Neonatal screening for inherited metabolic disorders

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Neonatal screening for inherited metabolic disordersaims at the earliest possible recognition of disordersin order to intervene. sometimes this intervention includeseffective treatment ~o prevent the most seriousconsequences of the disorder. although such therapy ispresently available for only a small proportion of the••veral thousands known genetic disorders. other objective.of screening are to provide recurrence risk information toparents. determine incidence in a population. reduce exposureto harmful drugs or environment. and provide forresearch purposes.In 1962 Guthrie described a bacterial growth inhibitionassay for measuring blood phenylalanine concentrationto screen for phenylketonuria (PKU) that requiredonly a few DROPs of blood spotted on filter paper anddired. New born screening for genetic disorders otherthan PKU was consequently introduced. The.nature andnumber of newborn screening tests vary widely in differentlocalities and may include some or all of the followinglcordblood. newborn nursery blood. newborn follow-upblood • and/or newborn follow-up urine. The three main.ethods of screening aret the microbiological, the chrcxa-.atographic and the chemical method.Newborn Whole-blood specimens are collected on filterpaper after heel stick after the infant has begun to ingestprotein and prior to discharge from the nursery ,usually day 3 to 5. Bacterial inhibition assays by usingdried blood discS are developed by Guthrie for screeningprogramms to detect some metabolic disordrs by measuringthe concentrations of metabolies in the blood. Forexample, measuring concentrations of phenylalanine forPKO, of galactose for galactosemia, of leucine for maplesyruP urine disease, of methionine for one of the threeaetiologies of hornoCystinemia and of tyrosine for tyrosinemia.It must be emphasized that a single abnormal screeningtest result does not establish a specific diagnosiS.Screening tests usually differ from diagnostic tests inregard to specificity, sensitivity and other importantcharacteristics. The abnormality reflected by the pOsitivesc~eening test result may have more than one possible9eoetic or nongenetic cause, and the aetiology in eachparticular case must be ascertained. Moreover, transientabnormalities and artifacts must be distinguished. Confirmationof PKU'and other inborn errors of met•abolismrequires additional blood specimens as well as urine testin9.If these further tests yield abnormal results, specificdiagnostic evaluation must be carried out before anappropriate plan of management can be formulated.The goal of screening for that group is mainly toprevent irreversable brain damage and consequent mentalretardation in the

affected neonates.Newborn urine specimens from the diaper are collectedby the parents on filter paper when the infant is 3 to5 weeks old using a kit given to tbem at the time tbenewborn leaves tbe bospital. Filter paper urine specimenscan be analyzed either by unidimensional paper or thinlayercbromatograpby. Some metabolic disorders and cOnditionsdetected by screening newborn urine are cystinuria,biatidinemia, Hartnup disease, metbylmalonic aciduria ,ar9ininosuccinic aciduria, cystatbioninuria, nonketotichyperglycinemia and hyperprolinemia. Some conditions areprobably benign including. Hartnup disease and hyperprolinemia.Two of the disorders involve defects in renal transportrather than inborn errors of metabolism. viz •• oyatinuriaand Hartnup disease. In most other disorders involvingaminoaciduria an extrarenal metabolic disturbanceleads to accumulation in plasma of one or more aminoacida.which are filtered in amounts that exceed the reabsorptioncapacity of the nephron. A variety of confirmatory teatsare available. These include apot tests of urine forspecific compounds, two-dimensional chromatography, .leotrophoresisand gas chromatography - mass spectrometry,The goal of screening for that group is also mainlyto prevent or minimize irreversable damage.In addition to tests for classical inborn errors of••tabolism newborn genetic screening may include testsfor some or all of the following genetic disorderss con-9enital hypothyroidism, congenital adrenal hyperplasia,cystic fibrosis, Ouchenne muscular dystrophy, familialhyper cholesterolemia, adenosine deaminase (ADA) deficiency,oC- antitrypsim deficiency, glucose -6- phos- . pbate dehydrogenase (G-6-PD) deficiency and si~kle cellThe goals of that group are variable. For congenitalhypothyroidism, congenital adrenal hyperplasia and familialhypercholesterolemia, the goal is to prevent orminimize irreversable damage. For ADA deficiency andsickle cell anemia, the earlier the diagnosis is establi’h~,.the 1Il0reoutcome may be improved. For OC’1- antitryp.indeficiency and G-6-PO deficiency, the screening may beUDdertaken to reduce to harmful drugs or enviroment inthe future. Lastly, for ouchenne muscular dystrophy andcy.tic fibrosis, the goal of screening is to educate parent.on recurrence risks.