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ABSTRACTS

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## Plenary Sessions

Failure of Australia antigenemia to prevent acute epidemic hepatitis in an institution for the mentally retarded. Dale E. Dietzman, Earl B. Matthew, David L. Madden, and John L. Sever. *NIH, Bethesda, Md.*

A major epidemic of short incubation acute infectious hepatitis occurred among 3500 patients in an institution for the mentally retarded. A total of 375 clinical cases were diagnosed and 245 subclinical cases were estimated on the basis of SGPT levels. Serial serum samples were obtained from 1104 patients during the epidemic. Australia antigenemia (Au) was determined by gel diffusion and complement fixation techniques. The institutional incidence of Au was 7.9% (87/1104). Three years earlier the incidence was approximately 8% (4/49). The current incidence was higher in males (10.6%) than females (4.4%), and higher in patients under age 15 years (12.8%) than older patients (5.7%). The incidence in patients with Down's syndrome was 22.9% (21/105). The attack rate for epidemic hepatitis varied among the infected wards (86%–20%) and was higher for younger, ambulatory, and more severely retarded patients. The attack rate for patients with Au was not significantly different from other patients in the same wards. On the 11 study wards, acute hepatitis occurred in 62.7% (32/51) of patients with Au, and 60.3% (238/395) of patients without Au. Only a few patients with acute Australia antigen hepatitis were detected and were excluded from these statistics.

Failure of penicillin to control a nursery epidemic of streptococcal infection. John C. Ribble, Margaret Heagarty, and Richard B. Roberts. *The New York Hosp.-Cornell Univ. Med. Ctr., New York, N.Y.*

During the winter of 1969–1970 there were two outbreaks of streptococcal infection (group A-M type 9) in one of our newborn nurseries. In a 4-month period covering both outbreaks 20% of the infants were infected, but at the height of the epidemic more than 85% were involved. There were two deaths due to streptococcal bacteremia and meningitis. When the first outbreak was identified, penicillin was given to all babies for the duration of their stay in the nursery. No new infections occurred although type 9 streptococcus was not totally eradicated from the infants previously infected. Two weeks after discontinuation of the penicillin regimen, there was a recurrence of infection with type 9 streptococcus. During the second outbreak the use of penicillin failed to prevent spread of the infection and 18/59 infants acquired streptococci even though they had received penicillin since birth. The streptococci were not resistant to penicillin. The failure was associated with an increased prevalence of penicillin-resistant *Staphylococcus aureus* on the umbilical cords. During the first outbreak 28% of the babies had resistant *S. aureus* on their cords; in the second outbreak 58% had resistant staphylococci ($P$ less than 0.001). In the second outbreak 16/18 (89%) of the infants who acquired streptococci were carriers of resistant *S. aureus* whereas 18/41 (44%) babies who did not acquire streptococci were carriers of staphylococci ($P$ less than 0.001). These findings indicate that penicillin-resistant staphylococci on the umbilicus may interfere with the ability of penicillin to prevent colonization of the cord with group A streptococci.

A new disorder of phenylalanine metabolism associated with ataxia, convulsions, and retardation: methylmandelic aciduria. O. Rennert, R. Julius, A. Aylsworth, C. Williams, and M. Greer. *Univ. of Florida Col. of Med., Gainesville, Fla.*

Two brothers, aged 1.5 and 6 years presented with ataxia, convulsions, and mental retardation. In both cases symptoms appeared between 1 and 1.5 years of age, initially with ataxia and seizures. The subsequent course was marked by increasing severity of symptoms interrupted by intermittent periods of remission. In the older boy attacks were of such severity that he exhibited dysarthria, dysphagia, convulsions, and coma. Diagnostic studies included investigation of blood, cerebrospinal fluid and urine for amino acids, keto acids, certain organic acids, and ammonia. The offending metabolite, methyl mandelate, was identified by use of gas chromatography and mass spectroscopy. Intermediates were identified by gas chromatography, thin layer, and paper chromatography. Protein restriction to 0.5 g/kg/24 hr effected a reversal of symptoms in both patients; protein loading (2.0 g/kg/24 hr) was tolerated for several days before nystagamus and ataxia were induced. The same level of protein loading in which phenylalanine was maintained at 150 mg/kg induced convulsions within 12 hr. The postulated pathway operative in this disorder is: phenylalanine → phenylethylamine → phenylethanolamine → mandelic aldehyde →mandelic acid. Two older male siblings were apparently affected and both died prior to 7 years of age. The pattern of inheritance in this family is that of a sex-linked recessive trait.

Alterations in red cell metabolism and oxygen transport produced by hypophosphatemia. S. TRAVIS, H. SUGERMAN, M. DELIVORIA-PAPADOPOULOS, L. MILLER, and F. OSKI. *Univ. of Pennsylvania Sch. of Med., Philadelphia, Penna.*

Intravenous hyperalimentation (IVH) is now employed in the management of patients with gastrointestinal disease or debility. After 7–10 days IVH therapy, five patients were found to have serum phosphorus ($P_i$) values of <1.0 mg/100 ml. Associated with this were striking changes in red cell glycolytic intermediates and ATP. These included a significant decrease in *glucose 6-phosphate, fructose 6-phosphate, 2,3-diphosphoglycerate,* 3-phosphoglycerate, and ATP, and a marked increase in the concentration of total triose phosphates (fructose diphosphate, glyceraldehyde 3-phosphate, and dehydroxyacetone phosphate). Associated with the decrease in 2, 3-DPG (mean 2.59 μmoles/ml RBC; normal 5.2 ± 0.4) and ATP (mean 0.41; normal 1.2 ± 0.2) was an increase in the affinity of hemoglobin for oxygen. The mean $P_{50}$ was 19.5 mm Hg (normal 27.0). On administration of phosphate or discontinuation of IVH, the abnormalities reverted to normal. There was a significant correlation between the serum $P_i$ concentration and the level of total triose phosphates illustrating the regulatory role of plasma $P_i$ in red cell metabolism at the glyceraldehyde 3-phosphate dehydrogenase step where it serves as a cofactor. These studies demonstrated that the serum $P_i$ influences oxygen transport and release to the tissues, and is an important factor in the delicate regulation of red cell metabolism. Thus, hypophosphatemia is not an innocuous laboratory finding, but can have clinical consequences.

Regulation of morphogenetic cellular behavior by surface-associated acid mucopolysaccharide-protein complexes (MPS). MERTON R. BERNFIELD and SHIB D. BANERJEE. *Stanford Univ. Sch. of Med., Stanford, Calif.*

We have previously shown that normal epithelial organogenesis requires the presence of MPS at the basal epithelial surface. The relationship of this MPS to differential cell proliferation and selective changes in shape of cells and cell groups was investigated in mouse embryo salivary glands in organ culture. Cellular proliferation was assessed by $^3$H-thymidine autoradiography and changes in tissue shape by sensitivity to cytochalasin B, an agent which reversibly disrupts the 50 Å intracellular contractile microfilaments. Ultrastructurally, microfilaments are unaltered by removal of surface MPS and surface materials are not affected by cytochalasin. Accumulation of newly synthesized MPS at the basal epithelial surface precedes the formation of lobules and is maximal at sites of incipient branching. Proliferating cells are subjacent to the sites of maximal MPS accumulation, even after loss of the branching pattern induced by cytochalasin. Cell proliferation occurs in a uniform zone near the surface under circumstances where surface MPS is equivalently distributed. Reappearance of lobules after removal of cytochalasin occurs at sites determined by the surface-associated material and is prevented by removing MPS from the epithelial surface. Removal of surface MPS causes normally branched organs to become "ball-like" rudiments which do not form in the presence of cytochalasin. Thus, surface-associated MPS determines sites of cellular proliferation and controls changes in tissue shape that result from integrated microfilament contractility. Since proliferation and change in shape are universal properties of cells, it is likely that abnormalities in surface-associated MPS are involved in clinically significant aberrations in organogenesis.

Immunoassay of serum digoxin levels in children: therapeutic implications. BERNARD L. MIRKIN and RICCI LARESE. *Univ. of Minnesota, Minneapolis, Minn.*

The uptake of digoxin (D) was studied in pediatric patients with congenital cardiac defects who were receiving therapeutic doses of D. The concentration of D in serum was determined by immunoassay (New Engl. J. Med., *281:* 1212 (1969)). All subjects received D twice daily for a minimum of 3 days before the investigation. Serum samples were obtained prior to and 1, 2, 4, 6, 8, and 12 hr after administration of D. The uptake of oral D was studied in seven patients receiving maintenance doses of 0.08–0.095 mg/kg/24 hr. D levels prior to administration of a maintenance dose averaged 2.9 mμg/ml. The initial peak concentration of D occurred 2 hr after the oral dose and ranged from 4.5–6.7 mμg/ml. A second elevation in D was also noted 4–8 hr after D administration in all seven subjects. In two patients, parenteral (IM) and oral uptake studies were performed. Maximum serum concentrations were obtained 1 hr after IM administration. The peak concentrations were similar to those obtained after an oral dose. D intoxication documented by EKG occurred in three children with D levels of 4.4, 6.8, and 10.0 mμg/ml. Several patients undergoing cardiac surgery developed elevations in serum D, which were two to five times that of preoperative levels. This increment was noted 1 hr after initiating extracorporeal circulation and persisted at least 2 hr after cessation of circulatory assistance. The elevated serum D concentration correlates with the period of extreme D sensitivity which has been noted postoperatively in such patients. These studies suggest that the determination of serum digoxin levels and their correlation with clinical response may prove useful in regulating digoxin therapy.

The heterogeneity of sphingomyelin lipidoses (Niemann-Pick disease). HOWARD R. SLOAN and DONALD S. FREDRICKSON. *NIH, Bethesda, Md.*

The advent of intrauterine diagnosis requires reevaluation of the several phenotypes of Niemann-Pick disease, divided by Crocker in 1961 (J. Neurochem., *7:* 69) into four groups, primarily on the basis of clinical manifestations. Sphingomyelin and *sphingomyelin-cleaving activity (Sphase)* have been determined in livers from 24 patients (five kindly provided by A. C. Crocker). The sphingomyelin contents (milligrams per gram dry weight) were: controls (12), 7 ± 2; type A (11), 255 ± 30; type B (6), 240 ± 35; type C (4), 25 ± 5; and type D (3), 20 ± 5. With sphingomyelin-$^{14}$C as substrate the Sphase activities of the livers were: controls (15), 7.5 ± 1.8 units (nmoles cleaved/mg protein/hr); type A (8), 0.33 ± 0.17 unit; type B (7), 0.75 ± 0.38; type C (4), 8.2 ± 2.1; and type D (3), 7.1 ± 2.3. Similar enzymatic results were obtained in preparations derived from skin fibroblasts: controls (17), 39 ± 5.6 units (nmoles cleaved/million cells/hr); type A (9), 0.15 ± 0.05; type B (5), 1.2 ± 0.51; type C (3), 32 ± 8.1; and type D (2) 41 ± 5.1.

Deficient Sphase is characteristic of only types A and B Niemann-Pick disease. Despite the apparent similarity of the enzymatic defects, A is invariably fatal while B is compatible with normal development. Neither chemical, biochemical, nor pathologic examinations can distinguish between these two types of Niemann-Pick disease. The key to phenotyping remains the clinical course of an affected sibling. Types C and D have a more protracted course, are incompatible with normal life, and appear to be due to mutations at loci quote different from those involved in types A and B Niemann-Pick disease.

Undifferentiated Wilm's tumors in infancy—induction of renal structures by organ culture. JOHN F. S. CROCKER and ROBERT L. VERNIER. *Univ. of Minnesota Hosps., Minneapolis, Minn.*

A group of renal tumors has been described in newborns which differ from Wilm's tumors by the absence of recognizable renal structures, the presence of only sheets of primitive cells, and the lack of metastases. Waisman *et al.* have emphasized that these children have a much better prognosis than children with other Wilm's tumors. The differences in the tumors in infants raise questions regarding the embryonic origin of the cells. In order to test the hypothesis that the tumors represent primitive undifferentiated metanephrogenic cells, we have studied tumors from two neonates and grown one by organ culture methods in an attempt to induce nephron formation in the tumor cells.

Grobstein and others have shown that metanephrogenic cells may be induced by fetal mouse dorsal brain or spinal cord. Small (approximately 1 sq mm) portions of tumor were placed in organ culture adjacent to fetal mouse brain for 48–96 hr. Tumor tissue adjacent to the neural tissue demonstrated palisading of cells within 48 hr and primitive nephronlike structures within 96 hr. Tubular and glomerular organelles were best seen in the areas of near contact between the tissues.

These studies demonstrate that this form of embryoma is of renal origin. Further investigation of this interesting tumor may give insight into the process of embryonic neoplasia.

Diagnosis of trisomy 22 with quinacrine fluorescence. HOPE H. PUNNETT, MILDRED L. KISTENMACHER, and MARIA A. TORO-SOLA. *Temple Univ. Sch. of Med. and St. Christopher's Hosp. for Children, Philadelphia, Penna.*

The possibility that trisomy 22 is a distinct clinical entity has been suggested by reports in the literature of 10 patients with similar congenital abnormalities and an extra G group chromosome, in whom the diagnosis of trisomy 21 or XYY has been excluded. It is now possible to distinguish chromosome 21 from 22 using the quinacrine fluorescence technique of Caspersson (Exp. Cell Res., *60:* 315 (1970)). The more brightly fluorescing G chromosome which occurs in triplicate in Down's syndrome has been identified as chromosome 21; chromosome 22 has weaker fluorescence (Caspersson *et al.:* Exp. Cell Res., *63:* 240 (1970)). The identification of chromosomes with similar morphology but different genetic content by fluorescence is an important adjunct to clinical diagnosis which has previously dictated the designation of extra chromosomes as 21 or 22.

We have studied two male children with an extra G group chromosome and similar congenital defects, including micrognathia, high arched palate, low set, large, floppy ears with cutaneous tags and/or pits, epicanthal folds, proximally inserted long thumbs, sandal gap of the feet, abnormalities of external genitalia, and undescended testes. *Case 1* (Punnett and Vaughan: 3rd Int. Congr. Hum. Genet. (abstracts)) at age 6 years is physically and mentally retarded. *Case 2* had failure to thrive and died at 6 weeks of age of infection. Preliminary fluorescence studies of the chromosomes of *case 2* suggest that he represents another case of trisomy 22. We are now restudying *case 1* and two other retarded, nonmongoloid children with extra G chromosomes, using fluorescence.

Effect of thyrotropin-releasing factor (TRF) on serum TSH: an approach to distinguishing hypothalamic from pituitary forms of idiopathic hypopituitary dwarfism. BRUCE H. COSTOM, MELVIN M. GRUMBACH, and SELNA L. KAPLAN. *Univ. of California, San Francisco, San Francisco, Calif.*

Recently, the molecular structure of ovine and porcine TRF (PCA-His-Pro-$NH_2$) has been reported and TRF synthesized. We suggested previously that the primary defect in some patients with idiopathic hypopituitarism is failure to secrete hypothalamic hypophysiotropic-releasing factors and not a pituitary defect. To test the hypothesis, synthetic TRF (500 $\mu$g) was given IV and venous samples obtained at 0, 5, 10, 20, 30, 45, 60, and 120 min for determination of serum TSH by radioimmunoassay in three groups: *I,* 11 normal children; *II,* eight with isolated growth hormone deficiency and normal thyroid function; *III,* nine with idiopathic hypopituitary dwarfism, including documented TSH deficiency. The mean fasting serum TSH value in *I* was 3.5 $\mu$U/ml and 3.3 $\mu$U/ml in *II,* with a brisk rise in serum TSH in both groups, peak levels of 10–40 $\mu$U/ml at 30–45 min, and a fall toward base line levels at 120 min. All *III* children had basal TSH levels of $<2.0$ $\mu$U/ml; one failed to respond to TRF; eight exhibited a rise in serum TSH with peak values comparable to *I* and *II.* The increase in TSH tended to be slower but more sustained than normal, with high values persisting at 120 min in many. The results indicate that the TRF test is useful in distinguishing between primary hypothalamic and pituitary forms of TSH deficiency, and that in many cases of insufficient TSH TRF deficiency exists. Further, they strongly suggest that deficiency of growth hormone-releasing factor (GRF), owing to a defect at the level of the hypothalamic neurosecretory neurone, is a common cause of idiopathic hypopituitary dwarfism. GRF, like TRF, appears to be a small peptide and when available may provide a practical substitute for HGH in the treatment of such patients.

Continuous negative chest wall pressure in hyaline membrane disease. D. VIDYASAGAR and VICTOR CHERNICK. *Univ. of Manitoba and Children's Hosp., Winnipeg, Canada.*

Gregory *et al.* (SPR, 1970) reported that in spontaneously breathing infants with hyaline membrane disease (HMD) a continuous positive airway pressure applied via an endotracheal tube elevated $Pa_{O_2}$ and reduced the alveolar-arterial oxygen tension difference ($A\text{-}aD_{O_2}$). We have modified the Air-Shields incubator-respirator so that a continuous negative pressure (5–15 cm $H_2O$) is applied to the chest wall (CNP) while the upper airway is at atmospheric pressure. Continuous positive pressure at the airway and CNP have a similar influence on transpulmonary pressure but CNP does not impede venous return. Eleven infants with severe HMD (initial $Pa_{O_2}$ 17–40 mm Hg; $FI_{O_2}$ 0.60–1.00) have been treated with CNP. Artificial ventilation and endotracheal intubation were avoided. In all infants $Pa_{O_2}$ increased (mean $Pa_{O_2}$ 88 mm Hg) and $A\text{-}aD_{O_2}$ decreased. It was possible to decrease $FI_{O_2}$ to less than 0.60 within an average of 40 hr after initiating treatment. All infants survived. CNP was also used in the treatment of 13 infants with severe HMD who required endotracheal intubation and artificial ventilation because of apnea or $Pa_{CO_2}$ >70 mm Hg. Again $Pa_{O_2}$ increased significantly and it was possible to decrease $FI_{O_2}$. Six of these infants died. CNP therefore resulted in an overall survival rate of 75%. The survival rate of infants with severe HMD treated with artificial ventilation has previously been 30% in our nursery. This study suggests that CNP is a very important adjunct to the treatment of severe HMD.

Correlations of ultrastructure and function in human subcutaneous adipose tissue. MILAN NOVAK, ELLEN MONKUS, and VICTORIANO PARDO. *Univ. of Miami Sch. of Med., Miami, Fla.* (Intr. by William W. Cleveland.)

On electron microscopic examination subcutaneous "white" adipose tissue cells from human neonates were markedly different from the large signet ring cells found in adults. Neonatal adipose cells had a thicker cytoplasmic layer and frequently more than one fat vacuole. Some cells contained numerous, closely packed, ovoid, or rod-shaped mitochondria. Although glycogen granules are not normally found in white adipose tissue, they were seen in certain cells of the neonate (0–4 hr). On light microscopy neonatal cells had a mean diameter of 42 mμ, compared with 99 μ in adults, and 20–50% contained more than one vacuole. Oxygen consumption of these cells is of particular interest, since respiratory enzymes are known to be localized on the mitochondria. *In vitro* oxygen consumption of isolated adipocytes was 0.18 ($\mu$M $O_2$/100 μg DNA/60 min) in neonatees ($n = 30$) and 0.28 in adults ($n = 12$). Since the mammalian diploid cell contains a constant amount of DNA, this implies that the individual neonatal adipose cell has an average oxygen consumption of about two-thirds that of an adult; however, it has only one-half the diameter and one-twelfth the volume of the adult cell. The morphologic and biochemical characteristics of neonatal adipose cells suggests that the subcutaneous adipose tissue in human neonates may have some important metabolic function, in addition to its role as source of substrates for energy processes.

Prenatal prediction of the respiratory distress syndrome (RDS). ROBERT C. BORER, JR., LOUIS GLUCK, ROGER K. FREEMAN, and MARIE V. KULOVICH. *Univ. of California, San Diego Sch. of Med., LaJolla, and Los Angeles County-Univ. of California Med. Ctr., Los Angeles, Calif.*

Fetal lung development was assessed by the phospholipids in amniotic fluid (PLAF). The surface-active phospholipids lecithin (Lec) and sphingomyelin (Sph) were separated by thin layer chromatography on precoated mylar strips, detected with bromothymol blue, and quantified by planimetry. One hundred twelve amniotic fluids from 96 patients (gestations from 12–43 weeks) were examined for Lec and Sph. A marked increase in the Lec/Sph concentration ratio occurred between 34 and 36 weeks of gestation. A PLAF (Lec)/(Sph) ratio below 1.50 defined an immature lung while a PLAF (Lec)/(Sph) ratio above 1.80 defined a mature fetal lung.

PLAF analysis was performed prospectively in 86 pregnancies with 3 or fewer days between amniocentesis and delivery. All fetuses assessed by PLAF to have mature lung function were correctly identified. RDS developed in 10 of 12 newborn infants in whom PLAF predicted immature lungs. Transitional lung development was predicted in seven fetuses of whom three associated infants had neonatal RDS. PLAF predicted 97% of neonatal lung function correctly compared with a 50% accuracy predicting fetal maturity by simultaneous amniotic fluid measures of creatinine and Nile blue sulfate. PLAF offers a useful clinical test for evaluating fetal lung maturity in high risk obstetrical patients.

The influence of intravascular coagulation in glomerulonephritis. JULIE R. INGELFINGER, ANTHONY P. FLETCHER, NORMA ALKJAERSIG, BARBARA R. COLE, and ALAN M. ROBSON. *Washington Univ. Sch. of Med., St. Louis, Mo.*

Evidence, mainly from animal studies, suggests that intrarenal (glomerular) fibrin deposition may occur during glomerulonephritis, and may contribute to disease chronicity. A new method for detecting intravascular fibrin deposition, plasma fibrinogen chromatography, has been employed in the study of 58 children with glomerulonephritis. The method detects the presence of specific fibrinogen-fibrin complexes and fibrinogen derivatives produced *in vivo* during intravascular fibrin deposition and/or its lysis and can detect clinically silent thrombosis (Fletcher *et al.*: Trans. Amer. Ass. Physicians, 1970). Plasma chromatographic abnormalities indicative of intravascular fibrin deposition were observed in each of the 35 children with acute glomerulonephritis. In 13 of these patients, serial studies later demonstrated evidence of fibrin lysis and the chromatographic abnormalities disappeared with clinical healing. Abnormal findings were observed in 20 of 24 children with biopsy-proven chronic glomerulonephritis and appeared to correlate with disease activity. Seven children with chronic glomerulonephritis and persistent chromatographic abnormalities received long term anticoagulation. In the four patients with rapidly progressive glomerulonephritis, remarkable clinical improvement followed anticoagulation; the remaining three patients have shown no progression of their disease since being anticoagulated. Our data are consistent with the hypothesis that under certain circumstances glomerular fibrin deposition plays a significant role in the progression of chronic glomerulonephritis and that this process may be ameliorated by anticoagulation.

Acute acquired immunologic deficiency due to lymphocytotoxin. SHIH-WEN HUANG, DORIS LATTOS, and RICHARD HONG. *Univ. of Wisconsin Med. Ctr., Madison, Wisc.*

It is known that lymphocytotoxin occurs in autoimmune diseases, infectious mononucleosis, immunization, and some viral infections, particularly rubella and rubeola. Its biologic significance is still incompletely defined and the association of acquired lymphopenia and exacerbation of clinical disease is seldom appreciated. We have observed five patients, 10–17 years, previously completely healthy who developed mild symptoms of malaise, sore throat, and fever. Worsening of symptoms occurred and lymphopenia was noted. One had scalded skin syndrome and oral candidiasis; another had Stevens-Johnson syndrome and a third died of overwhelming varicella. Two others had less severe symptomatology with pneumonitis and herpes gingivostomatitis. All five showed lymphocytotoxin with absolute counts of lymphocytes from 156–1000/cu mm. Lymphopenia disappeared gradually with improvement except in the fatal case. The earliest recovery was seen in 1 week but in one case neutropenia was also present and lymphopenia persisted for more than 2 months. Although the five cases manifested diverse acute symptomatology, they seemed to follow the same clinical course (*i.e.*, started with prolonged minor illness followed by the development of lymphocytotoxin and lymphopenia, super imposition of another viral or bacterial infection with the development of a fulminant picture). These cases may represent examples of a "transient, acquired immunity deficiency" triggered by viral infections. The original infecting agent was not defined; however, a rise in measles antibody titer (1:32 → 1:256) was shown in one patient.

A familial defect of chemotaxis. A new inborn error of neutrophil function. MICHAEL E. MILLER and THOMAS SCHON-

AUER. *Univ. of Pennsylvania Sch. of Med. and U. S. Naval Hosp., Philadelphia, Penna.*

Among the recognized causes of increased susceptibility to infection, the syndrome of chronic granulomatous disease is the only entity thus far associated with a primary, inborn error of neutrophil (PMN) function; *i.e.*, deficient bactericidal activity. We now describe an entirely different *familial* disorder of PMN function, a deficiency of chemotaxis. A 10-year-old Caucasian female with congenital icthyosis and a 9-year history of recalcitrant *T. rubum* infection was studied. Humoral and cellular immunity were normal. Study of PMNS from peripheral blood, or from standardized bone marrow suspensions of the child revealed normal phagocytic and bactericidal activities. However, marrow or peripheral blood PMNS from the child showed almost no chemotactic activity when stimulated by chemotactic factor (CF) generated from pooled, normal human serum by incubation with either gram-negative or gram-positive bacteria or preformed antigen-antibody complex. By contrast, when CF was generated from the patient's serum, normal chemotaxis occurred with PMNS from control subjects. An identical defect was found in peripheral blood PMNS from her father, who has been plagued with a lifetime history of recurrent boils and skin infections. Random mobility of PMNS from both child and father was normal when studied by the method of capillary tube migration. The precise defect in this family appears, therefore, to involve a specific abnormality of chemotactic receptors, rather than a generalized disorder of PMN mobility.

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