, Groups IIIa and IIIb are both accepted as dilated nonobstructive patterns in this study, but, as mentioned above, a masked obstruction cannot be ruled out and the patients should be followed.

There is no one set method for diagnosing obstructions[9,10]. Direct renal perfusion studies, IVP, and parenchymal mean transit times are often used. Diuretic renography is a highly sensitive non-invasive technique which does not require urinary tract instrumentation and provides information about the functional status of kidneys.

We conclude that diuretic renography is highly specific for nonobstructed kidneys, however, poorly functioning obstructed kidneys can lower the sensitivity of the technique.

Acknowledgement

We would like to express our sincere thanks to our colleagues in the Departments of Urology, Pediatric Surgery and Nephrology at the Hacettepe University Faculty of Medicine for their help in providing the patients for this study.

REFERENCES

1. Sty JR, Starshak RJ, Miller JH. *Pediatric Nuclear Medicine.* Norwalk: Appleton-Century-Crofts, 1983, pp 171-172.
2. Shore RM, Uehling DT, Bruskewitz R, Polcyn RE. Evaluation of obstructive uropathy with diuretic renography. *Am J Dis Child* 137:236, 1983.
3. O'Reilly PH, Testa HJ, Lawson RS, et al. Diuresis renography in equivocal urinary tract obstruction. *Br J Urol* 50:76, 1978.

4. Koff SA, Thrall JH, Keyes JW Jr. Assessment of hydroureteronephrosis in children using diuretic radionuclide urography. *J Urol* 123:531, 1980.
5. Koff SA, Thrall JH, Keyes JW Jr. Diuretic radionuclide urography: a non-invasive method for evaluating nephroureteral dilatation. *J Urol* 122:451, 1979.
6. English PJ, Testa HJ, Gosling JA, Cohen SJ. Idiopathic hydronephrosis in childhood-a comparison between diuresis renography and upper urinary tract morphology. *Br J Urol* 54:603, 1982.
7. Senac MO Jr, Miller JH, Stanley P. Evaluation of obstructive uropathy in children: radionuclide renography vs. the Whitaker test. *A J R* 143:11, 1984.
8. Whitfield HN, Britton KE, Hendry WF, et al. The distinction between obstructive uropathy and nephropathy by radioisotope transit times. *Br J Urol* 50:433, 1978.
9. Neal DE, Simpson W, Bartholomew P, Keavey PM. Comparison of dynamic computed tomography, diuresis renography and DTPA parenchymal transit time in the assessment of dilatation of the upper urinary tract. *Br J Urol* 57:515, 1985.
10. Merrick MV. *Essentials of Nuclear Medicine.* New York: Churchill Livingstone, 1984, pp 109.
11. Putman CE, Ravin CE. *Textbook of Diagnostic Imaging,* Vol. 1. Philadelphia: WB Saunders, 1988, pp 101.
12. O'Reilly PH, Testa HJ, Lawson RS, et al. Diuresis renography in equivocal urinary tract obstruction. *Br J Urol* 56:84, 1984.
13. Blue PW, Manier SM, Ghaed N. Masked obstruction of the renal collecting system. *Clin Nucl Med* 12:497, 1987.
14. O'Reilly PH. Current status of diuretic renography. In Freeman LM, Weissmann HS (eds). *Nuclear Medicine Annual* 1987, New York: Raven, 1987 pp 173-192.

The Turkish Journal of Pediatrics 33:245-246, 1991

HYDATID DISEASE PRESENTING AS AN INTRASCROTAL MASS IN A CHILD*

*Fatih Kızılcan MD***, F. Cahit Tanyel MD***, Nebil Büyükpamukçu MD**** Akgün Hiçsönmez MD****

SUMMARY: Kızılcan F, Tanyel FC, Büyükpamukçu N, Hiçsönmez A. (Department of Pediatric Surgery, Hacettepe University Faculty of Medicine, Ankara, Turkey). Hydatid disease presenting as an intrascrotal mass in a child. Turk J Pediatr 33: 245-246, 1991.

A thirteen-year-old boy with the preliminary diagnosis of hydrocele of the cord who underwent surgery is presented. Ultimate diagnosis of hydatid disease was established by surgical exploration and histopathologic examination of the specimen. Although it is a rare occurrence, hydatid disease should be considered as a diagnostic possibility in endemic areas. *Key words: echinococcus cysts, scrotal swelling.*

Scrotal swelling is one of the common causes of hospital admissions among children. Although many conditions are encountered in its etiology, scrotal swelling resulting from hydatid disease is not reported in children[1,2].

Hydatid disease presenting as a scrotal mass is described to call attention to this unreported etiologic possibility among children in endemic areas.

Case Report

A thirteen-year-old boy was hospitalized because of a painless scrotal mass which was first noted four days prior to admission. Past history was noncontributory. Physical examination revealed a painless, cystic, transilluminable mass measuring 4 × 4 cm and located in the left hemiscrotum, proximal to the testis. There were no other pathological findings. A complete blood count, urinalysis and chest roentgenogram were normal. The patient underwent surgical intervention with the initial diagnosis of hydrocele of the cord.

The mass was found to be located intravaginally during surgical exploration carried out through the left inguinal incision. The capsula was ruptured during dissection of the cystic mass. Following the drainage of clear fluid, the appearance of the germinative membrane through the rupture clarified the etiology to be hydatid disease (Fig. 1).

* From the Department of Pediatric Surgery, Hacettepe University Faculty of Medicine, Ankara.
** Resident in Pediatric Surgery, Hacettepe University Faculty of Medicine.
*** Associate Professor of Pediatric Surgery, Hacettepe University Faculty of Medicine.
**** Professor of Pediatric Surgery, Hacettepe University Faculty of Medicine.

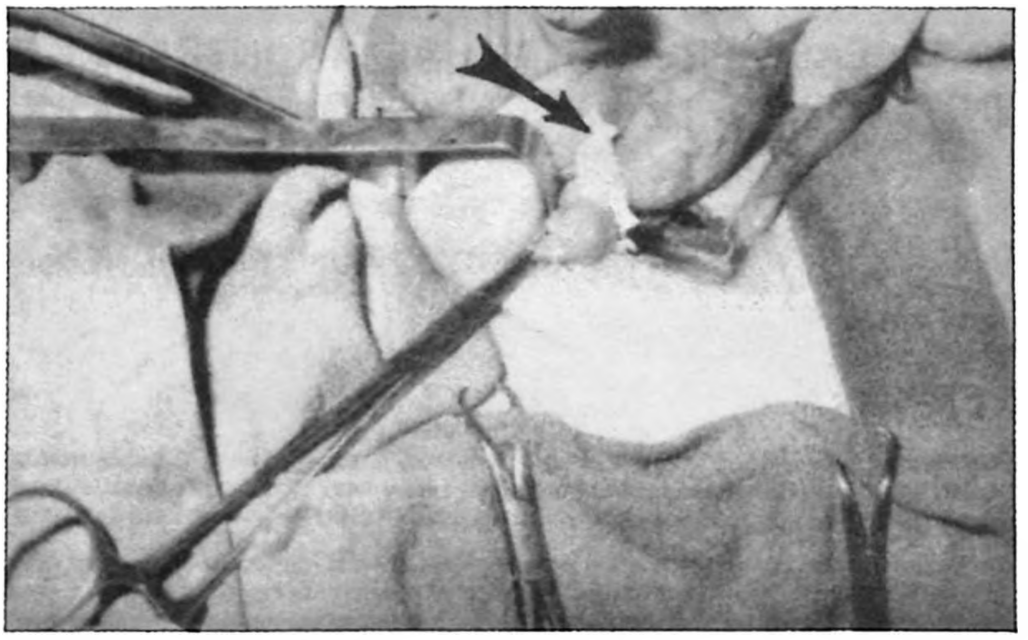

Fig. 1: Protrusion of the germinative membrane (arrow).

Further investigation using ultrasonography disclosed an additional hydatid cyst located in the left lobe of the liver. The patient will undergo further surgery for hepatic involvement after the completion of a course of mebendazole treatment.

Discussion

Hydatid disease is also a common cause of hospitalization in endemic areas[3]. The cysts are commonly located in the liver, lung and brain. In addition to these sites, many rare locations such as thyroid and salivary glands and retroperitoneum have been reported[4,5]. The scrotum is a rather uncommon site, with only one adult patient being reported[6].

Even though the scrotum is a rare site for hydatid disease, it should neverthless be taken into consideration in the etiology of scrotal swelling of children in endemic areas.

REFERENCES

1. Klauber GT, Sant GR. Disorders of the male external genitalia. In Kelalis PP, King LR, Belman AB (eds). *Clinical Pediatric Urology*. Philadelphia: WB Saunders, 1985, pp 825-863.
2. Paola AS, Khan SA. Clinical evaluation of scrotal masses: an overview. *Hosp Pract* 24:255, 1989.
3. Hiçsönmez A. Hydatid cysts in childhood: analysis of 208 cases. *Prog Pediatr Surg* 15:87, 1980.
4. Ceyhan M, Büyükpamukçu N. Obstructive jaundice due to hydatid cyst in a rare location. *Turk J Pediatr* 27:177, 1985.
5. Gürses N, Baysal K, Gürses N. Hydatid cyst in the thyroid and submandibular salivary glands in a child. *Z Kinderchir* 41:362, 1986.
6. Halim A, Vaezzadeh K. Hydatid disease of the genitourinary tract. *Br J Urol* 52:75, 1980.

The Turkish Journal of Pediatrics 33:247-252, 1991

OCULOCEREBRAL HYPOPIGMENTATION SYNDROME (CROSS SYNDROME)*

*Hasan Özkan MD***, Erbil Ünsal MD**, Galip Köse MD****

SUMMARY: Özkan H, Ünsal E, Köse G. (Department of Pediatrics, Dokuz Eylül University Faculty of Medicine, İzmir, Turkey). Oculocerebral hypopigmentation syndrome (Cross syndrome). Turk J Pediatr 33: 247-252, 1991.

A typical case of Cross syndrome with hypopigmentation, mental and psychomotor retardation, spasticity, bilateral optic atrophy and dental defects in a three-year-old boy is presented. The clinical features of this rare syndrome are discussed. *Key words: Cross syndrome, albinism.*

The oculocerebral hypopigmentation syndrome, also known as Cross syndrome, is an extremely rare form of albinism which is associated with mental retardation, spasticity, athetoid movements, and ocular and stomatologic anomalies[1]. It appears to be transmitted as an autosomal recessive trait.

This report presents a three-year-old child affected with ocular, stomatologic and neurologic disturbances including hypopigmentation.

Case Report

A three-year-old boy was admitted to our department with failure-to-thrive. The child was the product of a third-degree consanguineous marriage. The father aged 27, and the mother, aged 22, are healthy, and normally pigmented. The patient's one-year-old sister, who was blonde with blue eyes and white skin, evidenced hypopigmentation. She was mentally retarded and both her upper and lower extremities were spastic. Her head remained in a hyperextended position and she had a weak, high-pitched cry.

The patient, who was born in a hospital evidenced cyanosis of the extremities during the first five-ten minutes postnatally. He did not cry for a while. After receiving oxygen he returned to normal. At 11 months of age, he was first admitted to a university hospital because of failure-to-thrive, and his delayed psychomotor development was first recorded there. He was then reportedly unable to sit unaided. Physical examination (Figs. 1, 2) revealed a weight of 7850 g (below the third percentile), a height of 92 cm (between 10th-25th percentiles) and a head circumference of 45 cm (below the third percentile). There was

* From the Department of Pediatrics, Dokuz Eylül University Faculty of Medicine, İzmir.

** Resident in Pediatrics, Dokuz Eylül University Faculty of Medicine.

*** Professor of Pediatrics, Dokuz Eylül University, Faculty of Medicine.

Fig. 1: A three-year-old boy exhibiting oculocerebral hypopigmentation syndrome (Cross syndrome).

Fig. 2: Cross syndrome in a three-year-old male child.

significant hypopigmentation, the hair was extremely blond, the skin was white, and the eyes were light blue. He was severely retarded. Interaction with the environment was poor and undifferentiated. He was able to sit unaided, but was unable to stand up or walk. He was generally hypertonic. The deep tendon reflexes were symmetrically normal. Stomatologic examination revealed widely spaced discolored teeth. He also had gingival hypertrophy and grinding and rumination movements. The ophthalmologic examination revealed bilateral optic atrophy. Routine laboratory tests were normal including blood cell counts, blood electrolytes, urea and glucose. Plasma and urinary amino acid chromatography, serum iron and iron binding capacity, copper, ceruloplasmin, magnesium and thyroid function tests were within normal limits. Screening for intrauterine-acquired infections such as toxoplasmosis, rubella, cytomegalovirus and syphilis were negative. Although the bones were normal structurally, skeletal X-ray examination demonstrated a bone age of six months. The computerized tomographic scan of the brain showed calcification in the basal ganglia (Fig. 3).

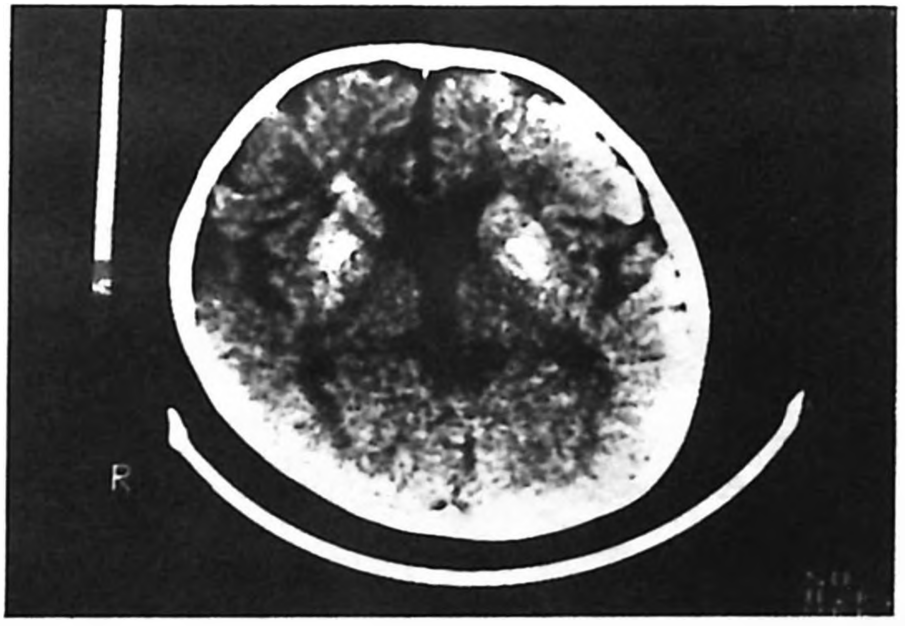

Fig. 3: A computerized tomographic scan of the brain revealing calcification in the basal ganglia.

Biopsy of the sural nerve showed no metachromatic substances. A skin biopsy was performed in order to confirm the clinical diagnosis of oculocutaneous albinism. There was amelanosis in the epidermis as seen by hematoxylin-eosin and Fontana staining (Fig. 4). The biopsy material stained with a tyrosinase stain, was positive (Figs. 5, 6).

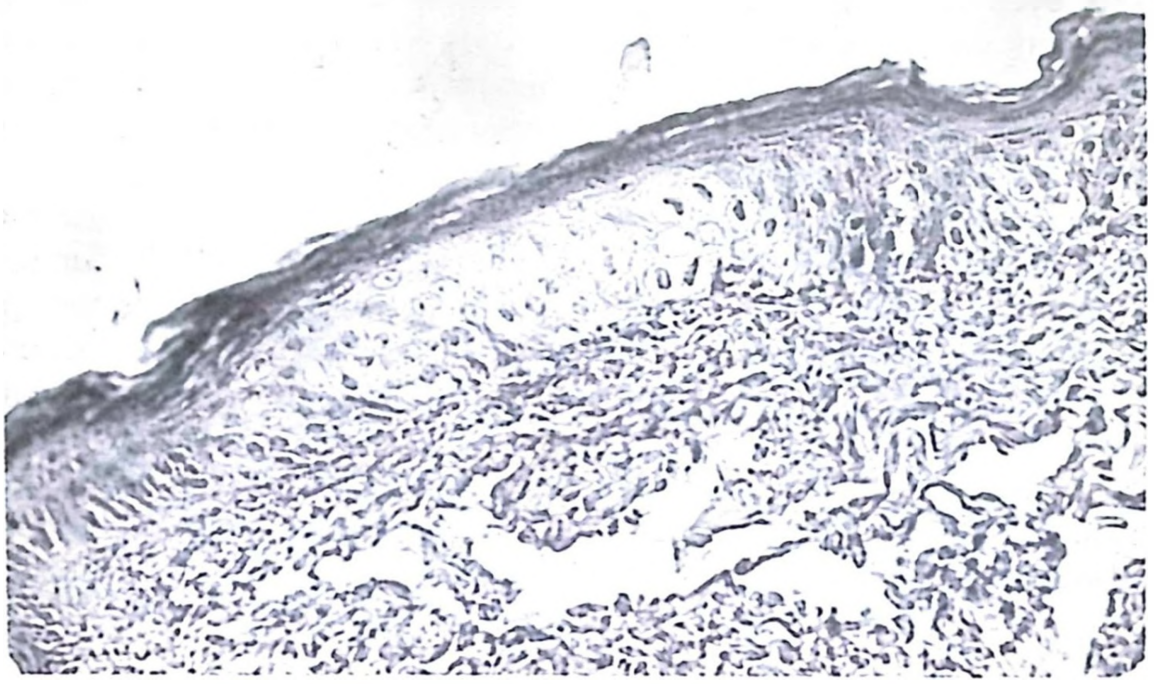

Fig. 4: Hematoxylin-eosin and Fontana staining illustrating amelanosis in the epidermis.

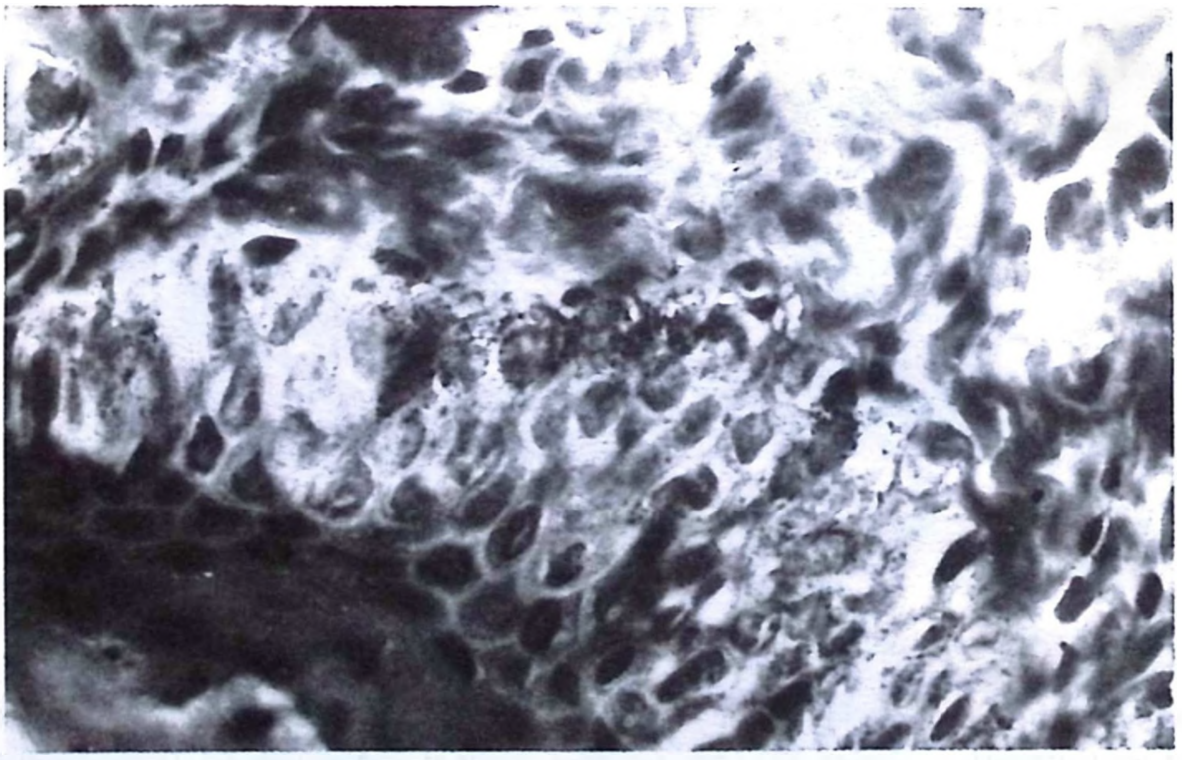

Fig. 5: The biopsy material stained with a tyrosinase stain yielding positive results.

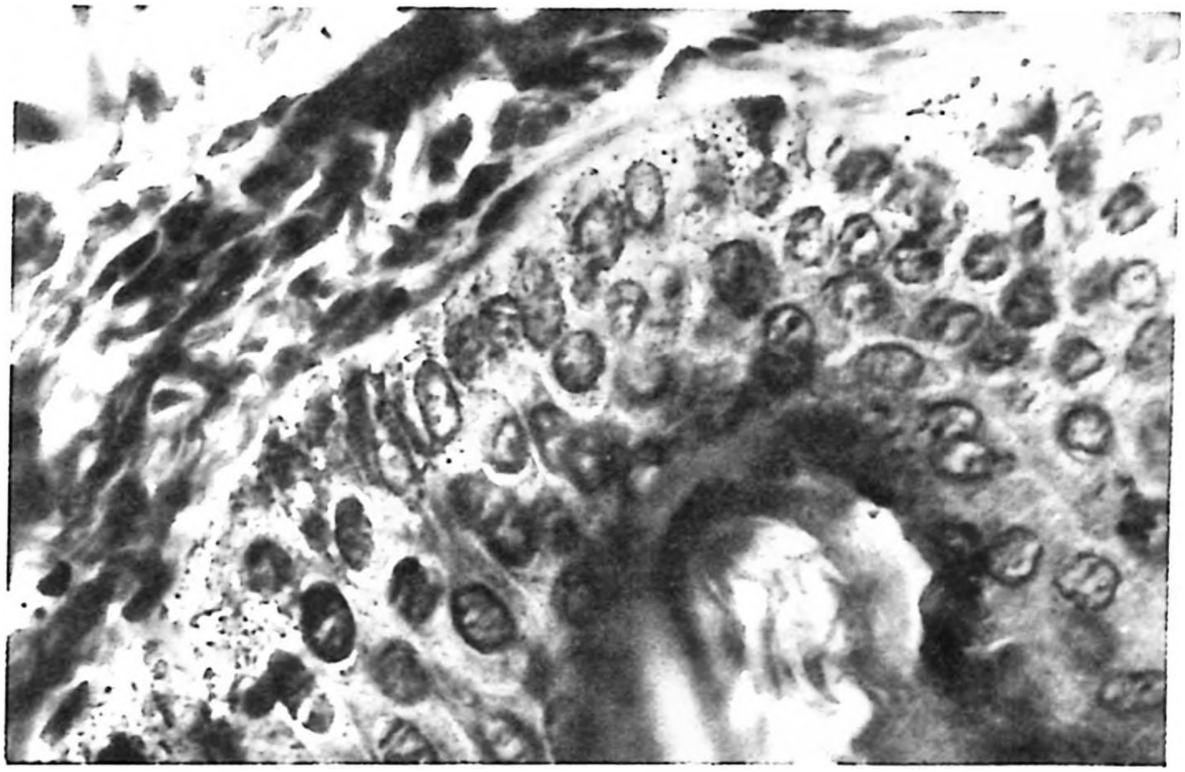

Fig. 6: Tyrosinase staining used on biopsy material yielding a positive result.

Discussion

The patient's findings including motor and mental retardation, significant hypopigmentation of the eyes and skin, bilateral optic atrophy, neurologic abnormalities such as spasticity, widely spaced and discolored teeth and gingival hypertrophy suggested the oculocerebral hypopigmentation syndrome. This very rare syndrome was first reported in three siblings in an Amish family in Ohio[1]. Later, several cases were reported from Germany, Italy, Great Britain and Belgium[2,3]. The clinical features observed in our patient were similar to those seen in nine previously reported cases[1-3]. All the patients presented with hypopigmentation, severe psychomotor retardation and neurologic and ocular disturbances. In addition, dental anomalies and consanguinity were present, as in the cases reported from Ohio, Italy and Belgium[1-3]. Computerized tomographic scan of the brain of our patient showed basal ganglia calcification in a pattern similar to that seen in hypoparathyroidism, pseudohypoparathyroidism (Albright's syndrome), familial calcification of the basal ganglia, Fahr's syndrome, Cockayne's syndrome, lead and carbon monoxide poisoning, and irradiation with methotrexate therapy[5]. We excluded such etiologies of basal ganglia calcification because of past history, physical examination and laboratory results. Tyrosinase staining of the skin biopsy revealed enzyme activity. This feature of pigment disorder resembles that found in patients with Cross syndrome[1-4]. Therefore, albinism

associated with neurologic, ocular and dental defects strongly supports the diagnosis of Cross syndrome in our patient.

REFERENCES

1. Cross HE, McKusick VA, Breen W. A new oculocerebral syndrome with hypopigmentation. *J Pediatr* 70:398, 1967.
2. Courtens W, Broeckx W, Ledoux M, Vamosa E. Oculocerebral hypopigmentation syndrome (Cross syndrome) in a Gipsy child. *Acta Paediatr Scand* 78:806, 1989.
3. Fryns JP, Dereymaeker AM, Heremans G, et al. Oculocerebral syndrome with hypopigmentation (Cross syndrome). Report of two siblings born to consanguineous parents. *Clin Genet* 34:81, 1988.
4. Goodman RM. Pigmentation of the skin and disorders of melanin metabolism. *Clin Dermatol* 3:265, 1985.
5. Sutton D. *Textbook of Radiology and Medical Imaging.* Edinburgh: Churchill Livingstone, 1987, p 1469.

The Turkish Journal of Pediatrics 33:253-266, 1991

FAILURE TO BREATHE AT BIRTH: CAUSES AND ASSESSMENT*

*NR Clifford Roberton MA, MB, FRCP***

SUMMARY: Roberton NRC. (Rosie Maternity Hospital, Cambridge, United Kingdom). Failure to breathe at birth: causes and assessment. Turk J Pediatr 33: 253-266, 1991.

A frequent misconception is that delayed onset of respiration is the result of intrapartum asphyxia. However, many factors other than asphyxia can delay the onset of respiration after delivery. To understand the effect of asphyxia on both the fetus and the neonate, and in particular in delaying the onset of spontaneous respiration, it is convenient to consider chronic partial asphyxia and acute asphyxia separately. In this article, the values of the Apgar score and cord blood pH were also evaluated. *Key words: resuscitation, asphyxia, newborn, Apgar score, cord blood pH.*

One of the most important reasons for women delivering in hospital is that if the baby is not breathing within two or three minutes of delivery a physician (usually a pediatrician) or a midwife will be present who can rapidly and efficiently resuscitate the baby. If necessary, this will be carried out by intubation and positive pressure ventilation.

Reports spread over twenty years are very consistent in reporting that about one neonate in fifty requires active resuscitation in the labor ward. Gupta and Tizard[1] found that 5.7 percent of all deliveries were apneic at one minute of age, and that a quarter of these needed intubation in the labor ward. More recently, Milner and Vyas[2] reported that 2.1 percent of all newborn babies required intubation and intermittent positive pressure ventilation (IPPV) in the labor ward.

For those responsible for this resuscitation it is crucial to recognize that there are many causes for a baby failing to breathe immediately after delivery (Table I). For these reasons, it is both inappropriate and dangerous to assume that failure to breathe by two or three minutes of age is always due to asphyxia, and to follow this misdiagnosis with blind therapy using bicarbonate or albumin.

CAUSES OF FAILURE TO BREATHE AT BIRTH (Table I)

Acute asphyxia

Although this is often thought of as the principal cause of failure to breathe after delivery, this is not so, and it is probably responsible for neonatal apnea only if the

* From Rosie Maternity Hospital, Cambridge, United Kingdom.

** Consultant Pediatrician, Rosie Maternity Hospital, Associate Lecturer in Pediatrics, Cambridge University, Cambridge, and Fellow in Fitzwilliam College, Cambridge.

TABLE I: Factors Other Than Asphyxia which May Delay the Onset of Respiration After Delivery

1. Drugs - depressing the CNS
2. Trauma - especially to the CNS
3. Prematurity - in particular surfactant deficient, stiff lungs.
4. Sepsis, especially Group B Streptococci
5. Muscle weakness - due to prematurity or primary muscle disease
6. Anemia
7. Congenital malformations - obstructing the airway or preventing lung expansion.
   - neurological, impairing respiratory control.

fetus has suffered some acute episode such as an antepartum hemorrhage or cord prolapse.

Nevertheless, the animal model for acute asphyxia has been of enormous value in explaining the physiology of asphyxia, and in providing the theoretical basis for the management of resuscitation[3]. Acute *postnatal* asphyxia induced in newborn animals by delivering them in good condition by cesarean section and then preventing them from breathing by immediately sealing their heads in a bag of saline follows a very characteristic pattern (Fig. 1). After a few shallow "breaths" which, by the nature of the experiment cannot result in any gas exchange, the animal stops "breathing". This early period of apnea, so called primary apnea may last for up to 10 minutes. However, after 1-2 minutes in primary apnea, the animal usually starts to gasp. The gasps occur with increasing frequency and vigor but then decrease in frequency and vigor until the animal literally reaches the last gasp. The heart rate falls rapidly after the onset of asphyxia, plateaus or may rise slightly in primary apnea and early in the phase of gasping, then begins to slow. Cardiac activity continues for 10 minutes or more after the last gasp. The period between the last gasp and cardiac arrest is known as secondary or terminal apnea. The changes in blood pressure parallel those in heart rate.

By the end of terminal apnea the $PaCO_2$ may exceed 100 mmHg and the PaO_2 is zero. Throughout the asphyxial episode the baby's pH falls from normal (pH 7.30, H^+ 50 nmol/L) to a pH < 6.5 ($H^+ > 300$ nmol/L). The relevance of these data to human perinatal care is that the response of a human baby immediately after delivery will depend on his pH. If his pH is > 7.25 ($H^+ < 55$ nmol/L) when delivered, he may be transiently apneic in primary apnea, but in the absence of other pathology (Table I) regular respiration will soon start. If he is in the phase of gasping, he will also rapidly settle into a pattern of regular respiration. If his pH has

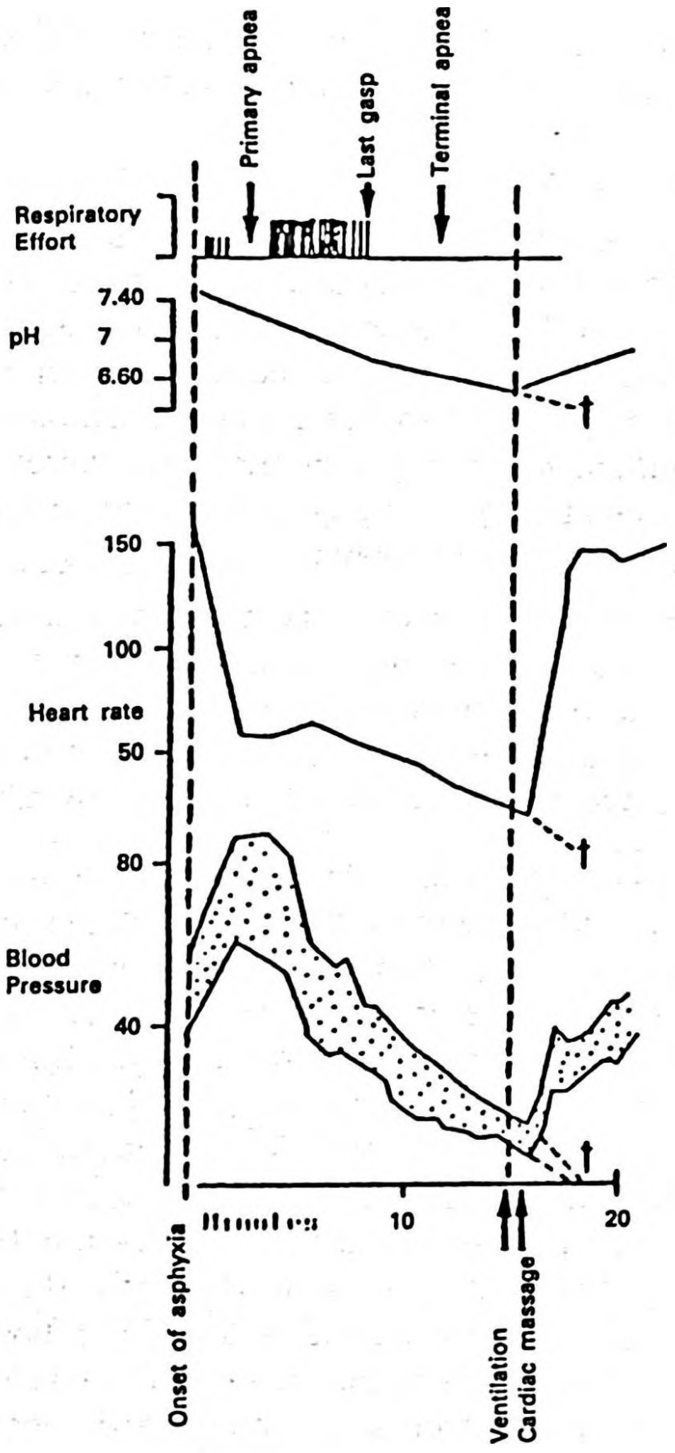

Fig. 1. Physiological changes during asphyxia and resuscitation of a newborn animal[42].

fallen to 7-7.10 (H^+ 80-100 nmol/L) he may still breathe adequately, but, particularly if there is some other complication such as heavy sedation or prematurity (see below), the primary apnea may be prolonged[4,5] or the gasping efforts may be too weak to establish alveolar ventilation. Still more severe intrapartum asphyxia will result in the delivery of an infant with a pH < 7.00 (H^+ > 100 nmol/L) who is more likely to be limp, bradycardic and in terminal apnea. A

baby born in terminal apnea will stay apneic irrespective of what therapies are given unless he is actively resuscitated by intubation and IPPV.

Chronic partial asphyxia

If asphyxia is responsible for apnea after delivery, it is very likely that this has followed events which lead to the gradual development of fetal hypoxemia and chronic partial asphyxia. This can occur before or during labor. For example, some hours or even days before delivery, a fetus may suffer a hypoxic/asphyxial insult which is not severe enough to kill him, but can cause neurological damage[6,7]. As he has not suffered *intrapartum asphyxia* he may well, therefore, show no signs of respiratory depression at birth, have a good Apgar score and establish regular breathing without any apparent problems.

Chronic partial asphyxia in labor is more common and corresponds to animal experiments in which pregnant monkeys were given an excess of halothane for periods of 4-6 hours to make them hypotensive, and their fetuses therefore became hypoxemic and acidemic. The monkeys were then delivered and their babies suffered widespread cortical, mid-brain and cerebellar damage[8].

The human counterpart of this will occur in situations such as the growth retarded fetus who already has reduced umbilical blood flow[9] which falls even further during the normal uterine contractions of labor, during recurrent episodes of umbilical cord occlusions due to entanglement round a fetal part, or compression of the cord between the presenting part and the pelvis. During these episodes, the fetal blood pressure will be sustained initially usually with a normal heart rate, though a bradycardia occasionally develops. The cardiac output is diverted to the placenta, adrenals, brain and myocardium[10-12]. The fetal PO_2 and pH fall, and energy is produced by anerobic metabolism. Since the PCO_2 also rises, a combined metabolic and respiratory acidemia develops. These changes resolve rapidly if normal utero-placental function is restored[13]. If, however, the adverse episodes are long lasting or recurrent, then the circulation will eventually fail, and the brain and heart will become ischemic and possibly permanently damaged[11,12].

If episodes of partial asphyxia have been relatively transient the fetus will not be seriously affected if delivered promptly, although his respiration may be depressed and he may be acidemic with a poor Apgar score; he will respond quickly to resuscitation and be normal thereafter.

Sequelae are likely to occur, however, if severe or prolonged chronic partial asphyxia has occurred[8]. The baby will then be born in poor condition, and will be apneic with a low Apgar score. If cord blood gas analysis is carried out he will have a marked metabolic, and in some cases respiratory acidemia with a pH < 7.00 (H^+

> 100 nmol/L). How much brain damage he has suffered can only be assessed, however, by his clinical condition in the next 12-24 hours and whether or not he develops hypoxic ischemic encephalopathy (HIE).

The fact that prenatal asphyxia can evolve in different ways has important clinical and medico-legal implications, of which the most important are:

1. Most babies who have signs of fetal distress, a low Apgar score or acidemia on cord blood gas analyses are normal in the neonatal period and on follow-up.
2. Intrauterine problems, days or weeks before labor can cause severe long-term neurological defects, yet the baby may show few, if any, neurological abnormalities in the neonatal period.
3. In the absence of clinically apparent HIE in the neonatal period, it is highly unlikely that intrapartum events were responsible for neurological sequelae.
4. Even where an "obvious" severe intrapartum asphyxial event such as a difficult breech extraction is followed by clinical HIE, it is difficult to know whether long-term neurological sequelae were solely the result of the intrapartum event, or were contributed to by neurological damage which had antedated labor by days or weeks. Making such a value judgement is even more difficult where the evidence of intrapartum asphyxia was just changes in the fetal heart rate pattern, or a fetal pH in the 7.0-7.20 range, both of which are normally associated with a good prognosis (Group 1 above).

Pre-existing neurological disease

It is crucial to remember that babies with abnormal brains or muscles may not breathe when delivered. There may be a congenital central nervous system (CNS) abnormality[14] (Table II) or severe acquired brain damage antedating delivery at any

TABLE II: Neurological Causes of Persisting Hypoventilation and Failure to Respond to Resuscitation[14]

Structural CNS malformations
Severe antenatal brain damage
Fractured cervical spine with cord damage
Dystrophia myotonica
Congenital myopathies
Werdnig-Hoffman disease
Brain tumor
Degenerative brain disorders
Ondine's curse (central hypoventilation syndrome).

stage during embryonic or fetal life. There may be primary muscle disease such as dystrophia myotonica or a congenital muscular dystrophy. In all these situations, although, the baby has not suffered any intrapartum asphyxia and will have normal blood gases when born, postnatal apnea may be complete and prolonged unless adequate resuscitation by IPPV is started promptly.

Depression of the respiratory center

Pharmacological

Virtually all the drugs which are used as analgesics, sedatives or general anesthetics during labor can cross the placenta, and depress the neonate's respiration[15]. The drugs are much more likely to cause postnatal apnea in premature babies or in those who have also suffered some degree of intrapartum asphyxia[4]. Only if the level of drug in the baby's plasma is very high, will this cause respiratory depression in an otherwise completely normal term baby. If, however, respiration is absent, as in animal experiments of acute asphyxia, there will be prolongation of primary apnea, and unless artificial ventilation is established, the neonate will become progressively hypoxemic and acidemic with all that that entails.

Hypocapnia

Maternal $PaCO_2$ may fall in women using one of the breathing techniques associated with "natural" childbirth, or in those over-using inhaled analgesics such as Entonox^R. Hyperventilation may be involuntary during general anesthesia. Since fetal $PaCO_2$ is in equilibrium with that of the mother, this may result in a baby being born with a $PaCO_2$ less than 30 mmHg in which case he will lack the CO_2 drive to ventilation, and may remain apneic until his $PaCO_2$ rises sufficiently to stimulate the respiratory center[16]. Maternal hypocapnia may also reduce placental blood flow, and thereby cause fetal hypoxemia and acidemia[17].

Trauma

It is difficult to separate the effects of fetal trauma from those of asphyxia. Tentorial tears, often with co-existing subdural hemorrhages used to be found in infants who had been difficult forceps rotations or traumatic breech extractions, in whom traumatic distortion of the fetal skull was combined with severe asphyxia. Precisely what causes the apnea in such babies after delivery, the asphyxia, the intracranial hemorrhage or the trauma is speculative. However, endorphin levels are higher in the cord blood of infants exposed to the physical stresses of vaginal delivery[18] and these substances can depress neonatal ventilation[19].

A rare traumatic cause of delayed onset of respiration at birth is injury, or trans-section of the cervical spinal cord. Depending on the level of the injury both the intercostal muscles and the diaphragm will be paralyzed, and apnea will result.

This type of injury seems to be virtually limited to babies who are extended breech presentations[20].

Prematurity

The Apgar score is low in premature babies[21] (Fig. 2) and active resuscitation is frequently required (Table III). However, the low score is not a sign of asphyxia and correlates much better with gestation[21-24] (Fig. 2). Goldenberg et al[22] did, however, show that preterm neonates with a low pH are more likely to have a low Apgar score. It is also clear, that whatever the cause of the low Apgar score in preterm babies, the score is a good marker of the high risk neonate who is more likely to die[25,26].

TABLE III: Percentage of Infants Requiring Positive Pressure Ventilation for Resuscitation[25]

Gestation	Number of Births	Requiring IPPV (%)
< 28	173	49
29 - 32	288	18
33 - 34	415	8
35 - 36	1340	2
37 - 38	5895	0.7
> 39	24,726	0.4

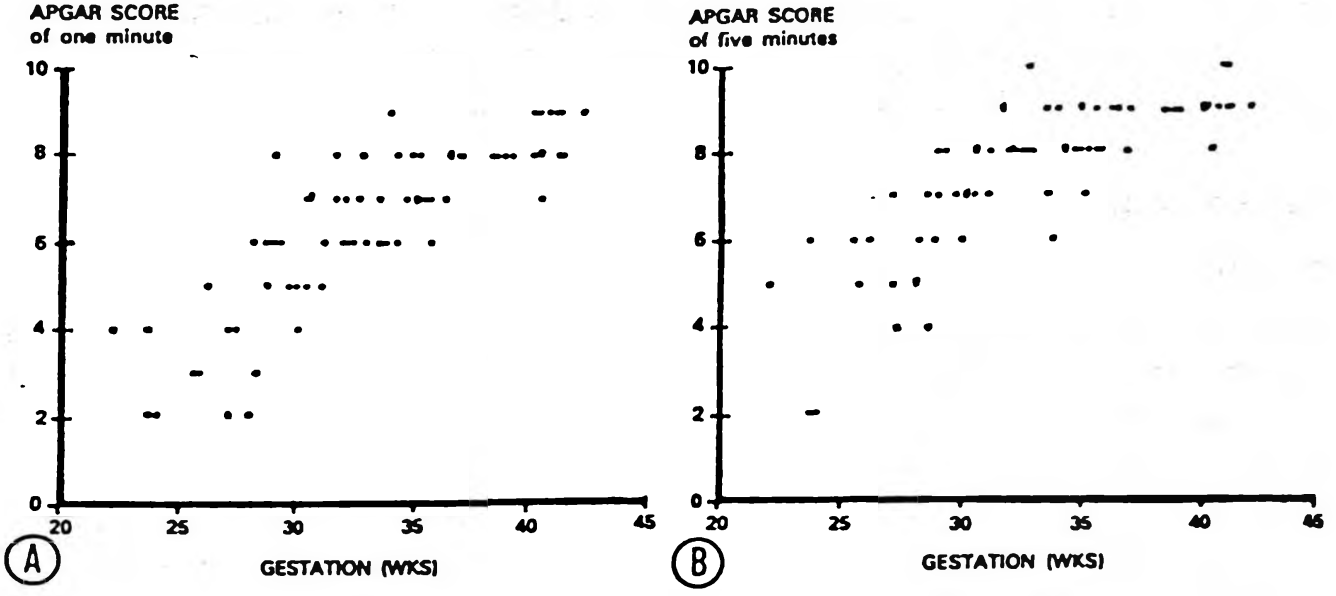

Fig. 2. Scattergram of 1 minute (A), and 5 minutes (B) Apgar scores plotted against gestation[21].

Anemia

The severely anemic neonate is often in heart failure. He lacks hemoglobin to carry oxygen to the tissues, and is therefore, more susceptible to asphyxia. Without hemoglobin, he lacks one of the body's major buffers, and may therefore, be more acidemic[27]. Severely anemic neonates may, therefore, be in very poor condition at delivery, and not only breathe inadequately, but also respond poorly to resuscitation. Although severe asphyxia causes pallor in its own right, anemia must always be excluded in a pale infant responding poorly to resuscitation. Of the two likely causes of severe anemia at birth, rhesus incompatibility and fetal hemorrhage, the former is usually expected. Unexpected severe anemia is, therefore, usually due to fetal hemorrhage, and needs prompt transfusion.

Sepsis

Babies suffering from severe intrapartum infection, both preterm and at term, classically due to Listeria[28] or Group B streptococci[29,30] can be born with very poor Apgar scores. They are critically ill at the time of birth with hypotension, acidemia and a septicemia, but may not actually be asphyxiated[30]. Although the outlook for these babies is grave, the condition must be diagnosed and vigorous anti-infection therapy commenced in addition to treating their apnea.

Congenital malformations

Malformations, in particular those affecting the lungs and airway can cause major problems at resuscitation. The babies are not usually asphyxiated, and their one minute Apgar may be reasonable, but they may then become hypoxic and acidemic with a poor color, hyptonia and inadequate respiration. Characteristically, therefore, these babies start with a reasonable Apgar score of say 6 or 7, but this actually deteriorates during the next 5-10 minutes. Typical examples are babies with diaphragmatic hernia, or one of the other causes of pulmonary hypoplasia.

Assessing the apneic baby

History

Hopefully the person responsible for the resuscitation will have ascertained whether there is a history of any of the above problems. In particular, he must know about:

1. Gestation
2. Evidence of perinatal infection.
   a) Maternal pyrexia
   b) evidence of maternal genital infection
   c) positive cultures of high vaginal swabs

3. Perinatal drug use.
   a) Sedation
   b) Analgesia including — parenteral opiates
      — inhaled agents
      — general anesthesia
   c) Other drugs likely to decrease respiration
      — anticonvulsants
      — psychotropics
4. Blood loss per vaginam which could have been fetal
   — abruptio/placenta previa
   — vasa previa
   — twin-twin transfusion
5. Known episodes of trauma which may or may not induce asphyxia
   a) difficult/failed forceps
   b) breech extraction
6. Recognized antecedents of genuine asphyxia
   a) changes in fetal heart rate pattern
   b) meconium staining
   c) fetal acid-base measurement.

With this as a historical background, the attendant should then be able to use the Apgar score and any other available data to plan his management of the baby in the next 10 minutes.

Clinical examination

Taking the Apgar score does in fact make the physician examine the baby. In addition to assessing the factors relevant to the Apgar score, other relevant factors to look for during the very rapid initial clinical assessment include:

1. Meconium staining
   — may mean asphyxia
   — may cause problems with resuscitation.
2. Dysmorphic features
   — in particular those that would suggest the pulmonary hypoplasia of Potter's syndrome or other conditions with a small chest - e.g., short limbed dwarfism.
3. Evidence for congenital malformations that would compromise resuscitation e.g., hydrops, or the scaphoid abdomen of diaphragmatic hernia.
4. Evidence of infection
   — smell: purulent liquor, skin rash

5. Evidence of hemorrhage
   — recent: poor pulse volume, marked pallor of mucus membranes
   — chronic hepatosplenomegaly, edema
6. Evidence of early neonatal lung disease
   — marked dyspnea, if any respiratory efforts present
   — stiff lungs difficult to inflate by IPPV.

Apgar score

The traditional way of assessing the newborn is to use the Apgar score devised by Virginia Apgar[31] in 1953 which grades five clinical features with scores of 0-2 at 1 minute of age (Table IV). In recent years, there has been a tendency to belittle the Apgar score because it is a poor index of asphyxia i.e. hypoxemia and acidemia (Table V)[32,33] and has little prognostic value[34,35]. This view is completely unjustifiable, since it takes a blinkered view of its purpose. If a baby has a poor Apgar score, he has a problem[36]. It could be any of the problems listed in Table I, but which ever one is present, the sooner it is diagnosed and managed appropriately, the better. The components of the score do not carry equivalent physiological weight. Heart rate and respiration are clearly more important than reflex responsiveness. It is for this reason that a narrative description of the baby's condition at birth and his response to resuscitation must be recorded in the notes. Never just say that a baby has an Apgar score of 5 at 1 minute: accurately describe his condition. For instance, "at 1 minute he was apneic. had blue hands and feet, a heart rate of 90 and normal tone: he grimaced when sucked out", or "at 1 minute the infant was pale with a heart rate of 120 and gasped twice, but he was limp and cried when sucked out". In both these situations, the Apgar score is 5 but they have very different clinical and physiological implications. In addition to

TABLE IV: Apgar Score

	Score		
Clinical feature	0	1	2
Heart rate	0	< 100	> 100
Respiration	Absent	Gasping or irregular	Regular or crying lustily
Muscle tone	Limp	Diminished, or normal with no movements	Normal with active movements
Response to pharyngeal catheter	Nil	Grimace	Cough
Color of trunk	White	Blue	Pink

TABLE V: Mean pH Base Deficit of Infant With Different Apgar Scores[32]

	1 min Apgar score								
	1	2	3	4	5	6	7	8	9
No of infants	5	12	17	11	22	30	62	147	589
pH mean	7.17	7.12	7.10	7.22	7.18	7.17	7.19	7.20	7.21
SD	0.5	0.13	0.13	0.10	0.08	0.09	0.08	0.07	0.08
BD (mEq/L)	10.6	11.8	11.5	7.8	9.6	10.6	8.8	8.4	7.9
Mean SD	4.0	5.9	6.3	5.5	4.3	3.2	4.1	3.7	3.6

BD = base deficit
SD = standard deviation

taking the Apgar score at 1 minute of age, it is traditional to record the scores at 5, 10, 15 and 20 minutes of age. This adds little to the narrative account in the notes of the baby's response, but improvement in the Apgar score from 0-20 minutes is an internationally understood and accepted shorthand for describing the success, or otherwise of the resuscitative effort, and the 15 and 20 minute scores show some correlation with subsequent neurological development[37].

Cord blood analysis

This is the only other piece of data which can be available in the labor ward to help one diagnose the cause of a baby's failure to breathe. It is the most satisfactory way of assessing whether or not asphyxia rather than one of the other conditions listed in Table I is present [38]. Ideally, therefore, at all deliveries, a blood gas should be measured on a sample drawn from the umbilical artery in a section of the umbilical cord double clamped immediately after delivery[39]. Since low Apgar scores are not often due to asphyxia, it is not surprising that there is a poor relationship between Apgar score and pH[32,40]. Two percent of babies with normal Apgar scores have a pH < 7.10 ($H^+ > 80$ nmol/L) and most babies with a pH < 7.10 ($H^+ > 80$ nmol/L) will have normal Apgar scores. However, if both the Apgar score and the pH are abnormal, and no other problems are detected (Table I), it strongly suggests that there was recent asphyxia[38,40,41]. However, it is only when umbilical artery pH values are < 7.00 ($H^+ > 100$ nmol/L) that low Apgar scores are common, or are still reduced at 5 minutes of age[40] (Fig. 3). However, even this degree of acidemia is a poor marker of subsequent neurological damage[35].

On the basis of the clinical history, the clinical examination, the Apgar score and the cord blood gas analysis, it is therefore usually possible to arrive at an accurate

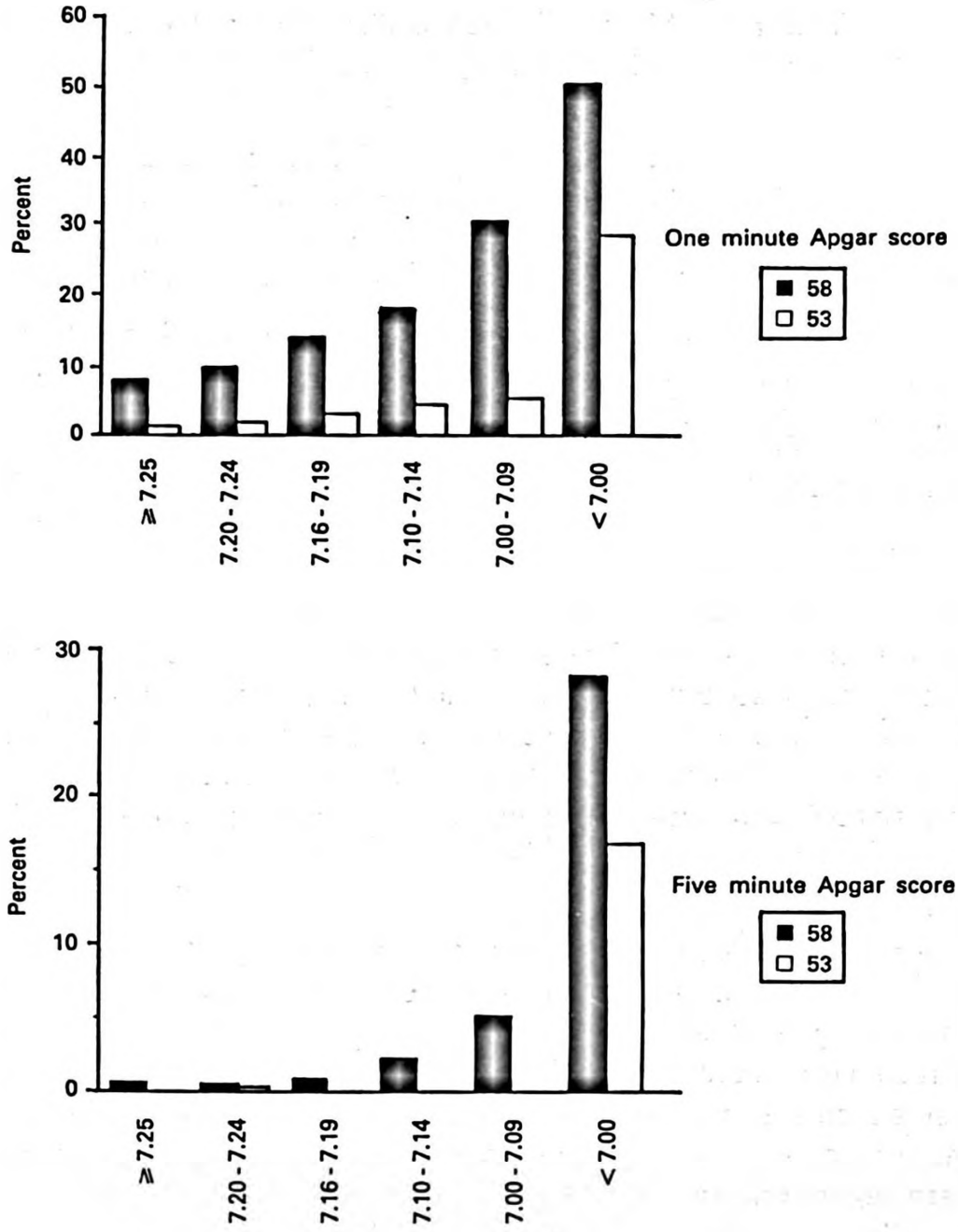

Fig. 3. Relationship between umbilical artery pH levels and Apgar scores at 1 (top) and 5 (bottom) minutes[40].

diagnosis within 5-10 minutes of age of the cause of a baby being apneic immediately after delivery and being slow in responding to resuscitation. Once this diagnosis has been established, the appropiate treatment can then be given.

REFERENCES

1. Gupta JM, Tizard JP. The sequence of events in neonatal apnoea. *Lancet* 2:55, 1967.
2. Milner AD, Vyas M. Resuscitation of the newborn. In Milner AD, Martin RJ (eds). *Neonatal and Pediatric Respiratory Medicine.* London: Butterworth, 1985, p. 16.

NOTICE TO AUTHORS

The Turkish Journal of Pediatrics publishes original articles, case reports and reviews of the literature in the field of pediatrics in English, and it will consider papers from authors of all countries. Original articles should report scientific findings within the pediatric field of interest. Case reports should contain accounts of rare syndromes, new diagnostic tools and methods, new kinds of treatment and laboratory research with foreseeable practical application. Review articles should contain an objective account of different points of view and an internationally representative bibliography. Authors considering submission of review articles of medical progress are encouraged to consult with the Editor before submission. Papers should in general not exceed 15 written pages for original articles or 7 for case reports and reviews of the literature, including tables, figures and illustrations. All papers are subject to editorial revision for the purpose of conformity to the style adopted by *The Turkish Journal of Pediatrics*, and authors may be requested to shorten or revise their papers.

Statements and opinions expressed in the articles therein are those of the author(s) and not necessarily those of the Editor or publisher; the Editor and publisher disclaim any responsibility or liability for such material. Neither the Editor nor the publisher guarantees, warrants, or endorses any product or service advertised in this publication; neither do they guarantee any claim made by the manufacturer of such product or service.

We recommend that all manuscripts be approved for submission by the department chairman or head of the institution in which the study has been done. All manuscripts must be accompanied by the following **written statement**, signed by the author(s): "The author(s) transfer(s) all copyright ownership of the manuscript entitled (title of article) to *The Turkish Journal of Pediatrics* in the event the work is published. The author(s) warrant(s) that the article is original, is not for consideration by another journal, and has not been previously published (except in a congress report), and has been prepared according to the manuscript rules" (as described below). Papers describing research involving human subjects should indicate that informed consent was obtained from the parents or guardians of the children who served as subjects and, when appropriate, from the subjects themselves.

Preparation of Manuscript

Contributors are requested to pay particular attention to the following rules governing the preparation of manuscripts. Failure to follow these rules is frequent cause of delay in the publication of articles and may result in rejection of otherwise acceptable manuscripts. Manuscripts should be sent in duplicate (original and one photocopy acceptable) to the Editorial Secretary, *Turkish Journal of Pediatrics*, P.K. 66, 06240 Samanpazarı, Ankara, Turkey. Manuscripts, whether rejected or published, are not returned to the authors but original illustrations which are rejected are returned upon request of the author.

Format Manuscripts should be typed, double-spaced, on one side of the paper only, with wide margins.

Title Page A separate title page should include authors' names and academic degrees; departmental and institutional affiliations of each author, and sources of financial assistance, if any. Designate one author as the correspondent, and provide address and business and home telephone numbers. Galley proofs will be sent to the corresponding author, as will order forms for reprints at a later date.

Contents Each original article should contain the following sections: Introduction, Material and Methods, Results, Discussion and Abstract, and each Case Report should contain an Introduction, Case Report, Discussion and Abstract.

Abbreviations Abbreviations must conform to accepted standards. Laboratory slang, clinical jargon and colloquialism must be avoided.

Tables Tables should be numbered with Roman numerals according to order of mention in the text. Each table must be typed double-spaced on a separate sheet of paper and a concise title supplied for each. Tables should be self-explanatory and supplement, not duplicate the text. If a table or any data therein have been previously published, a footnote must give full credit to the original source.

Figures Figures and illustrations should be of direct interest to the subject of the paper and numbered with Arabic numerals according to order of reference in the text. Figures should be drawn on white paper and photographs must be clear prints. The name of the first author and the number of the figure or illustration must be written in pencil on the back of each, with an arrow indicating the top side. Original drawings of graphs should be prepared in black India ink or typographic (press-apply) lettering. Typewritten or freehand lettering is unacceptable. All lettering must be professional, in proportion to the drawing, graph, or photograph. Do not send original art work, x-ray films, or ECG strips. A list of legends for the figures and illustrations must be provided on a separate page.

Summary / Abstract An informative abstract not exceeding 150 words must accompany each manuscript, typed on a separate sheet. Unexplained abbreviations and references are not allowed.

References References to the literature should be limited to those cited by the author, arranged and numbered according to order of mention in the text. All authors of an article or book should be listed where there are four or fewer. If more than four, the first three names should be given followed by the indication "et al". In a manuscript underlining indicates italics.

References to journal articles:

Example : 1. Noack G, Freyschuss I. The early detection of pneumothorax with transthoracic impedance in newborn infants. *Acta Paediatr Scand* 66:677, 1977.

Names of journals are to be abbreviated in accordance with the style of *Index Medicus.*

References to books:

Example : 2. Praat RTC. *The Genetics of Neurological Disorders.* London: Oxford University Press, 1967, pp. 173-174.

References to chapters in books:

Example : 3. Kissane JM. Development of the kidney and congenital malformations. In Heptinstall RH (ed). *Pathology of the Kidney* (2nd ed) Vol. 1. Boston: Little, Brown and Co, 1974, pp. 69-109.

Key Words Authors are requested to list on a separate sheet of paper key words related to their article. These will be used in compiling an index for the volume of the journal in which the article appears.

Proofs and Reprints Galley proofs will be sent to the corresponding (or principal) author by the printer. The master proof should be returned to the Managing Editor together with the manuscript within two days, and by air mail if received by air mail. Thirty reprints of articles published are sent free of charge to the corresponding author.

Announcements Announcements of scheduled meetings, symposia, or postgraduate courses may be sent for consideration to the publisher at least 5 months in advance of the meeting date.

Books for Review Books and monographs, domestic or foreign, may be sent to the Editor for consideration for review. No books are returned, nor acknowledgement made of books received.

Advertising Communications of a business nature and all advertising communications should be addressed to the Journal's Editor.

Copyright All rights reserved. Apart from any relaxations permitted under national copyright laws, no part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form or by any means without the prior written permission of the copyright owners. Permission is not required to copy abstracts of papers or of articles on condition that a full reference to the source is shown. Multiple copying of the contents without permission is always illegal.

Checklist

Please check your article as described below before sending it to the Editor.

- Letter of submission
- Signed "Statement" (which is written on a separate paper) as described above
- Two copies of article (one original and one photocopy will be acceptable).
- Title page
  - Title of article
  - Name(s), academic degrees, and affiliations of author(s)
  - Name, address, and business and home telephone numbers of corresponding author
- Article proper
  - Original articles: Introduction, Material and Methods, Results, Discussion, Abstract
  - Case Reports: Introduction, Case Report, Discussion, Abstract
  - Key words
- References on a separate sheet
- Tables on a separate sheet
- Legends on a separate sheet
- Illustrations properly labelled (one set of glossy prints and one set of photocopies).

3. Dawes GS. *Fetal and Neonatal Physiology.* Chicago: Year BK, 1968, pp. 141-159.
4. Moore WM, Davis JA. Response of the newborn rabbit to acute anoxia and variations due to narcotic agents. *Br J Anaesth* 38:787, 1966.
5. Campbell AG, Milligan JE, Talner NS. The effect of pre-treatment with pentobarbital, meperidine, or hyperbaric oxygen on the response to anoxia and resuscitation in newborn rabbits. *J Pediatr* 72:518, 1968.
6. Stoddard RA, Clark SL, Minton SD. In utero ischemic injury: sonographic diagnosis and medicolegal implications. *Am J Obstet Gynecol* 159:23, 1988.
7. Nijhuis JG, Kruyt N, van Wijck JA. Fetal brain death. Two case reports. *Br J Obstet Gynecol* 95:197, 1988.
8. Brann AW Jr, Myers RE. Central nervous system findings in the newborn monkey following severe in utero partial asphyxia. *Neurology (Minneap)* 25:327, 1975.
9. Hackett GA, Campbell S, Gamsu H, et al. Doppler studies in the growth retarded fetus and prediction of neonatal necrotising enterocolitis, haemorrhage, and neonatal morbidity. *Br Med J* 294:13, 1987.
10. Bocking AD, Gagnon R, White SE, et al. Circulatory responses to prolonged hypoxemia in fetal sheep. *Am J Obstet Gynecol* 159:1418, 1988.
11. Richardson BS. Fetal adaptive responses to asphyxia. *Clin Perinatol* 16:595, 1989.
12. Block BS, Schlafer DH, Wentworth RA, et al. Intrauterine asphyxia and the breakdown of physiologic circulatory compensation in fetal sheep. *Am J Obstet Gynecol* 162:1325, 1990.
13. Patriarco MS, Viechnicki BM, Hutchinson TA, et al. A study on intrauterine fetal resuscitation with terbutaline. *Am J Obstet Gynecol* 157:384, 1987.
14. Brazy JE, Kinney HC, Oakes WJ. Central nervous system structural lesions causing apnea at birth. *J Pediatr* 11:163, 1987.
15. Barrier G, Sureau C. Effects of anaesthetic and analgesic drugs on labour, fetus and neonate. *Clin Obstet Gynaecol* 9:351, 1982.
16. Moya F, Morishima HO, Shnider SM, James LS. Influence of maternal hyperventilation on the newborn infant. *Am J Obstet Gynecol* 91:76, 1965.
17. Motoyama EK, Rivard G, Acheson F, Cook CD. Adverse effect of maternal hyperventilation on the foetus. *Lancet* 1:286, 1966.
18. Abboud TK. Maternal and fetal beta endorphin: effects of pregnancy and labour. *Arch Dis Child* 63:707, 1988.
19. Hazinski TA, Grunstein MM, Schlueter MA, Tooley WH. Effect of naloxone on ventilation in newborn rabbits. *J Appl Physiol* 50:713, 1981.
20. Westgren M, Grundsell H, Ingemarsson I, et al. Hypertension of the fetal head in breech presentation. A study with long-term follow-up. *Br J Obstet Gynaecol* 88:101, 1981.
21. Catlin EA, Carpenter MW, Brann BS 4th, et al. The Apgar score revisited: influence of gestational ages. *J Pediatr* 109:865, 1986.
22. Goldenberg RL, Huddleston JF, Nelson KG. Apgar scores and umbilical arterial pH in preterm newborn infants. *Am J Obstet Gynecol* 149:651, 1984.
23. Perkins RP, Papile LA. The very low birthweight infant: incidence and significance of low Apgar scores, "asphyxia", and morbidity findings at delivery. *Am J Perinatol* 2:108, 1985.
24. Luthy DA, Shy KK, Strickland D, et al. Status of infants at birth and risk for adverse neonatal events and long-term sequelae: a study in low birth weight infants. *Am J Obstet Gynecol* 157:676, 1987.
25. MacDonald HM, Mulligan JC, Allen AC, Taylor PM. Neonatal asphyxia. I. Relationship of obstetric and neonatal complications to neonatal mortality in 38,405 consecutive deliveries. *J Pediatr* 96:898, 1990.

26. Behnke M, Carter RL, Hardt NS, et al. The relationship of Apgar scores, gestational age, and birthweight to survival of low-birthweight infants. *Am J Perinatol* 4:121, 1987.

27. Soothill PW, Nicolaides KH, Rodeck CH. Effect of anaemia on fetal acid-base status. *Br J Obstet Gynaecol* 94:880, 1987.

28. Boucher M, Yonekura ML. Perinatal listeriosis (early-onset): correlation of antenatal manifestations and neonatal outcome. *Obstet Gynecol* 68:593, 1986.

29. Peevy KJ, Chalhub EG. Occult group B streptococcal infection: an important cause of intrauterine asphyxia. *Am J Obstet Gynecol* 146:989, 1983.

30. Maberry MC, Ramin SM, Gilstrap LC 3d, et al. Intrapartum asphyxia in pregnancies complicated by intra-amniotic infection. *Obstet Gynecol* 76:351, 1990.

31. Apgar V. Proposal for new method of evaluation of newborn infant. *Anesth Analg* 32:260, 1953.

32. Sykes GS, Molloy PM, Johnson P, et al. Do Apgar scores indicate asphyxia? *Lancet* 1:494, 1982.

33. Silverman F, Suidan J, Wasserman J, et al. The Apgar score: is it enough? *Obstet Gynecol* 66:331, 1985.

34. Dennis J, Johnson AM, Mutch L, et al. Acid-base status at birth and neurodevelopmental outcome at four and one-half years. *Am J Obstet Gynecol* 161:213, 1989.

35. Fee SC, Malee K, Deddish R, et al. Severe acidosis and subsequent neurologic status. *Am J Obstet Gynecol* 162:802, 1990.

36. American Academy of Pediatrics Committee on Fetus and Newborn: Use and abuse of the Apgar score. *Pediatrics* 78:1148, 1986.

37. Nelson KB, Ellenberg JH. Apgar scores as predictors of chronic neurologic disability. *Pediatrics* 68:36, 1981.

38. Thorp JA, Sampson JE, Parisi VM, Creasy RK. Routine umbilical cord blood gas determinations? *Am J Obstet Gynecol* 161:600, 1989.

39. Johnson JW, Richards RS, Wagaman RA. The cause for routine umbilical blood acid-base studies at delivery. *Am J Obstet Gynecol* 162:621, 1990.

40. Gilstrap LC 3d, Leveno KJ, Burris J, et al. Diagnosis of birth asphyxia on the basis of fetal pH, Apgar score and newborn cerebral dysfunction. *Am J Obstet Gynecol* 161:825, 1989.

41. Steer PJ, Eigbe F, Lissauer TJ, Beard RW. Interrelationships among abnormal cardiotocograms in labour, meconium staining of the amniotic fluid, arterial cord blood pH, and Apgar scores. *Obstet Gynecol* 74:715, 1989.

42. Dawes GS, Jacobson HN, Mott JC, et al. The treatment of asphyxiated, mature foetal lambs and rhesus monkeys with intravenous glucose and sodium carbonate. *J Physiol (London)* 169:167, 1963.

ANNOUNCEMENTS

MEETINGS

ANTALYA, 25-29 OCTOBER 1992

FIRST INTERNATIONAL CONGRESS ON ADOLESCENCE DISORDERS AND NEW APPROACHES

Inquiries to: Congress Secretariat
Prof. Sevim Dinçer Cengiz, MD
Meşrutiyet Caddesi 3/12
Kızılay
ANKARA, TURKEY

AUTHOR INDEX TO VOLUME 33

AJİ YAFET Dolli 35
AKANSEL Gür 59
AKGÜR Feza M. 55
AKINCI Ayşehan 153
AKSOY Muzaffer 195
AKTÜRK Fadıl 139
AKYÜZ Canan 185
ANLAR Banu 199
ARDA Oktay 85
ARISOY Nil 35
AYDINOĞLU Halil 117
AYGUN Kemal 143
AYTER Şükriye 79
BAKIR TÜLAY 43
BEKSAÇ Sinan 79
BERKEL İzzet A. 205
BERNAY İrem 235
BEŞBAŞ Nesrin 135
BOZALIOĞLU Hamza 43
BOZER Yüksel A. 27, 99
BÖKE Erkmen 27
BROCA de Alain 121
BULUT Melih 59, 167
BÜYÜKGEBİZ Atilla 19
BÜYÜKPAMUKÇU Nebil A. 55, 245
CEYHAN Mehmet 13, 217
CİLİV Gönenç 19
COŞKUN Turgay 79, 181
ÇAĞLAYAN Suat 117
ÇAKAR Nur 79
ÇETİN HASAN 153
DEMİRCİN Metin 99
DEMİRSOY Sadık 159
DİNÇER Cumhur 221
DİNÇER Fitnat 221
DOĞAN Rıza 27, 173
DURAK Hatice 235
ERBAŞ Deniz 159
ERBENGİ Günaydın 235
ERBİL Hasan 111
ERCAN Oya 85
ERSOY Fügen 163, 205
EROUD Tatiana 1
FEVILLE MICHELLE 121
FATTİ Richard A. 1
GÖKALP Ziya Hamit 221
GÖÇMEN Ayhan 163
GÜĞÜŞ Safiye 49
GÜLMEZ İbrahim 191
GÜMÜŞTEKİN Enis 43
GÜR İnci 153
GÜSANOĞLU Enver 159
GÜTUN Şükrü 153
GÜZAN Eyüp 99
GÜNÖNMEZ Akgün 55, 245
GÜRCAN Cem 191
GÜVEMİR Bedri 111
KANRA Güler 13, 217
KANSOY Savaş 117
KARACAGİL Mustafa 191
KARADENİZ Ceyda 185
KINIK Erol 19
KIZILCAN Fatih 245
KOÇAK Nurten 49
KOMŞUOĞLU Sezer Ş. 139
KÖSE Galip 247
KREMP Odile 121
KUTLUK Tezer 185
KÜÇÜKALİ Türkan 185
LEKE Lekombe 121
OKTAY Hamiyet 205
ORAN Olcay 231
ÖZALP İmran 79, 181
ÖZBAY Gülşen 85
ÖZGÜÇ Meral 79
ÖZKAN Hasan 247
ÖZKUTLU Süheyla 173
ÖZORAN Solmaz Afet 139
ÖZORAN Yavuz 43, 139
PAŞAOĞLU İlhan 27, 99, 173
RISBOURG Bernard 121
ROBERTON Clifford N.R. 65, 253
SAATÇİ Ümit 135
SALTIK Ahmet 143
SANAL Özden 1, 163, 205
SARIALİOĞLU Faik 185
SARIOĞLU Ayşe 35
SEÇKİN Ebru 117
SEVER Lale 35
SINAV Satvet 111
SUNGUR İsmet 143
SÜLLÜ Yüksel 111
SÜZEN Bikem 139
TANYEL F. Cahit 55, 245
TATLIŞEN Atilla 191
TEKANT Gonca 59, 167
TEKİNALP Gülsevin 181, 231
TEZCAN İlhan 163
TEZİÇ Tahsin 43, 153
TOPAL Burhan 13
TOPALOĞLU Rezan 135
TURGUTALP Havvanur 139
ULUTUNCEL Nergis 235
ULUKUTLU Lamia 85
ÜNER HAŞMET 55
ÜNSAL Erbil 247
VURAL Mehmet 121
YALAZ Kalbiye 49
YAPRAK Işın 117
YENİAY İhsan 163
YILMAZ Engin 79
YILMAZ Necati 59
YURDAKÖK Murat 231
ZORLUTUNA Ahmet 221

ARTICLE INDEX TO VOLUME 33

A Case of Neurenteric Cyst 139
A Different Approach to Sleep Problems of Infancy: Swaddling Above the Waist 117
Acute Hemorrhagic Leukoencephalitis 49
An Experimental Study on the Use of Fibrin Sealants in Strabismus Surgery 111
Contrast Material-Induced Acute Renal Failure in a Diabetic Patient 135
Creation of Right Ventricle-Pulmonary Artery Continuity Without Cardiopulmonary Bypass 173
Diagnosis and Treatment of Intraspinal Lipomas 221
Diuretic Renography in Children: A Non-invasive Method for the Assessment of Upper Urinary Tract Pathologies 235
Elimination of Maternal Antibodies Against Measles 217
Encopretic Children: Experience With Fifty Cases 167
Failure to Breathe at Birth: Causes and Assessment 253
Fused Pelvic Kidney Drained by a Single Ureter 59
Gastric Involvement in Childhood Non-Hodgkin's Lymphoma: A Case Report 43
Gene Mapping Using Linkage Analysis 1
Hereditary Fructose Intolerance in a Patient With Phenylketonuria 181
Hydatid Disease Presenting as an Intrascrotal Mass in a Child 245
IgG Subclass Deficiency in Children With Recurrent Infections 163
Intestinal Effects of Iron Deficiency Anemia in Children 85
Intrauterine Intussusception: A Rare Cause of Ileal Atresia Which Can Lead to a Confusion in Diagnosis 55
Lipids and Lipoproteins in the Sexual Maturation Stages of Male Adolescents 19
Multiple Primary Malignancy: A Report on Langerhans Cell Histiocytosis Associated with Hodgkin's Disease 185
Neonatal Thermoregulation 121
Neural Cell Adhesion Molecules 199
Oculocerebral Hypopigmentation Syndrome (Cross Syndrome) 247
Prenatal Diagnosis of Cystic Fibrosis in a Turkish Family 79
Pulmonary Hypertension due to Chronic Upper Airway Obstruction: A Clinical Review and Report of Four Cases 35
Risk of Tuberculosis Infection in Edirne Primary Schools and a Review of Its Epidemiological Indices 143
Rotavirus Diarrhea in Newborn Infants 153
Serological Evaluation of 52 Children Immunized With the Combined Measles, Mumps and Rubella Vaccine 13
Sodium and Potassium Levels in Colostrum 231
Surgical Treatment of Renovascular Hypertension in Children 27
The Effect of Aprotinin (Trasylol) on Post-operative Bleeding in Cyanotic Congenital Heart Disease 99
The Effect of Epidermal Growth Factor on Serum Zinc Levels 159
The History of Beta-Thalassemia in Turkey 195
The Management of Meconium Aspiration Syndrome 65
Twenty-year Follow-up of 160 Patients With Ataxia-Telangiectasia 205
Urethrocutaneous Fistula Due to a Coil of Hair 191

KEY WORD INDEX TO VOLUME 33

acute necrotizing hemorrhagic leukoencephalitis 49
acute renal failure 135
adenoid hypertrophy 35
adenotonsillectomy 35
adhesion molecule 199
AIR variation rate 143
albinism 247
annual infection risk (AIR) 143
AIR variation rate 143
Apgar score 253
aprotinin 99
arterial hypertension 27
asphyxia 253
ataxia-telangiectasia 205
cellular immunity 205
childhood tumors 43, 185
clinical features 205
colostrum 231
contrast material 135
cord blood pH 253
Cross syndrome 247
cyanotic congenital heart disease 99
cystic fibrosis 79
diarrhea 153
discoid 59
DNA amplification 79
d-xylose malabsorption 85
echinococcus cysts 245
encopresis 167
enterogenous cyst 139
epidermal growth factor 159
extraocular muscles 111
fecal soiling 167
fibrin sealant 111
fused pelvic kidney 59
gammaglobulin 163
gastric involvement 43
Gene mapping 1
hemoglobinopathies 195
hereditary fructose intolerance 181
Hodgkin's disease 185
humoral immunity 205
IgG subclass deficiency 163
ileal atresia 55
immunoglobulin superfamily 199
integrin 199
intestinal mucosa 85
intestinoma 139
intraspinal lipoma 221
intrauterine intussusception 55
iron deficiency anemia 85
kidney 59
KM 19 polymorphism 79
Langerhans cell histiocytosis 185
linkage analysis 1
lipids 19
lipoproteins 19
male adolescents 19
malignancy 205
maternal antibodies against measles 217
measles 13
measles vaccination 217
meconium aspiration syndrome 65
mitochondria 85
multiple primary malignancy 185
mumps 13
necrotizing enterocolitis 153
neonate 121
neonatal intestinal obstruction 55
neural cell adhesion molecule 199
neurenteric cyst 139
newborn 65, 253
non-Hodgkin's lymphoma 43
penile tourniquet syndrome 191
phenylketonuria 181
postoperative bleeding 99
potassium 231
prenatal diagnosis 79
pulmonary artery stenosis 173
pulmonary hypertension 35
radioisotope renography 235
radionuclide imaging 235
recurrent infections 163
rehabilitation 221
renal artery stenosis 27
renovascular hypertension 27
restriction fragment length polymorphism 1
resuscitation 253
rotavirus 153
rubella 13
scrotal swelling 245
serum zinc level 159
sleep problems 117
sodium 231
Southern blotting 1
strabismus surgery 111
strength of PPD 143
surgical intervention 221
swaddling 117
Tanner sexual maturation stages 19
Tb epidemiology 143
Tb immunization 143
teratoid cyst 139
tetralogy of Fallot 173
thalassemia 195
thermoregulation 121
tonsil hypertrophy 35
type 1 diabetes mellitus 135
urethrocutaneous fistula 191
vaccination 13