identical to a normal serum phosphorus concentration in blood, about 3.3 mg/dL. If the serum phosphate concentration rises above this level, phosphaturia occurs, and the serum phosphorus declines to 3.3 mg/dL. If the serum phosphate concentration declines below 3.3 mg/dL, filtered phosphate is entirely reabsorbed, and urinary phosphate excretion declines to zero.

The TmP can be considered as a dam in the phosphate reservoir, over which excess phosphate spills and whose level controls the concentration of serum phosphorus. The TmP is not fixed but can be moved upward or downward, depending on metabolic needs and prevailing metabolic conditions (described later).

The TRP or $FE_{Pi}$ can be readily calculated, and the TmP can be derived from the nomogram of Bijvoet, which is shown in Figure 72-9. This process proves enormously useful in clinical practice because it is the central starting point for determining whether hypophosphatemia is principally renal or nonrenal in origin.

## Parathyroid Hormone and Phosphatonins

PTH has long been appreciated to be phosphaturic; it lowers the TmP or, more accurately, inhibits proximal renal tubular phosphate reabsorption. This characteristic explains the hypophosphatemia associated with primary and secondary hyperparathyroidism and the hyperphosphatemia associated with hypoparathyroid states. Excessive PTH lowers the TmP, whereas low PTH values allow the TmP to rise to supranormal levels.

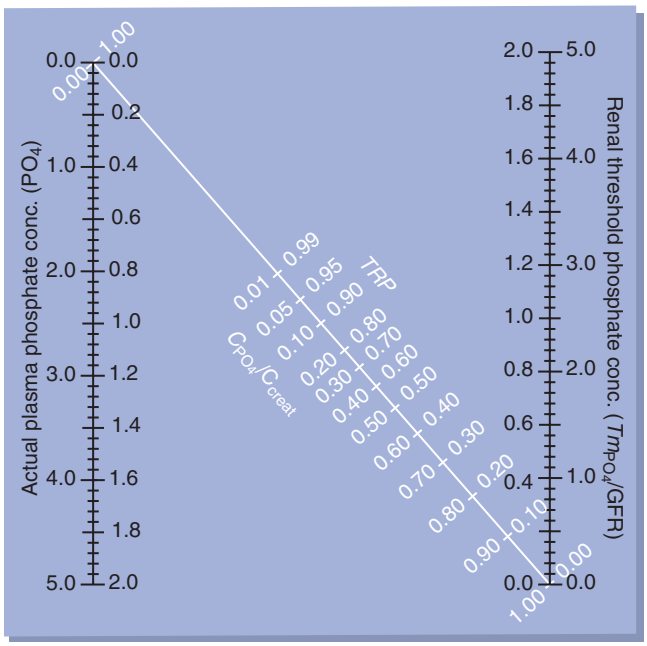


**FIGURE 72-9** Nomogram shows the tubular maximum for the phosphorus glomerular filtration rate (TmP-GFR). It allows conversion of the fractional excretion of phosphorus (or its inverse, the tubular reabsorption of filtered phosphate [TRP]) into the TmP-GFR. The TRP is calculated, and a line is drawn extending from the serum phosphorus level *(left vertical line)*, through the TRP *(middle diagonal line)*, to the *right vertical line*, which represents the TmP/GFR. TmP values are provided in millimolar and milligram per deciliter units. TmP values below 1.0 mmol or 2.5 mg/dL are abnormal and indicate phosphaturia. $C_{creat}$, Creatinine concentration; $C_{PO4}$, phosphate concentration. (From Walton RJ, Bijvoet OL: Nomogram for derivation of renal threshold phosphate concentration, Lancet 2:309–310, 1975.)

The TmP level is regulated by other factors.. For example, experimental dietary phosphorus deprivation in laboratory animals and humans leads to a PTH-independent increase in the TmP, and high-phosphate feeding results in a PTH-independent decline in the TmP. For decades, investigators in this area have postulated the existence of a phosphaturic hormones called *phosphatonins,* one of which is fibroblast growth factor-23 (FGF-23). This field has progressed rapidly over the past decade, but much remains to be worked out. The main physiologic points are that a hormonal system independent of PTH also regulates renal phosphorus handling and that the kidney is the prime regulatory organ for phosphate homeostasis.

## REGULATION OF SERUM MAGNESIUM

Magnesium is a divalent cation. Magnesium homeostasis parallels phosphorus homeostasis. Magnesium and phosphate are principally intracellular, with concentrations inside the cell that far exceed those outside the cell. Both substances govern key intracellular regulatory processes. In the case of magnesium, these processes include fundamental events such as DNA replication and transcription, translation of RNA, the use of adenosine triphosphate as an energy source, and regulated peptide hormone secretion.

Both substances are abundant inside all kinds of cells. Because they are well supplied in vegetarian and carnivorous diets, little evolutionary pressure exists to develop a complex regulatory network, and as with phosphate, serum magnesium concentrations are not tightly regulated. Because magnesium is principally intracellular, measurement of serum levels may provide false estimates of actual total body and intracellular magnesium status. Because magnesium is essential for fundamental processes such as gene transcription and cellular energy use, life-threatening magnesium deficiency is often unrecognized because its symptoms are frustratingly nonspecific: weakness, respirator dependence, diffuses neurologic syndromes (including seizures), and cardiovascular collapse.

Magnesium has a molecular weight of 24 (1 mole = 24 g), and because it is divalent, one equivalent is 12 g. Blood magnesium measurements are often provided in milligrams per deciliter (mg/dL) or milliequivalents per liter (mEq/L); oral magnesium supplements are expressed in milligrams per tablet or milliequivalents per vial; and urinary magnesium excretion values are given in milliequivalents or milligrams per 24 hours. Constructing a black box for magnesium is helpful (Fig. 72-10), and the magnesium values are provided in milligram and milliequivalent units.

As with phosphorus, magnesium has quantitatively important interfaces with the intestine, skeleton, intracellular supplies, and kidney. At the level of the intestine, magnesium is widely available in normal diets, and regulation is limited; the body absorbs about one third of what is ingested. In normal circumstances, dietary magnesium is abundant, absorption is ample, and magnesium deficiency does not occur. However, deficiency may occur with alcoholism, in intensive care unit settings in which adequate nutrition often is not provided, or with intestinal malabsorption.

At the level of the skeleton, magnesium is incorporated into the hydroxyapatite crystal as mineralization of osteoid occurs, and it is released by osteoclastic bone resorption (see Figs. 72-1 and 72-3). In quantitative terms, these fluxes are small.