mon in the former group. Hypercholesterolemia is common in "normal" school children. Family studies in this population will lead to the detection of many adults with hyperlipoproteinemia and an increased probability of developing vascular disease.

The stale-fish syndrome: A new metabolic disorder associated with trimethylaminuria. JAMES R. HUMBERT, KEITH B. HAMMOND, WM. E. HATHAWAY, JEAN MARCOUX, and DONOUGH O'BRIEN. *Univ. of Colorado Med. Ctr., Denver, Colo.*

In a six-year-old girl with a history of recurrent pulmonary infections and a mild bleeding tendency, a strikingly fishy smell was detected in the sweat and urine. She resembled a Turner syndrome phenotypically and had splenomegaly. Chromosomes were normal. Hematocrit was 30–34%, WBC 3,150–9,000/cu mm, platelet count 150,000–250,000/cu mm. Red blood cell (RBC) survival studies showed a slightly decreased half-time due to splenic sequestration; RBC volume was normal, but plasma volume was increased (60 ml/k). RBC's showed increased resistance to filtration through a 3 μ pore filter; this finding suggested increased cell membrane rigidity. Bleeding time was prolonged, platelet aggregation to collagen and adhesiveness to glass beads was decreased. Leukocyte adhesiveness to glass was decreased in 16 of 23 tests performed; other tests of leukocyte function were normal. The patient's mother, sister, maternal grandmother and maternal uncle also showed decreased leukocyte adhesiveness, but no other defects. Examination of the patient's urine by gas chromatography demonstrated the presence of excessive trimethylamine (TMA). This substance, a metabolite of choline, has a characteristic odor of decaying fish. When an oral choline load was given to the patient, she excreted large amounts of TMA in her urine as compared to a normal control. In addition, oral loading doses of TMA produced the fishy smell in the patient but not in the controls. This patient represents a new clinical and metabolic syndrome in which a disorder of choline metabolism, possibly due to TMA oxidase deficiency, may explain the defective membrane function of platelets, neutrophils and RBC's, and the accumulation of trimethylamine.

Net acid balance (NAB) in metabolic acidosis. ROBERT W. WINTERS, JAMES C. CHAN, EUGENE L. KLENK, GAIL S. WILLIAMS, and RALPH B. DELL. *Columbia Univ. Coll. of Phys. and Surg., New York, N. Y.*

In previous studies from this laboratory the principles for the determination of the balance (intake minus output) of non-carbonic, non-metabolizable, non-metabolized acid (net acid) have been validated and applied to healthy, growing infants. To determine NAB requires the independent measurement of all components of net acid intake (sulfuric and organic acid production plus net acid generated by skeletal mineralization minus net base intake) and net acid output (renal net acid excretion).

In the present study NAB was determined over 3–8 day balance periods in 11 infants developing ($n = 3$) or recovering from ($n = 8$) diarrhea, ileostomy, renal or late metabolic acidosis. Four studies on infants having no significant change in acid-base status over the period of study served as controls. NAB was significantly positive during the development of acidosis and negative during recovery. A close ($r > 0.9$) linear relationship was found between NAB (mEq/kg) and the measured change in blood base excess (Δ BE, mEq/l) over the period of study such that the virtual volume of retained net base or acid approximated 50% of the body weight suggesting considerable involvement of non-ECF buffers. To our knowledge this study represents the first complete quantitative measurement of the total magnitude and the separate components of net base retained (during recovery) or net acid retained (during development) in metabolic acidosis.

Opposing metabolic effects of theophylline and dibutyryl cyclic AMP. DAVID BAUM, CAROL STOWERS, and JAMES FRENCH. *Univ. of Wash. Sch. of Med., Seattle, Wash.*

Both dibutyryl cyclic AMP (DCAMP) and theophylline have been used to increase cyclic AMP (CAMP) levels in studies suggesting CAMP to be a link between catecholamines and their metabolic effects. However, DCAMP and CAMP have different effects on *in vitro* lipolysis. Since theophylline increases CAMP levels by inhibiting its phosphodiesterase, theophylline and DCAMP could effect lipolysis differently. To provide an *in vivo* evaluation of the effects of DCAMP and theophylline upon lipolysis, comparison of glycerol and free fatty acid (FFA) levels was made in puppies receiving these agents under basal conditions and during epinephrine (E) stimulation.

Theophylline infusions given to six puppies resulted in plasma glycerol (160 ± 36% mean control; mean ± S.E.) and FFA (175 ± 32%) increases, while DCAMP given to five others produced falls in glycerol (−23 ± 6%) and FFA (−24 ± 9%) levels. Prolonged glycerol (245 ± 33%) and FFA (160 ± 36%) elevations were sustained in six puppies during 75-minute E infusions. Five puppies receiving similar E infusions with similar glycerol and FFA elevations had added increases in glycerol (147 ± 41%) and FFA (85 ± 19%) when theophylline was administered after 30 minutes of E. However, when DCAMP was added instead of theophylline in five other animals receiving E, glycerol (−108 ± 16%) and FFA (−82 ± 17%) levels fell.

These observations demonstrate that DCAMP and theophylline produce opposite effects on basal and catecholamine-stimulated lipolysis in the puppy, and suggest the need for added caution in the use of these agents as tools for the study of CAMP.

Propionyl-CoA carboxylase deficiency (propionicacidemia): A cause of non-ketotic hyperglycinemia. MAURICE J. MAHONEY, Y. EDWARD HSIA, and LEON E. ROSENBERG. *Yale Univ. Sch. of Med., New Haven, Conn.*

Propionyl-CoA carboxylase deficiency is now thought to be the primary enzyme defect in the disease previously called "ketotic hyperglycinemia". In a 10 month old girl with mental retardation and seizures, who never showed clinical attacks of ketoacidosis while eating a usual infant diet, we found hyperglycinuria, modest hyperglycinemia (2.4–2.9 mg%; normal 1.6 ± 0.3 mg%), and an impaired plasma clearance of glycine after an oral load. Studies of glycine catabolism by leukocytes in vitro were normal but a severe defect in propionate oxidation was present. In addition, propionyl-CoA carboxylase activity in extracts of cultured fibroblasts was less than 1% of normal. To investigate propionate metabolism in vivo, oral amino acid loads were given. Isoleucine, a propionyl-CoA precursor, led to vomiting, lethargy, ketonuria, hyperlactatemia, and hyperammonemia within 1 day. Valine, which is metabolized to methylmalonyl-CoA, the product of the deficient enzyme, caused hyperammonemia but no symptoms, no ketonuria, and no increase in lactate over a five day period. Plasma glycine remained between 3.1 and 5.1 mg% during the oral isoleucine and valine loads. Thus, propionyl-CoA carboxylase deficiency need not cause clinical attacks of ketoacidosis and must be considered in any infant with even slightly elevated plasma and urine glycine concentrations.