clinical example of supervised machine learning with convolutional neural networks is the histopathological detection of lymph node metastases in breast cancer patients (Table 488-1).

The three remaining types of machine learning have not been as widely applied to clinical problems to date, but we believe this is likely to shift in coming years. These include unsupervised learning, semi-supervised learning, and reinforcement learning. Unsupervised learning, in contrast to supervised learning, encompasses methods that use *unlabeled* input data, where the goal is to discover the "structure" present in the data. A researcher may use unsupervised methods to determine whether or not the data lie on a low-dimensional "manifold" that is "embedded" in a higher-dimensional space. For example, a researcher may obtain gene-expression measurements from more than 20,000 protein-coding genes for a large group of asthma patients and then "project" each patient into a lower-dimensional space to visualize and understand structure present in the dataset, or may group asthma patients by similarity across all gene-expression values. Classical linear methods include principal component analysis (PCA) and contemporary nonlinear approaches include uniform manifold and approximation and projection (UMAP) (Table 488-1). Semi-supervised learning is a hybrid between supervised and unsupervised learning, with methods that use *both* labeled data and unlabeled data. These algorithms exploit the (often low-dimensional) structure of unlabeled data to learn better models than may be possible in a purely supervised setting where labeled data may be scarce. Finally, reinforcement learning is a distinct subfield of machine learning that focuses on optimizing the iterative decision-making of an "agent" that is equipped with a cumulative "reward" function, and thus must navigate a trade-off between exploration and exploitation of its environment, distinct from the other three subfields of machine learning where the entire learning signal (i.e., dataset) is presented at once. This approach to learning has been successful in teaching computers to play games at world-expert levels (e.g., Google's AlphaGo Zero).

Modern Medical Machine Learning