Louisiana Medicaid

Provider Update

Volume 25, Issue 4 **July/August 2008**

LaCHIP Affordable Plan Update

The Department of Health and Hospitals started enrolling children in the LaCHIP Affordable Plan on May 19, 2008. In just over 6 weeks, 622 Louisiana children had been approved for this new program. The LaCHIP Affordable Plan is offered to families with income that exceeds the limits for the no cost LaCHIP program. Children may enroll in the program during their annual renewal process as well as through new applications. LaCHIP Affordable Plan benefits are administered by the State of Louisiana Office of Group Benefits (OGB); therefore claims are not processed by Unisys.

Since some children were eligible for Medicaid benefits in the past, many may still have their old Medicaid eligibility cards. Health care providers must verify coverage through the LaCHIP Affordable Plan by asking to see the child's current benefits eligibility ID card. When eligibility status is checked in MEVS, REVS, and e-MEVS, a message will inform providers that the child is enrolled in the LaCHIP Affordable Plan, as well as provide OGB contact information for billing. A message will also be generated, if a request for other billing activities, such as prior authorization, is received by Unisys. It will inform both the provider and recipient that the child is enrolled in the LaCHIP Affordable Plan, and prior authorization requests are not administered by Unisys. The notice will refer recipients and providers to OGB member services for billing information.

For more information about LaCHIP and the Affordable Plan, visit www.lachip.org and click on the LaCHIP Affordable Plan link. You may also call 1-877-2LaCHIP (252-2447) for information.

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Direct Service Worker Registry

The Department of Health and Hospitals (DHH) has established a registry of direct service workers (DSW) as directed by Act 306 of the 2005 Regular Legislative Session. A direct service worker is an unlicensed person who provides face-to-face personal care or other services and support to the elderly or persons with disabilities to enhance their well-being. The registry maintains the names of individuals who, either by work experience or training, are eligible to register as direct service workers. The registry also allows employers to verify if a potential employee is in good standing with no findings of abuse, neglect, misappropriation or exploitation against them. Providers are required to verify the status of workers, via the registry, prior to making an offer of employment.

A Rule was promulgated in the November 20, 2006 *Louisiana Register* which outlined the training requirements for direct service workers. Intermediate care facilities for the developmentally disabled, personal care attendant, supervised independent living, respite, adult day care and adult day health care providers must be in compliance with these requirements by November 20, 2008. Payment for dates of service after November 20, 2008 may be denied and/or the provider agency may be sanctioned if claims are submitted for services provided by a worker who is not on the DSW registry.

The registry may be accessed online at www.labenfa.com. Click on the link for the DSW registry. When the screen opens, enter the Social Security number of the worker and click on "Search". There is also a hyperlink to the DSW registry on the DHH Health Standards home page at http://www.dhh.state.la.us/offices/?ID=112 along with other useful information on the registry including a list of trainers who have been approved to teach the DSW training curriculum. Providers are **not** allowed to offer DSW training to workers unless the curriculum has been approved by DHH.

Providers who have submitted the names of workers who meet the criteria for being grandfathered to the registry or who have successfully completed the DSW training curriculum for placement on the registry and they have not yet been added, may contact Cathy Oglesby at the DSW registry at (225) 295-8575. For questions concerning approval of a training curriculum or other registry requirements, please contact Candace Andrus, RN, Program Manager at (225) 342-5794.

Addition of Immunization Administration Codes Policy Clarification and Claim Recycles

Since the initial notice concerning the implementation of additional immunization administration procedure codes was published, work has been completed to change the system logic to accommodate billing changes. Effective for dates of service on or after October 1, 2007, initial programming was completed to allow the billing of these procedure codes on incoming claims. In an effort to assist providers with resubmitting claims for correct payment, we have taken steps to systematically recycle claims related to this implementation.

These immunization administration procedure codes, which include 90465-90468, 90473, and 90474, must be billed appropriately for claims payment. Please refer to the Current Procedural Terminology (CPT) coding book for additional instruction on using these codes. The fall 2007 annual provider workshops included information regarding the correct usage of these immunization administration codes. These training materials are located on the LA Medicaid web site and can be accessed using the following links: www.lamedicaid.com, link - > Training, link - > Provider Training Packets, links - > 2007 Training Materials for KIDMED and Professional Services.

On November 6, 2007, the initial recycle of denied claims related to the implementation of these codes were processed. However, some claims were denied as duplicates because the recycled claims were processed at the same time as claims that had been resubmitted by providers. It should be noted that any claims billed with incorrect administration codes were not recycled. Providers are required to resubmit these claims using correct administration codes for the vaccines administered.

Policy and system changes were made to allow providers to "split bill" initial administration code/detail line and each additional administration code/detail line. As long as the initial administration claim has been previously paid, each additional administration code claim should process correctly.

Medicaid policy requires providers to bill administration codes and detail lines that accompany these codes in correct sequence (i.e., initial administration code followed by detail line, and each additional administration code(s) followed by detail lines). However, since providers are allowed to bill private payers without code sequencing, claims will not deny if billed out of sequence **as long as** all components are present and billed with correct administration codes **and** the initial administration code/detail processes with or prior to each additional administration code(s)/detail. Claim denials that were billed out of sequence **will not** be recycled since these claims submissions did not follow existing Medicaid policy. Providers are responsible for resubmitting any denials that fall within this category.

A second systematic claims recycle was performed in June 2008. This recycle included claims with dates of service between January 1, 2006 and September 30, 2007 that were billed with additional immunization administration procedure codes and were denied for error edits 210 (Provider not certified for this procedure), 232 (Procedure/Type of Service not covered by Program), 234 (P/F Age Restriction), and 299 (Procedure/Drug not covered by Medicaid).

A third claims recycle will be performed after the second recycle (claims with dates of service January 2006 through September 2007) have been processed. This recycle will include claims that denied as duplicates in the original recycle of November 6, 2007. When these recycles are completed, providers should reconcile their accounts to determine if they need to resubmit or void any claims in order to rectify any other outstanding issues regarding the payment of their immunization claims. For claims beyond the one year timely filing period, contact your Provider Relations Field Representative to coordinate receipt of these claims by September 30, 2008 for processing.

Please contact Unisys Provider Relations at (800) 473-2783 or (225) 924-5040 if you have any questions.

Pneumococcal Vaccine Clarification

Providers should take note that there are two CPT codes for pneumococcal vaccines and the appropriate code must be used when submitting a claim.

- When providing the recommended childhood pneumococcal **conjugate** vaccine (PCV) which is included in the Office of Public Health and the Advisory Committee on Immunization Practices (ACIP) Immunization Schedules, code 90669 should be billed. This vaccine is available from the Vaccines for Children Program.
- If the pneumococcal **polysaccharide** vaccine (PPV) is administered to immunosuppressed recipients over the age of 2 years, code 90732 should be billed. Medicaid will reimburse the provider for the administration as well as for the vaccine as this vaccine is not currently available from the Vaccines for Children Program. Medical record documentation must reflect the need for the use of the PPV vaccine.

Psychiatric Services

Effective for dates of service on or after October 1, 2007, Louisiana Medicaid began reimbursing professional service providers for specified Current Procedural Terminology (CPT) procedure codes pertaining to psychiatric services (current codes 90801-90802, 90804-90815, 96101) delivered in the office or other outpatient facility setting as outlined in the *Current Procedural Terminology* manual. This policy is applicable to physician services furnished through the Professional Services Program and mental health services provided in rural health clinics (RHC) and federally qualified health centers (FQHCs). RHCs and FQHCs should enter the appropriate psychiatric procedure codes as encounter detail lines when submitting claims for these services. The following guidelines are applicable for the submission of claims using the specified CPT procedure codes for psychiatric services:

- Psychiatric Diagnostic or Evaluative Interview Procedures (current code range 90801-90802) and designated Psychiatric Therapeutic Procedures (current code range 90804-90815) are counted toward the outpatient visit service limit allowed per calendar year for adult recipients (age 21 and older). Providers should assist recipients in the management of their limited yearly outpatient visits.

- Psychiatric Diagnostic or Evaluative Interview Procedures (either code 90801 or 90802) are reimbursable once per 365 days per attending provider.

- Psychological Testing (current code 96101) is reimbursable once per 365 days per attending provider. Providers should bill all applicable units of service related to this procedure code on one date of service and not divide the units amongst multiple dates of service or claim lines. Procedure code 96101 is **not** counted toward the outpatient visit service limit allowed per calendar year for adult recipients (age 21 and older).

- If nationally approved changes occur to CPT codes for psychiatric services at a future date, providers are to follow the most accurate coding available for covered services for that particular date of service, unless otherwise directed.

Adjunct Services

Effective for dates of service on and after October 21, 2007, Louisiana Medicaid reimburses providers for the following Current Procedural Terminology (CPT) procedure codes for adjunct services: CPT codes 99050 (Services at times other than regularly scheduled office hours…) and 99051 (Services at regularly scheduled evening, weekend, or holiday hours…). These procedures are outlined in the *Current Procedural Terminology* manual under "Special Services, Procedures and Reports".

The intent of this policy is to facilitate recipient access to services during non-typical hours primarily to reduce the inappropriate use of the hospital emergency department. The reimbursement for the adjunct codes is intended to assist with coverage of the additional administrative costs associated with staffing during these times. The intent is not for providers to alter their existing business hours for the purpose of maximizing reimbursement.

These adjunct codes are reimbursed in addition to the reimbursement for outpatient evaluation and management services when the services are rendered in settings other than hospital emergency departments between the hours of 5 p.m. and 8 a.m. Monday through Friday, on weekends (12 a.m. Saturday through midnight on Sunday), and State/Governor proclaimed legal holidays (12 a.m. through midnight). Refer to the *Louisiana Medicaid Professional Services Fee Schedule* on the Medicaid website for reimbursement information relative to these codes. Providers are instructed to bill usual and customary charges.

These adjunct codes are never reported alone, but rather in addition to another code or codes describing the service related to that patient visit or encounter. The following examples illustrate the appropriate use of adjunct procedure codes.

- If the existing office hours are Monday through Friday from 8 a.m. to5 p.m. and the physician treats the patient in the office at 7 p.m., then the provider may report the appropriate basic service (E/M visit code or encounter) and adjunct code (99050).

- If a patient is seen in the office on Saturday during existing office hours, then the provider may report the appropriate basic service (E/M visit code or encounter) and adjunct code (99051).

Rural health clinics (RHC) and federally qualified health centers (FQHC) will receive fee-for-service reimbursement for the adjunct services codes separate from, but in addition to, the PPS reimbursement for the associated encounter (T1015). The adjunct codes are not reimbursable for dental encounters. For those services that meet the guidelines outlined in this policy, the encounter and required detail line(s) for services provided to the recipient on a date of service should be reported as directed in current RHC/FQHC policy. If appropriate, the adjunct services code may also be reported as a detail line, but it **may not be submitted as the only "detail line" for an encounter**. The adjunct code will be reimbursed fee-for-service in addition to the payment for the encounter.

Documentation in the medical record relative to this reimbursement must include the time that the services were rendered. Should there be a post payment review of claims, providers may also be asked to submit documentation regarding the existing office hours during the timeframe being reviewed.

CommunityCARE Policy Revision
Post-Authorization of Emergency Room Visits

CommunityCARE policy requires post-authorization from the primary care physician (PCP) for the two lowest levels of emergency room (ER) services (CPT codes 99281 and 99282) and associated services. Currently, requests for post-authorization must be submitted to the PCP, along with appropriate documentation of presenting symptoms, the next business day following the date of service. Effective for dates of service on or after July 1, 2008, the time frame for submitting requests for post-authorization of ER visits has been extended from next business day following the date of service to 10 calendar days following the date of service.

Questions regarding CommunityCARE policy should be directed to Unisys Provider Relations at (800) 473-2783, or the CommunityCARE Hotline at (800) 259-4444.

CommunityCARE and NPI

CommunityCARE primary care physicians (PCPs) currently use their 7-digit Louisiana Medicaid legacy provider ID when issuing CommunityCARE referrals/authorizations. Effective immediately, PCPs should begin placing both their legacy provider ID **AND** the National Provider Identifier (NPI) registered with Louisiana Medicaid on all written referrals/authorizations. PCPs should continue to use only their 7-digit legacy ID when issuing ER post-authorizations via the e-RA system. PCPs enrolled as physician groups, rural health clinics (RHCs), or federally qualified health centers (FQHCs) should remember that enrollees are linked to the entire practice, not the individual physicians, and must issue referrals/authorizations with the legacy provider ID and NPI registered for the physician group, RHC, or FQHC.

Personal Care, Respite and SIL Providers

Moratorium on Licensing of Personal Care Attendant, Respite and Supervised Independent Living Providers

During the 2008 Regular Legislative Session, the Louisiana Legislature passed Act 328 (House Bill Number 1224) which places a moratorium on the licensure of providers for Personal Care Attendant (PCA), Supervised Independent Living (SIL) and Respite Care services. The moratorium, which is subject to approval by the Centers for Medicare and Medicaid Services, shall apply to any new applications received on or after July 1, 2008 and shall remain in effect until July 2010. The legislation does provide for exceptions in certain circumstances. Act 328 can be viewed at http://www.legis.state.la.us/ .

LT-PCS and Hospice Providers

Policy Clarification for Long Term-Personal Care Services and Hospice

Recipients may not concurrently receive Long Term-Personal Care Services (LT-PCS) and Hospice as personal care services is a component of hospice care. If a recipient is receiving hospice services and wishes to receive LT-PCS, the hospice services must be discontinued. Conversely, if a LT-PCS recipient elects to receive hospice care, the LT-PCS must be discontinued. Concurrent billing of these services for the same recipient does not comply with Medicaid policy and is considered to be duplicate billing. Providers who engage in this practice may be subject to recoupment of payments and/or sanctions.

All Providers

Preventive Medicine/KIDMED Reimbursement Changes

Reimbursement rates for preventive medicine services, including KIDMED medical screenings, were increased effective for dates of service on or after October 15, 2007 as part of the 2007 reimbursement changes and a system adjustment appeared on the RA dated June 17, 2008. If your claims for these services do not appear in the June 17, 2008 RA, then your billed charges were less than or equal to the fee on file prior to the rate increase. Claims where billed charges were less than or equal to the fee on file will not have systematic adjustments. For proper claim adjustment policy and procedures, providers should review the '2007 KIDMED Provider Training Manual', pages 30, 38 and/or 64 or the '2007 Professional Services Provider Training Manual', pages 121 or 128, as appropriate. DHH policy states that providers are to enter their usual and customary charges for the services rendered. You may contact Unisys Provider Relations at (800) 473-2783 if you have any questions.

Adjustment of Circumcision Claims

System changes have been made to correct age editing associated with CPT code 54150 for circumcisions. Claims that incorrectly denied for age restriction (Error 234) beginning with dates of service January 1, 2007 have been systematically adjusted and the adjustments are included in the June 24, 2008 remittance. For further questions, please contact Unisys Provider Relations at (800) 473-2783.

Providers of Newborn Care: CPT Code 99436

CPT procedure code 99436, "Attendance at delivery…stabilization of newborn", has been made payable effective for dates of service on or after June 1, 2008. Any policies directing providers to use other CPT codes for this service are no longer in effect. Providers are to follow CPT guidelines regarding which services may or may not be reported in addition to this code.

A Brief Overview of Drug Clearance and Dosing Considerations for Renal and Hepatic Insufficiency

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Clearance

Clearance is the volume of serum, plasma, or blood from which the drug is completely removed, or cleared, in a given time period. The two most common units used in measuring clearance are milliliters per minute (mL/min) or liters per hour (L/h); hence, clearance measures volume per unit time. Therefore, clearance is considered a major pharmacokinetic parameter because it determines the maintenance dose that is required to obtain a given steady-state serum concentration.

When we think of drug clearance, what should come to mind is total body clearance (CL_T), which encompasses the two major routes of drug elimination from the body: renal clearance (CL_R) and hepatic clearance (CL_H). ($CL_T = CL_R + CL_H$). However, since there are other contributing sources of drug clearance in the body, for example, biliary clearance and gut clearance, total body clearance may be defined as renal clearance plus non-renal clearance. ($CL_T = CL_R + CL_{NR}$)

Hepatic Clearance

Hepatic clearance of a drug is determined by blood flow to the liver, and the efficiency of the liver in extracting the drug from the blood stream. Efficiency is dependent upon protein binding, intrinsic clearance of the liver for the particular drug, and liver blood flow. An extraction ratio (ER) is the fraction of drug removed from the body by an organ, such as the liver. For drugs with high extraction ratios, the rate-limiting step for metabolism is how much drug can be delivered to the liver. By definition, a drug with a high extraction ratio would have an ER > 0.7 and therefore the liver is very efficient at removing the drug from the blood. This is of relevance since any condition that could decrease liver blood flow, such as congestive heart failure or liver disease, would disrupt hepatic clearance of high extraction drugs. However, the hepatic clearance of drugs with high extraction ratios does not change much when protein-binding displacement occurs. Some common drugs with high hepatic extraction ratios are lidocaine, morphine, propranolol, and most tricylic antidepressants. In contrast, for low extraction ratio drugs, blood flow to the liver is not rate limiting for metabolism. Therefore, a decreased blood flow to the liver, secondary to hepatic or cardiac disease, would not affect metabolism as much, because the capacity to metabolize the drug is very low. The degree of protein binding affects the hepatic clearance of drugs with low extraction ratios. When drug interactions cause drug molecules to become unattached from protein complexes, more unbound drug is able to leave the vascular system and enter the hepatocytes where they become metabolized and increase hepatic clearance.

Another factor that may affect the hepatic clearance of low extraction ratio drugs is the induction or inhibition of cytochrome P-450 enzyme system, which may increase or decrease the drug's intrinsic clearance (the ability of the enzyme to metabolize the drug) and alter its hepatic clearance. Some examples of drugs with low hepatic extraction ratios are valproic acid, warfarin, and phenytoin.

Most of the metabolic processes within the liver are classified as either Phase I reactions or Phase II reactions. Drugs may undergo Phase I metabolism followed by Phase II reactions. Phase I reactions are referred to as preparatory reactions and include hydrolysis, oxidation, and reduction reactions. Phase II reactions may be classified as conjugation reactions and result in the formation of acetates, glucoronides, and sulfates.

The two primary purposes for liver metabolism are to inactivate the drug and make it more water-soluble than the parent drug, facilitating elimination by the kidney.

The cytochrome p450 enzyme is the major hepatic enzyme system responsible for Phase I metabolism. The cytochrome p450 enzymes most important in drug metabolism are Cytochrome p450-1 (CYP1), CYP2, and CYP3. In addition to their action on specific drug substrates, they can also be induced or inhibited by other drugs, and as such, cause an increase or decrease in the plasma concentration of the drug that it metabolizes. The table below lists some common CYP isoenzymes and their drug substrates.

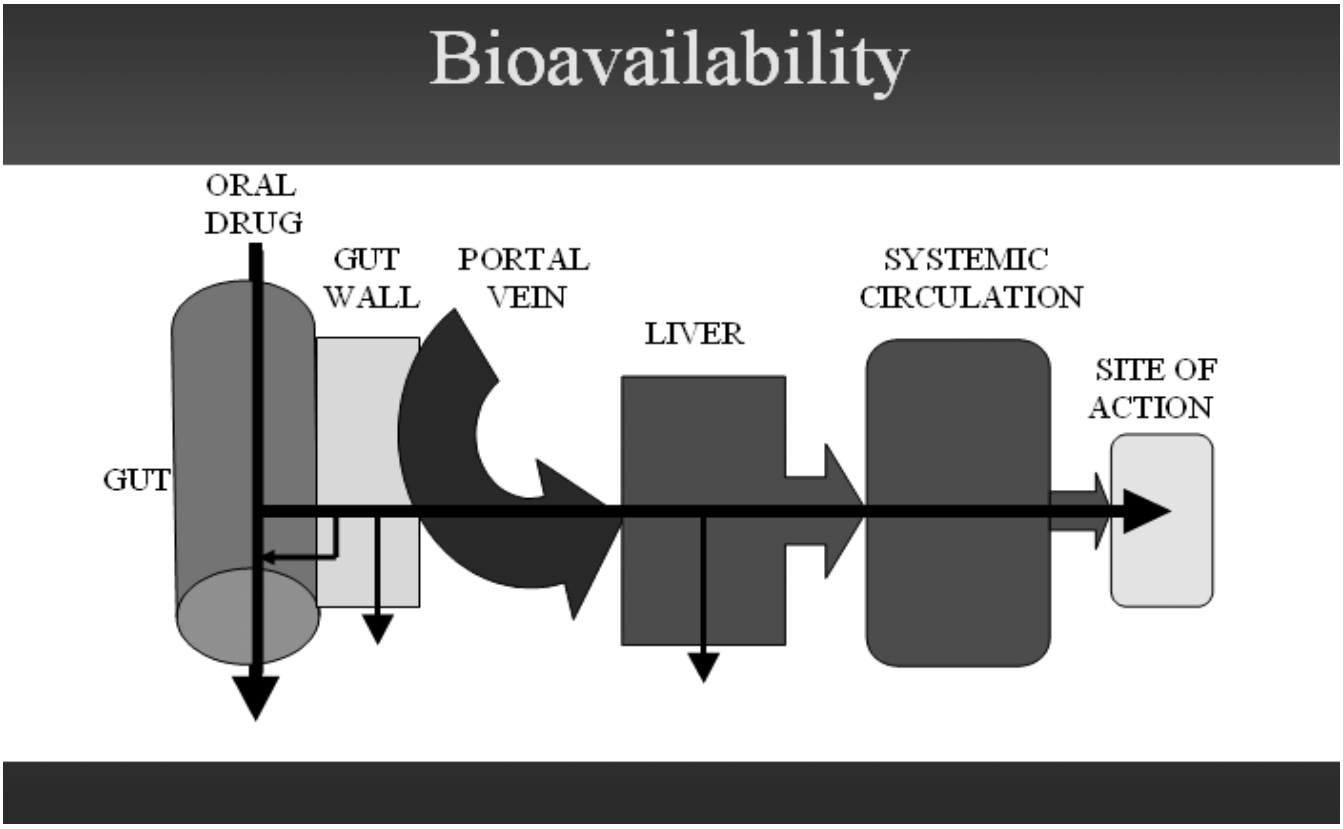
Drug-Metabolizing Enzymes and Selected Inhibitors and Inducers

ISOENZYME	DRUG	INHIBITORS	INDUCERS
CYP1A2	Caffeine, tacrine, theophylline, lidocaine, R-warfarin	Cimetidine, ciprofloxacin, erythromycin, tacrine	Omeprazole, smoking
CYP2B6	Cocaine, ifosfamide, cyclophosphamide	Chloramphenicol	Phenobarbital
CYP2C9/10	S-warfarin, phenytoin, tolbutamide, Diclofenac, piroxicam	Amiodarone, fluconazole, lovastatin	Rifampin, phenobarbital
CYP2C19	Diazepam, omeprazole, mephenytoin	Fluvoxamine, fluoxetine, Omeprazole, felbamate	Rifampin, phenobarbital
CYP2D6	Codeine, haloperidol, dextromethorphan, Tricyclic antidepressants, phenothiazines, metoprolol, propranolol, risperidone, encainide, paroxetine, sertraline, venlafaxine	Quinidine, fluoxetine, sertraline, amiodarone, propoxyphene	
CYP2E1	Acetaminophen, alcohol	Disulfiram	Isoniazid, alcohol
CYP3A3/4	Nifedipine, verapamil, cyclosporine, carbamazepine, terfenadine, cisapride, astemizole, tacrolimus, midazolam, alfentanil, diazepam, verapamil, loratadine, ifosfamide, cyclophosphamide	Erythromycin, cimetidine, clarithromycin, fluvoxamine, fluoxetine, ketoconazole, itraconazole, grapefruit juice, metronidazole, ritonavir, indinavir, mibefradil	Rifampin, phenytoin, carbamazepine

Table 9-1, p114, Dipiro, Concepts in Clinical Pharmacokinetics, 4th edition

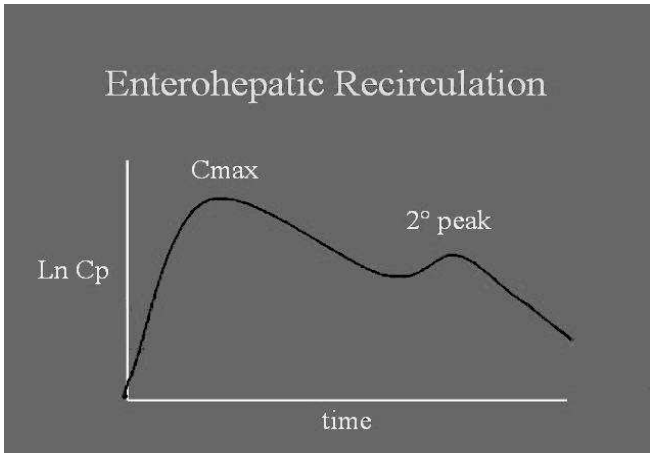
Drugs administered extravascularly release molecules from the dosage form which then pass through several biologic layers in order to reach the vascular system. In certain cases, the entire dose may not enter the systemic circulation. One common example of this is when a tablet is taken orally and does not dissolve completely; part of the dose is eliminated in the stool, thereby not benefitting the patient. The *bioavailability* of the drug is the fraction of the administered dose that is delivered to the systemic circulation.

When the extravascular dose is administered orally, a portion of the dose may be removed by transport proteins of the gastrointestinal tract wall or liver or may be metabolized by enzymes before it reaches the systemic circulation. This commonly occurs with drugs that are subject to gastrointestinal tract wall metabolism or that have a high liver extraction ratio. The loss of drug from these combined processes is known as *the first pass effect*, because these drugs are taken orally and must pass through the gastrointestinal tract wall and into the portal circulation of the liver before reaching the systemic circulation. Also to note is the effect of transport proteins, present in the gastrointestinal tract walls. These carriers can actively pump drug molecules that already have been absorbed back into the lumen of the gastrointestinal tract. The primary transport protein that interferes with drug absorption by this mechanism is known as P-glycoprotein (PGP). For example, if a drug administered orally has a hepatic extraction ratio of 0.75, a high liver ER, and is 100% absorbed from the gastrointestinal tract, only 25% of the original dose will enter the systemic circulation. To avoid this *first pass* phenomenon, the drug should be given by another route of administration.



Enterohepatic Recirculation

In addition to metabolism, the liver may remove drug from the blood by excretion of the parent compound or metabolite into the bile. The bile is then secreted into the gallbladder and periodically released into the intestines. The drug can then be reabsorbed back into the portal vein and again pass through the liver into the systemic circulation, causing a secondary peak in the plasma concentration-time curve.



Dipiro's Concepts in Clinical Pharmacokinetics, 4th Ed.

A common drug exposure consult with Poison Control Centers, prolonged toxicity of a medication caused by enterohepatic recirculation, can be safely managed in a hospital setting utilizing multiple-dose activated charcoal and close monitoring of drug levels until the culprit drug level is in therapeutic range. In a typical phenytoin toxicity, multiple-dose activated charcoal decreases serum phenytoin levels more rapidly, but has not been shown to shorten clinical course.

Renal Clearance

Because of the increasing incidence of acute and chronic renal failure, assessment of renal function has an important role in patient care. Also, because of the kidney's diverse roles - excretory, metabolic, and endocrine - assessment of renal function is necessary to maintain body homeostasis and metabolic activities.

Renal excretion of a drug is dependent on glomerular filtration, tubular secretion, and tubular reabsorption. All three of these processes must be considered in order to provide patients with appropriate dosing regimens of drugs that are renally cleared.

Patients who develop renal disease remain relatively asymptomatic until impairment has progressed to the point that systemic manifestations become evident. Diabetes mellitus and hypertension are the two most common causes of end-stage kidney disease, and as renal function declines, patients may experience development or exacerbation of related symptoms.

Presentation of Chronic Kidney Disease (CKD)

	Early CKD (Stages 1-2)	Late CKD (Stages 3-4)
General Symptoms	The patient may not appear in distress. Not likely present	Patient may have edema The patient may have fatigue, malaise, pruritus, nausea
Signs	Not likely present	May present with fluid retention, anemia, dyspnea, reduced urine output
Laboratory tests	Microalbuminuria Mildly-elevated S_{cr} and BUN	Persistent proteinuria Reduced GFR or CL_{cr} Abnormal urinalysis Renal ultrasound shows reduced kidney mass

BUN, blood urea nitrogen; CLcr, creatinine clearance; GFR, glomerular filtration rate; Scr, serum creatinine concentration.
Pharmacotherapy, 6th edition, p804

Qualitative and Semiquantitative Indices of Kidney Function

The National Kidney Foundation currently recommends that all patients with CKD, and those at increased risk for CKD, undergo comprehensive laboratory assessment for: (1) serum creatinine to estimate GFR, (2) albumin:creatinine ratio in a spot urine specimen, (3) examination of urine sediment for red and white blood cells, (4) renal ultrasonagraphy, (5) serum electrolytes including sodium, potassium, chloride, and bicarbonate, (6) urine pH, and (7) urine specific gravity. These tests can be followed as early markers of declining renal function.

Additional qualitative measures of renal function are: X-ray, CT scans, MRI, biopsy. These are useful in determining the etiology of kidney disease.

Cystatin C is the newest, proposed, endogenous marker of renal function. Cystatin C is a 13.3 kDa cysteine protease inhibitor which is produced by all nucleated cells, and its production appears to be independent of gender, age, body mass, nutritional status and inflammation. It is filtered, but has some reabsorption and catabolism in the proximal tubules. One advantage is that it appears to be more sensitive to early declines in renal function in comparison to serum creatinine. Proposed reference ranges are 0.54 to 1.21 mg/L in adults and 0.70 to 1.38 mg/L in children older than one year of age.

Physical exam may detect signs and symptoms of possible kidney dysfunction that could otherwise be overlooked by testing. Some examples of signs and symptoms detected by physical exam are: enlarged kidneys, distended bladder, and fluid overload, which may lead to increased weight, edema of lower extremities, CHF, pulmonary congestion, or increased blood pressure.

Quantitative Measures of Kidney Function

Quantitative measures of kidney function are most useful for the design of appropriate dosage regimens. Glomerular filtration rate (GFR) is considered to be the best overall indicator of renal function. Therefore, the need for GFR quantitation is of utmost importance. Inulin, radiolabeled markers (e.g., ^{125}I-iothalamate and ^{99m}Tc-DTPA), and contrast agents (e.g., iothalmate and iohexol) all have favorable characteristics toward quantitatively measuring kidney function. However, the high cost of some, demanding blood and urine collection and testing, make these underutilized clinically.

Following is a table comparing these quantitative measures of kidney function.

Sensitivity and Clinical Utility of Renal Function Tests

	Accuracy	Clinical Utility	Cost
Inulin Clearance	++++	+	$$$$
Radiolabeled Markers	+++	+	$$$
Nonisotopic contrast agents	+++	++	$$$
Creatinine clearance	++	+++	$$
Serum creatinine	+	++++	$

+, least acceptable; ++, adequate; +++, better; ++++, best. Pharmacotherapy, 6th ed. Table 41-4, p769.

Estimation of Creatinine Clearance

Creatinine is a metabolic product of creatine in muscle (normal Scr 0.5-1.5 mg/dl).
Creatinine is eliminated by both filtration and tubular secretion. Tubular secretion accounts for about 10% of total creatinine elimination in patients with normal renal function and up to 100% in patients with severe renal insufficiency. Therefore, as renal function declines, creatinine clearance becomes a less and less accurate measure of GFR.

Creatinine clearance is a good indicator of changes in glomerular filtration but not of changes in secretion or reabsorption. The most common clinical measure of renal function is creatinine clearance (CrCL) which is commonly estimated by the Cockcroft-Gault equation (normal CrCL being 120 ml/min). This formula is mostly used for estimating creatinine clearance in adults with stable renal function.

Cockcroft-Gault Equation

$$CrCL = \frac{(140 - age)(IBW)}{72 * SCr} \quad (\times 0.85 \text{ for females})$$

Males
Ideal Body Weight in Kg (IBW) = 50 + 2.3 * (inches over 5 feet tall)

Females
Ideal Body Weight in Kg (IBW) = 45.5 + 2.3 * (inches over 5 feet tall)

Modification of Diet in Renal Disease (MDRD) Study

The MDRD equation came from a study evaluating GFR in patients with CKD (GFR < 90 mL/min). Although it appears to have a weaker correlation with GFR than the Cockcroft-Gault equation, some healthcare practitioners encourage the use in patients without CKD. Therefore current evidence suggests that the MDRD equation should be reserved for patients with GFR < 90 mL/min.

MDRD Equations

GFR (ml/min/1.73m^2)

$=170 \times (Scr)^{-0.999} \times (age)^{-0.176} \times (SUN)^{-0.170} \times (Alb)^{+0.318} \times (0.762 \text{ if female}) \times (1.180 \text{ if black})$

SUN = serum urea nitrogen concentration

This is the 6-variable MDRD equation that takes into account three biochemical markers: serum creatinine (SCr), serum albumin (Alb), and serum urea nitrogen (SUN). Since not all patients have these laboratory tests ordered on a general basis, it becomes difficult to use the 6-variable MDRD equation, for lack of necessary values to plug into the equation.

A more simplified equation, the 4-variable MDRD equation, was developed to allow for simplicity in calculations. It also includes laboratory values more readily available on patient's charts.

GFR (ml/min/1.73m^2)

$= 186 \times (Scr)^{-1.154} \times (age)^{-0.203} \times (0.742 \text{ if female}) \times (1.210 \text{ if black})$

While there are advantages to using the MDRD equations for estimating GFR, further investigations are needed to determine statistical differences between results obtained using Cockcroft-Gault versus MDRD equations for dosage recommendations in chronic kidney disease patients.

24 Hour Urine Collection & Midpoint SCr

This method is the most accurate clinical measure of creatinine clearance because it is an actual calculation of creatinine clearance. It assumes that serum creatinine is at a steady-state level. However, patients with unstable renal function and those with hepatic disease may pose problems toward creatinine clearance calculations. Studies by Hull and colleagues and Caregaro and associates confirmed that measured creatinine clearance overestimated GFR by 50% in patients with hepatic disease, which could be due to increased tubular secretion of creatinine.

$$CrCL(mL/min) = \frac{\text{urine vol.(ml)} * \text{urine creatinine (mg/ml)}}{14.4 * Scr(mg/dL)}$$

Salazar and Corcoran Equations

This equation is a more accurate estimation of GFR than the Cockcroft-Gault equation for obese patients greater than 30% over ideal body weight.

Males

$$CrCL = \frac{(137 - age) * [(0.285 * ABW) + (12.1 * height^2)]}{51 * Scr}$$

Females

$$CrCL = \frac{(146 - age) * [(0.287 * ABW) + (9.74 * height^2)]}{60 * Scr}$$

Actual Body Weight in kilograms (ABW)
Height is the height in meters.

Also for 1 week old infants to 18 year old adolescents is the Schwartz equation, developed by GJ Schwartz and colleagues. The equation estimates creatinine clearance based on the child's age and length.

Schwartz Equation

$$CrCL = \frac{length\ (cm) * k}{Scr}$$

k = 0.45 for infants 1 to 52 weeks old
k = 0.55 for children 1 to 13 years old
k = 0.55 for adolescent females 13-18 years old
k = 0.7 for adolescent males 13-18 years old

Dosing Consideration for Diminished Renal Clearance

Renal insufficiency is accompanied by alterations in many other organs and systems within the body. These alterations result in the clinical manifestations of renal insufficiency including electrolyte disturbances, anemia, hyperlipidemia, hypertension, gastrointestinal changes, etc. Some of these changes may affect the disposition (ADME) of certain medications in the patient with renal insufficiency. Therefore, many dosage regimens require individualization based on the degree of the patient's renal insufficiency and other accompanying factors.

Steps to Adjust Drug Dosages for Patients with Renal Insufficiency

Step 1	Obtain history and relevant Demographic/clinical information	Record demographic information, obtain past medical history including history of renal disease, and record current laboratory information (e.g., serum creatinine)
Step 2	Estimate creatinine clearance	Use equation (e.g., Cockcroft-Gault) to estimate creatinine clearance, or calculate creatinine clearance from timed urine collection
Step 3	Review current medications	Identify drugs for which individualization of the treatment regimen will be necessary
Step 4	Calculate individualized treatment regimen	Determine treatment goals; calculate dosage regimen based on pharmacokinetic characteristics of the drug and the patient's renal function
Step 5	Monitoring	Monitor parameters of drug response and toxicity; monitor drugs levels if available/applicable
Step 6	Revise regimen	Adjust regimen based on drug response or change in patient status (including renal function) as warranted

Pharmacotherapy, 6th ed., Table 48-6, p 924

In conclusion, assessing a patient's hepatic and renal function status plays a vital role in providing the patient with individualized and patient-specific pharmaceutical care.

References:

1. Dipiro JT, Talbert RL, Yee GC, et al. Pharmacotherapy: A Pathophysiologic Approach. (6th ed). New York, NY; McGraw-Hill; 2005.

2. Bauer, LA. Clinical Pharmacokinetic and Pharmacodynamic Concepts. Applied Clinical Pharmacokinetics. New York, NY; McGraw-Hill; 2001; 1:7-21.

3. Dipiro JT, Spruill WJ, Wade WE, et al. Concepts in clinical pharmacokinetics. Bethesda, MD;American Society of Health System Pharmacists;2005. Lessons 1-3,6,7,9.

4. Dowling TC, Comstock TJ. Quantification of Renal Function. Pharmacotherapy: a Pathophysiologic Approach.. (6th ed). New York, NY; McGraw-Hill; 2005; 41:761-777.

5. Bauer, LA. Clinical Pharmacokinetics and Pharmacodynamics. Pharmacotherapy: a Pathophysiologic Approach. (6th ed). New York, NY; McGraw-Hill; 2005; 5:51-72.

6. Gibaldi M, Boyes RN, Feldman S. Influence of first pass effect on availability of drugs on oral administration. J Pharm Sci 1971; 60:1338-1340.

7. Wu C-Y, Benet LZ, Hebert MF et al. Differentiation of absorption and firstpass gut and hepatic metabolism in humans: Studies with cyclosporine. Clin Pharmacol Ther 1995; 58:492-497.

8. Wyte CD, Berk WA. Severe oral phenytoin overdose does not cause cardiovascular morbidity. Ann Emerg Med 1991; 20:508-512.

9. Heard K, Dart RC. Chemical and Biological Agents: Phenytoin. The 5 Minute Toxicology Consult. Philadelphia, PA;Lippincott Williams & Wilkens. 2000:578-579.

10. Kidd, RS. Renal Clearance Lecture. Department of Biopharmaceutical Sciences- Bernard J. Dunn School of Pharmacy; Shenandoah University. 2007.

11. Mueller BA. Acute Renal Failure. Pharmacotherapy: A Pathophysiologic Approach. (6th ed). New York, NY; McGraw-Hill; 2005;42:781-796.

12. Levey AS, Coresh J, Balk E, et al. National Kidney Foundation practice guidelines for chronic kidney disease: Evaluation, classification, and stratification. Ann Intern Med 2003; 139:137-147.

13. Cockroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. Nephron 1976; 16:31-41.

14. Levey AS, et al. Annals of Internal Med. 1999; 130:461-470.

15. Levey AS, et al. J Am Soc Nephrol 2000; 11:155A.

16. Hull JH, Hak LJ, Koch GC, et al. Influence of range of renal function and liver disease on predictability of creatinine clearance. Clin Pharmacol Ther 1981; 29:516-521.

17. Caregaro L, Menon F, Angeli P, et al. Limitations of serum creatinine level and creatinine clearance as filtration markers in cirrhosis. Arch Intern Med 1994; 154:201-205.

18. Randers E. Erlandsen EJ. Serum cystatin C as an endogenous marker of the renal function-A review. Clin Chem Lab Med 1999; 37:389-395.

19. Price CP, Finney H. Developments in the assessment of glomerular filtration rate. Clin Chim Acta 2000; 297:55-66.

20. Schwartz GJ, Brion LP, Spitzer A. The use of plasma creatinine concentration for estimating glomerular filtration rate in infants, children, and adolescents. Pediatr Clin North Am 1987; 34:571-590.

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