

fibrils. In health they are fine, delicate, smooth, and clear-cut in outline, like a thread of silk, and stain *internally*, with a uniform clear coffee-colored tint. In disease these become *granular* and *wrinkled* in outline, as though the firm smooth consistence of the fibre underwent a granulation with softening, and lost its cleanness of contour. Here and there, too, small irregular swellings are seen. *Internal changes* : These are very distinct in many specimens, and can leave no doubt in our mind that chemical alterations are taking place within the fibril. The most striking feature is discontinuous and uneven staining. The fine and delicate collateral or terminal fibril, which stained (if it stained at all) of a uniform clear coffee tint, is irregularly stained along its course, in some parts the pallor and want of staining almost indicating that the fibre is broken into separate fragments, till the most careful focussing and search will reveal the unstained intermediate parts. These streaks of discontinuous and irregular staining are so remarkably frequent and conspicuous in several specimens we have examined, that we have no doubt they represent what is a real pathological change going on within these naked nerve fibrils.

Correlation of Clinical with Pathological.

These two sets of changes in the naked collateral and terminal fibrils (internal and external) constitute, to our mind, the other element of earliest and recognisable change in the field of conjunction, whereby the pathways for the passage of nervous excitations from neuron to neuron, and from one complex group of neurons (nerve centre) to another, is thus rendered difficult or impossible. Both these sets of changes in the field of conjunction are, as far as the present author is aware, only recognisable with the use of Golgi's method and its modifications, the author having used for this purpose his own modification, published in the *British Medical Journal*, March, 1894. Our work in this line leads us to the view that it is here, in the changes in the anatomico-physiological junction

regions, in this field of conjunction, we find the earliest dynamical changes, and that these represent, on the psychical side, the diminished capacity of the neurons to be excitable to presentative sensorial stimulations (the equivalent of the softenings and obliterations of the protoplasmic contact-granules), and a diminished permeability in the pathways of nerve currents issuing from one neuron by its nervous process and its terminals to another neuron in the cortical area, the psychical counterpart of which would be a *slowness in the arousing of associated images, and delay of reaction time*. Finally, as regards the earlier and subtler nutritive changes within the cell body and nucleus. The physiology of nutrition is in the nerve cell elaborated to a high degree, and each nerve centre of this or that part of the central nervous system has its own intrinsic nutritive rhythm. In the alcoholic brain, the early and subtler changes affect, not merely the field of conjunction (produce *dynamical effects as far as the reception and transmission of nerve currents are concerned*), but the *trophic or nutritive focus* (cell body and nucleus) of each individual neuron. The *advanced* trophic changes, especially as shown in the polymorphic elements, we have already described and portrayed. The cells in this region are also favourable for the study of the *commencing* trophic changes in the neuron. The methods we have used for this purpose are four in number : (a) sublimate and alcohol fixing, and staining with Toluidine blue ; (b) frozen sections, stained with aniline blue-black ; (c) Nissl's methylene-blue method ; (d) Golgi's method. Each of these helps to supplement the other.

Commencing trophic changes in the cell bodies and nucleus. We are of opinion that these also are definite and recognisable, and further, that in certain respects (*viz.*, as elucidated by the aniline blue-black method) these have been abundantly described and figured by Bevan Lewis ("Text-book of Mental Disease," 1890). For our own part we would add certain details obtained by our investigations with the three other methods named, *viz.*, the Toluidine, Nissl, and Golgi methods. The first and second of these methods are useful for showing certain fine intra-

cellular and intra-nuclear changes which the aniline method does not help to show, while the third enables us to apply a certain test to identify what fragments of nerve-protoplasm still remain. Fortunately for us, not all the cells show equally advanced changes in the alcoholic brain, for while some show moderately advanced intra-cellular changes at once recognisable as such, others (neighbouring cells) on whom the stress—for some reason or other—has not fallen so severely will show us appearances consistent with health, or only faint indications of a commencing departure from the normal. This graduation of pathological changes helps us greatly, for it offers an intrinsic control method of distinct value. Keeping this in mind the earliest changes we see are: (a) Deeper staining, of cell body and protoplasmic processes (with aniline, Toluidine, and Nissl's method). (b) Swelling and softening (indistinctness of outline) of the intra-cellular chromatin rods, and increased intensity of their staining (with Nissl's method). (c) Thickening of intra-nuclear reticulum, and increased prominence of nucleoli (with Toluidine method). (d) Increase of the normal golden cell pigment which is present at or near the basal portion of the cell (with all three methods). We are not as yet in a position to state which of these four changes occurs first, or whether any two or more of them occur simultaneously; but certainly they all occur in the *earliest* stages, when the contemporaneous changes in the finest nervo-protoplasmic regions which we have before detailed occur. To us these four points mentioned indicate two things, viz.: (a) that there is increased functional activity in the cell body, and (b) that this is productive of a degradation in the form of nerve energy, the physical accompaniment of which is a softening and alteration of the blue chromatin rods and granules, and their gradual replacement by yellowish pigment. The increase and progress of pigmentation is the equivalent of the onset and progress of *degradation* in the functional activity of the cell—the replacement of living protoplasm by non-living pigmentary product as in senile decay and in chronic epilepsy: here (in chronic alcoholism) it is attended with the other intra-cellular changes of a more subtle kind,

viz., intensity of staining of cell protoplasm, and swelling and softening with increased staining of the intra-cellular chromatin rods and granules, the reservoirs for the building up and storage of nerve energy under high tension, *i.e.*, the pabulum of the cell. The earliest lesions, therefore, of alcoholism are of a nutritive and dynamical type, dynamical in so far as it affects the protoplasmic granules on the one hand and the nerve collaterals and terminals on the other which enter into the constitution of the nervo-protoplasmic plexuses (fields of conjunction) in the brain; and nutritional in so far as it affects the protoplasm and nucleus of the cell body and therefore interferes with the higher evolution and elaboration of nerve energy, and especially with the quasi-spontaneous or voluntary vivifications of former memory images which is the peculiar property of the cortical neuron during its period of increased functional activity.

But this is not the only result of the alcoholic lesion. Another outcome of it is the next group of symptoms.

Clinico-Psychological.

(b) Diminished faculty of *attention* and *volition*.

Here there is a slightly deeper involvement we think. In the mild amnesia we have considered there is the loss of *re-vivification* or re-rousing of past experienced mental images and states; here, even when the objective images are present, the capacity of receiving and registering them in the mind is diminished. On the psychical side this is, in other words, diminished power of attention. It may be that in one case this is mainly limited to the visual, in another to the olfactory, in a third to the kinæsthetic, or in a fourth, &c., to the auditory, &c., sphere, and that in other cases it extends to all these. The faculty of attention is an early one in the infant, and we think it is simpler in character and grade than volition. At least two sensorial elements enter into the composition of attention, viz.: (a) the special or local sense which is being active; (b) its special kinæsthetic auxiliary. The mode of evolution of each