The results are shown in Table III ("satisfactory" indicates that the disease is apparently arrested and no tubercle bacilli are found in the sputum). In the group where

TABLE III.—Results

	Satis- factory	Unsatis- factory	Died	Total
No alternative treatment:				
Pneumectomy	25 } 37	8 } 12	7 } 9	40 } 58
Lobectomy	12	4	2	18
Surgical alternative possible:				
Pneumectomy	4 } 12	1 } 2	1 } 1	5 } 15
Lobectomy	8	1	1	10
Conservative treatment possible:				
Pneumectomy		1		1
Lobectomy	4			4
Totals	53	15	10	78

resection was the only possible method of treatment 64% can be classified as satisfactory, 15% were dead, and 21% unsatisfactory. Where alternative surgical treatment was possible 80% were satisfactory, 7% dead, and 13% unsatisfactory.

Causes of Death.—Table IV shows the causes of death. In four cases the surgeon did not have a chance—in two the respiratory reserve was too low, but in both the possibility was recognized before operation; in the other two the operation was satisfactory, but the patients' resistance was not sufficient to deal with the remaining disease.

TABLE IV.—Causes of Death

Operative deaths	6
Lack of respiratory reserve	2
Directly following operation	2
Blood-transfusion disaster	1
Oedema of larynx	1
Post-operative deaths (failure of treatment) ..	..

Unsatisfactory Results.—In 15 cases classified as unsatisfactory the patients were still alive at the end of the period of observation. Three cases are in serious danger, and one is well except for a small sinus. Of the others the deterioration on the other side is slight in four cases, and there is a reasonable prospect that it will settle down.

TABLE V.—Unsatisfactory Results

Pneumectomy (obligatory)	8	Pneumectomy (choice)	1
Persistent sinus	1	Deterioration other lung	1
Deterioration other lung	4		
T.B. + ; ? cause	1		
Respiratory cripples	2		
Lobectomy (obligatory)	4	Lobectomy (choice)	1
Deterioration other lung	1	T.B. + same lung	1
T.B. + ; cause ?	1		
Spread other lung	2		
For Localized Disease: Pneumectomy	1		
Deterioration other lung	..		

Conclusions

Any investigator into the results of and indications for any particular mechanical form of treatment for pulmonary tuberculosis is confronted with the difficulty that if he allows a long enough time to elapse to enable him to reach a definite conclusion the method of treatment may have improved so much that the immediate mortality figures are out of date. In all probability the mortality figures obtained here would be reduced if the operations were performed to-day; but if advanced cases are tackled the mortality will be appreciable. Most cases dealt with have been followed for a minimum of two years.

It can be claimed, however, that this paper does confirm the opinion that in resection we have a method by which many cases unsuitable for any other form of surgical treatment can be rendered quiescent; a high proportion (64% of 58 cases) who would be dead or hopeless invalids have been rendered quiescent with a

good prospect of ultimate arrest of the disease. Resection has not yet proved itself superior to surgical collapse therapy in upper-zone disease.

The cases dealt with are mainly those which have shown a fair degree of resistance, and the findings are not applicable to cases in which the disease is recent in onset. The basic indication for resection in advanced cases is bronchial stenosis or its results.

As the cases were selected for operation by a number of physicians and include cases operated on by at least five surgeons the results may be regarded as representative of average high-class clinical work. The cases are not confined to one particular type.

It appears that if deterioration is going to occur in the opposite lung it will probably do so within a year of the start of convalescence. The likelihood of deterioration is high where the disease has shown signs of instability within the previous year or in patients over 50 years of age.

I acknowledge with gratitude the kindness of my colleagues at Brompton Hospital, who have allowed me to use their case notes and radiographs. The accuracy and success of the follow-up are entirely due to my registrar, Dr. M. R. Geake, to whom I tender my warm thanks.

SKIN LESIONS IN ORGANIC BRAIN DISEASE

BY

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During recent years many papers have been published on the psychological aspects of skin disease, yet comparatively little has been written on the subject of skin lesions found in association with organic brain disease. This discrepancy has not passed unnoticed by dermatologists, and MacKenna (1947) has commented on it in his introduction to Wittkower's article on the psychological aspects of seborrhoeic dermatitis. Posing the question, "To what degree does the mind influence the behaviour of the skin and its appendages?" he points out that the answer must concern itself with the cerebral control of the epidermis, and goes on to state that "a search of the literature indicates that from the dermatological standpoint there have not been any great advances since D. Krestin published his famous paper on 'The Seborrhoeic Facies as a Manifestation of Post-encephalitic Parkinsonism and Allied Disorders.'" Krestin's paper was published in 1927, and on the basis of 73 cases studied in the wards of the London Hospital he made the suggestion that the secretory disturbances described might "depend upon lesions in the neighbourhood of the third ventricle involving vegetative nerve centres."

More recent evidence that cerebral lesions can be followed by skin changes has emerged from the study of patients subjected to prefrontal leucotomy. Ziegler and Osgood (1945), in a careful study of the post-operative findings in 17 patients submitted to leucotomy, found that three suffered for a variable period post-operatively from a bullous eruption of the heels. These bullae healed slowly and were stated "to resemble

trophic ulcers in every way." No fewer than seven of their patients showed bilateral oedema of the legs and feet, and in these seven were included two of the three patients exhibiting bullae. All the patients showing oedema and/or bullous eruptions survived, so there was no necropsy evidence of the exact location of the leucotomy lesion in these cases. It is known, of course, that the cerebral course traversed by the leucotomy at the operation of prefrontal leucotomy can vary widely from case to case (Meyer and Beck, 1945), and clinicopathological correlation derived from a comparative study of the brains of patients dying some time after the operation has already yielded valuable information in relation to cerebral anatomy and cerebral function (Meyer, Beck, and McLardy, 1947; Meyer and McLardy, 1948, 1949).

A paper by McLardy (1950) deals more specifically with the necropsy findings in cases showing skin lesions following leucotomy. Analysing a series of 122 cases of post-leucotomy deaths, in which the time interval between operation and death ranged from five hours to five and a half years, McLardy segregated 14 cases which appeared to him to form a homogeneous group. The post-operative period of survival in these 14 cases was never less than five weeks or more than six months. He considered that all were "delayed post-operative deaths," the putative cause being "trophic deterioration." Of this group of 14, seven showed "remarkable similarity," in that they all became marasmic and died with multiple cutaneous septic sores within two to five months of operation, and, moreover, the area of the brain transected by the leucotomy in these seven cases was roughly similar.

The cases here reported concern four female patients suffering from some form of organic cerebral disease who developed skin lesions prior to death. (Two cases with cutaneous manifestations limited to the sacral area and heels have been discarded, since in these it was impossible to assess the part played by such factors as pressure and inanition.) In three of the four cases described the cerebral lesion was extensive; they therefore lack the localizing value of the circumscribed leucotomy transection. Nevertheless, in view of the few clinical reports extant on the subject of the cerebral control of the epidermis, the description of these four cases may be of value.

The accounts of the clinical examinations and necropsy findings are considerably abridged for reasons of space.

Case 1

Diagnosis: Glioblastoma

A married woman aged 68 was admitted on December 21, 1946. The first deviation from normal was noted 15 days before admission, when she was seen to repeat the process of preparing the house for the annual chimney-cleaning, although this had actually been carried out the previous day. Subsequently she showed a progressive failure in comprehension and practical ability. She was often incontinent.

Examination.—The patient was an elderly woman of healthy appearance, who walked into hospital. Detailed examination of the C.N.S. revealed no focal neurological signs in the somatic sphere. C.S.F.: normal pressure and constituents. In the mental sphere she showed marked defects of an aphasic and apractic type. Her mood was one of mild euphoria: she punctuated her remarks with smiles and was obviously unaware of her situation. A gross intellectual deterioration of such rapid onset, with no antecedent history of trauma or illness, made it reason-

ably certain that the underlying condition was that of a malignant tumour.

Skin Lesions.—Six days after admission, when the patient was still ambulant, a small abrasion was noted on the skin overlying the coccyx. Two days later a bullous lesion, resembling a second-degree burn, appeared in the same area. This extended rapidly during the course of a few hours, until both buttocks and the posterior aspects of both thighs were involved. During the next few days bullous eruptions appeared on both legs and feet. Sloughing quickly occurred in those areas submitted to pressure. Death occurred on January 8, 1947, 12 days from the date of the appearance of the bullae.

Necropsy Report

The presence of a cerebral tumour was confirmed, and histological examination showed this to be a glioblastoma multiforme. The bulk of the tumour lay in the base of the left hemisphere, extending from the frontal pole into the temporal lobe as far back as the level of the corpora mammillaria. It crossed the midline, however, to invade the base of the right frontal lobe and therefore gave the impression of a midline growth. At the level of the anterior horn the tumour extended to invade the left side of the corpus callosum. It compressed and displaced upwards the left lateral ventricle, while the right lateral ventricle was displaced to the right and dilated. A cyst was present in the right frontal lobe on the lateral aspect of the tumour. The tumour reached the surface anterior to the infundibulum, invading both gyri recti, surrounding the optic chiasma and nerves and left middle cerebral artery. Apart from small foci of recent infarction in both lungs, no abnormalities were detected in the other organs.

Case 2

Diagnosis: Carbon Monoxide Poisoning

A spinster aged 63 was admitted on January 2, 1948. Four weeks previously she had been admitted to a general hospital following an attempt at suicide by the inhalation of coal gas.

Examination.—A few small pustules were present on the right elbow. B.P. 150/90. No focal neurological signs elicited. Gait unsteady on rising from chair but improved on walking. C.S.F., negative. W.R., negative. W.B.C., 6,000. Mental testing showed severe memory defects and disorientation for time and place. It was obvious that a severe degree of cerebral damage had occurred as a result of prolonged exposure to coal gas.

Skin Lesions.—On January 7 the patient developed an acute rapidly advancing bullous eruption over the sacral region and buttocks. Penicillin therapy was instituted, and over the next ten days her general condition improved and the bullous eruption appeared to be healing. On January 18 she again relapsed, and from this date to her death on January 22 her temperature showed a step-ladder rise each night and the bullous eruption over the sacrum spread upward over the lumbar and dorsal vertebrae. Fresh bullous eruptions appeared over the right scapula, the antero-medial aspects of both legs, and right heel. (These bullae had all the appearance of superficial burns, and in fact those over the anterior aspect of both legs were referred to as such in the necropsy report.)

Necropsy Report

Sections of the brain were examined from all regions. The cortex showed loss and degeneration of nerve cells. In the white matter there were numerous irregular areas of demyelination of varying size and shape which were diffusely infiltrated by cerebral histiocytes containing much fat. Similar areas were present in the basal ganglia. The features were those of a typical case of subacute/chronic carbon monoxide poisoning showing active demyelination in white matter. Toxic changes were noted in heart, liver, and kidneys.

Case 3

Diagnosis: (1) Dermatitis Gangrenosa of Left Lower Limb Following Severe Pemphigus; (2) Subdural Haematoma Overlying Right Cerebral Hemisphere; (3) Depressive Psychosis

A married woman aged 53 was sent into hospital on August 15, 1946, as a case of involuntal depression. Examination, however, revealed that she was suffering from an organic cerebral condition with focal neurological signs and intellectual defects. Her relatives stated that six weeks previously she suddenly complained of intense headache over the right temple and thereafter lapsed into a "drowsy state," with incontinence. She reiterated questions regarding her husband and son—seemingly unaware that her husband had died two years previously. After two weeks she was admitted to a nursing-home. In her waking periods she showed understanding of questions and answered them correctly, although a minute or so later she forgot both the question and her reply. Later a depressive thought content became manifest—characterized by ideas of guilt and unworthiness; and after four weeks in the nursing-home it was judged necessary to admit her to a mental hospital.

Physical examination on admission showed:—C.N.S. (positive findings only): knee-jerks diminished on both sides; ankle-jerk diminished on right, absent on left. Bilateral extensor plantar response. A generalized hyperaesthesia to pinprick was present on admission and for three days thereafter. The C.S.F. was under normal pressure; protein, 75 mg. per 100 ml.; globulin, slight increase; cells, 1 per c.mm.; W.R. negative; colloidal gold, 0011000000; blood chemistry normal. Radiological examination of skull and chest negative.

Mental examination showed that she could answer simple questions about herself, but was unable to deal with questions requiring reasoning and calculation. She appreciated to some extent her intellectual disability. She had an amnesia for the previous four weeks. Her speech was slow, her voice monotonous, her response retarded. She yawned often during interrogation and made smacking movements with her lips.

After-course of Illness.—At the end of two weeks she had largely regained her mental clarity. C.S.F. protein, however, rose to 110 mg. per 100 ml. As her intellectual defects disappeared her depressive thought content became more prominent. On September 28 she was sent for more detailed neurological investigation, but this failed to reveal any lesion which could explain the original illness and the residual focal sign of bilateral extensor plantar response. On January 23, 1947, the C.S.F. protein gave a normal reading of 35 mg. per 100 ml. During the next eight months her condition remained static. She had regained her normal intellectual standard—so far as this could be assessed—although she was amnesic for the early period of her illness. The plantar response remained extensor. She was still deeply depressed. Electric convulsion therapy, which might have relieved the depression, was contra-indicated because of doubt concerning the exact nature of the cerebral lesion. Her physical condition was satisfactory and she occupied herself in daily domestic tasks in the ward.

Skin Lesions.—On October 29, 1947—that is, 14 months after admission—a widespread bullous eruption developed with dramatic suddenness over a wide area on the inner aspect of the left thigh and anterior surface of the left leg. The bullae varied in size, contained yellow serum, and had the appearance of an acute pemphigus. A minute crop of bullae appeared transiently over the left forearm. Her temperature rose to 99° F. (37.2°C.) on the day on which the eruption first appeared, but thereafter the temperature and pulse rate were normal until the terminal week of the illness. During the next four weeks the subcutaneous tissue in these affected areas progressively sloughed, so that the underlying muscles were clearly visible. At the same time,

bullae appeared progressively in neighbouring areas, so that finally the entire surface of the left lower limb, with the exception of a narrow strip on the posterior aspect of the limb and the sole of the foot, was involved in the eruption. In course of time erosion of the subcutaneous tissue occurred also in these later affected areas so that the final appearance was that of a widespread dermatitis gangrenosa. Blood transfusion and every variety of antibiotic were utilized throughout the long course of the illness. In the third month granulations appeared in some of the areas affected, but coincidentally the dorsum of the foot became grossly infected—the infecting organisms being resistant to penicillin. The patient now looked extremely toxic and had fluctuating oedema of the face and sacrum. In the terminal phase hydrothorax developed. Death occurred on February 27, 1948, four months after the first appearance of the skin lesions.

Necropsy Report

General Appearances.—The whole of the left leg was involved by an extensive and severe ulcerative process involving skin and subcutaneous tissue, and in places extending down to the underlying muscle. Some of the ulcers, especially those on the anterior aspect of the tibia, were healing well by granulation and were relatively free from infection, but others showed little or no sign of repair and were grossly infected.

Brain After Fixation.—Macroscopically, the inner layer of dura over the right frontal lobe on its supero-lateral aspect was discoloured with blood pigment and showed on its cortical surface "neomembrane," suggesting that at some previous date there had been a subdural haematoma which had since become absorbed. Microscopically, a section from the dural lesion showed that the inner aspect of dura was almost continuously lined by a thin layer of golden-brown haemosiderin pigment which lay mainly extracellularly. The "neomembrane" seen with the naked eye consisted of loose fibrovascular tissue with similar pigment deposits scattered within its substance. A section from basal ganglia revealed no striking abnormalities except for a few small irregular cystic spaces formed by degenerative changes in the neuroglia, probably of a chronic ischaemic nature. Findings in other organs were: right hydrothorax, partial collapse of lower lobe of left lung, "septic" spleen, and periportal fatty degeneration of liver cells.

Case 4

Diagnosis: Chronic Mania; Subdural Haematoma

This case differs from the previous three cases in that the skin lesion was not a bullous eruption. It also differs in that the patient had been in hospital for many years suffering from a long-term mental illness.

A spinster aged 42 was admitted on March 27, 1922. With advancing age her psychotic illness had rendered her uncommunicative, and accurate intellectual assessment was impossible. For two years she had been confined to bed because of a fractured neck of the femur.

Skin Lesions.—On November 10, 1950, she developed a slight rash on the face, and this erythematous rash later spread to involve her whole body. The upper and lower limbs were most severely affected, and the skin in these regions developed a shiny bright-red appearance with numerous petechial haemorrhages. Finally, the lower limbs became oedematous and bright purple in colour, and small areas of gangrene appeared over the heels and soles.

It was at first thought that the dermatitis was due to drug sensitivity, but when exacerbation and not amelioration followed the prohibition of the very small doses of drugs administered at infrequent intervals, and to which she had not previously shown intolerance, an organic cerebral lesion was suspected—largely on the basis of the knowledge gained from the foregoing three cases. The patient died on December 6, 1950, at the age of 70.

Necropsy Report

Brain After Fixation.—The dura: large subdural haematomata covered the supero-lateral surfaces of both hemispheres. On each side the haemorrhage was limited on its inner aspect by a well-defined thin membrane which extended over the entire haemorrhagic area and enclosed within itself and the dura several ounces of blood clot. External examination of cerebral hemispheres showed considerable flattening and compression from side to side of the right hemisphere, most pronounced in the fronto-parietal region. Microscopically the inner aspect of the dura covering the haematoma showed a well-defined layer of granulation tissue containing abundant haemosiderin pigment lying free or in histiocytes. Collagen fibril formation was well marked and proliferating capillaries were prominent. Sections were taken of the frontal cortex near the tip of the anterior horn. No pathological changes were noted.

Other Organs.—Skin lesions: the superficial layers of the dermis were swollen and oedematous and showed focal collagen degeneration. There was a fair degree of inflammatory cell infiltration, the majority of the cells were lymphocytes, but pyknotic polymorphs and histiocytes were also present. The capillary walls were swollen and in many places showed proliferation. Diffuse haemorrhage was present. The overlying epidermis showed degenerative changes. Eosinophil polymorphs were found in small numbers throughout the inflammatory infiltration. Lungs: pneumonic consolidation was present in both lower lobes. In addition, many of the small vessels showed both periarteritis and mesarteritis, the inflammatory cells being mainly polymorphs. This vasculitis was probably distinct from the pneumonic process.

Review of Literature

Apart from the trophic skin lesions described in post-leucotomy cases, there are few published reports of cutaneous disturbances in cerebral disease. Bullous eruptions have been described very occasionally as a concomitant of epidemic encephalitis. Stern (1936) states: "The origin of the trophic changes of the skin and joints found in occasional cases remains inexplicable. Gangrene and blisters on the hands have been described in both acute and chronic stages of the disease. . . . I personally have seen a severe case of chronic Parkinsonian encephalitis in which there occurred simultaneously a *pemphigus-like* disease. Whether there is any connexion between the two diseases is open to discussion." Rostowski (1939) has drawn attention to the "almost invariable" occurrence of bullous eruptions in "choreiform" encephalitis—"the parts most commonly affected being the circumoral region, the chin, the skin overlying the elbows and knuckles. The lesion commences as erythematous patches on which develop small or large vesicles containing first white and later yellow fluid. These vesicles enlarge and coalesce, ultimately rupture, and leave wounds which are difficult to heal." This author believes that "it is the cerebral infection which accounts for the skin lesion, and not the trauma to the skin resulting from the choreiform movements. That this is so is proved by the finding that such eruptions have never been seen in Sydenham's chorea, although the ceaseless movements may be of the same intensity as that seen in choreiform encephalitis" (Rostowski, personal communication).

More numerous, but still far from frequent, are the reports of bullous eruptions accompanying spinal-cord lesions. Cutaneous bullae are, of course, mentioned in textbook descriptions of myelitis and syringomyelia as occasional concomitants of these diseases, in which it is usually assumed that they are secondary to the sensory changes. Some authors believe, however, that these bullous eruptions, which so often resemble pemphigus in appearance, are the results of impaired skin nutrition, and are primary "trophic" changes, in the sense that the spinal-

cord lesion causes at one and the same time alterations in skin sensibility and in skin nutrition.

A typical report of this kind is that of Milian and Lelong (1922), and concerns a man of 66, with a syringomyelia of eleven years' duration, who had thrice had a "pemphigoid" eruption. The eruption was bilateral and symmetrical. On the third occasion the bullae were distributed over the anterior and posterior aspects of both forearms. The authors regarded these bullae as trophic in origin because they were localized to areas "which showed the maximum atrophy and sensory disturbance," and considered that they were due to involvement of the grey matter of the spinal cord, particularly those areas containing the sympathetic centres of the trunk and limbs. They were careful to point out that, although a myelopathic pathogenesis was the most likely one in their case, this did not necessarily apply in all cases of pemphigus. Again, Ormsby and Montgomery (1948), in assessing the evidence for and against a neuropathic aetiology of pemphigus, mention that pemphigus has been observed in patients with neurogenic conditions, and enumerate various reported cases in which lesions of the spinal roots and/or spinal cord have been found at necropsy. These few scattered references therefore suggest the possibility that bullous eruptions may arise from destruction of either cerebral or spinal-cord centres.

Cerebral Localization.—A determined attempt has been made by McLardy (1950) to delimit a particular area of the brain, damage to which might be held responsible for the appearance of cutaneous blisters and marasmus in a group of patients dying within two to five months of the operation of prefrontal leucotomy. His examination (mainly macroscopic) of the brains of seven such patients revealed that in each the operation had caused bilateral damage to the subcallosal fasciculus at the level of the head of the caudate nucleus. He also found associated damage to other areas—notably (a) the striatum (under which term he includes the caudate nucleus and putamen), and (b) the cortex and digital white matter of the superior frontal gyrus at the topographical level of Brodmann's (dysgranular) area 8 and (agranular) area 6—but quantitative destruction of these regions varied from case to case. From his findings in these seven cases, and also from evidence supplied by other relevant cases in a total series of 122 necropsies in patients dying after leucotomy, he constructs the hypothesis that the three cerebral regions enumerated contribute to a connected vital system—"a vital fronto-subcallosal-caudate system"—disruption of which is responsible for the fatal "trophic deterioration." His hypothesis stresses the subcallosal fasciculus as the most important component in this system, since it presumes that this fasciculus, in its rostral portion at least, mediates connexions between the caudate nucleus and Brodmann's cortical areas 8 and 6.

Discussion

During the period 1946–51 more than 200 patients with one or other form of organic cerebral disease were under observation in this particular female section of the hospital. The four cases described represent only a small fraction of the total organic cases, indicating that such severe cutaneous manifestations occur infrequently. It is easy to visualize how such skin lesions may be accepted as merely a terminal manifestation of inanition occurring in bed-ridden patients. It is therefore of interest to note that three of the cases here described were ambulant and in an apparently normal state of nutrition when the skin lesions first appeared; the fourth, although confined to bed, was capable of active movements and appeared in good physical health.

The first three cases form a homogeneous group in that the skin lesion presented initially as a bullous eruption. In Case 1 (cerebral tumour) and Case 2 (carbon monoxide poisoning) the cerebral destruction was massive and rapidly progressive, and the skin eruptions were likewise of brief

duration, death occurring within two to three weeks of the first appearance of the bullae. Death in these cases was presumably caused by the cerebral lesion, the skin eruptions being only a minor contributing factor. Conversely, in Case 3 (subdural haematoma), in which the cerebral lesion was more circumscribed and, if one may so describe it, less "lethal," the skin condition ran a prolonged course of exactly four months, during which time it showed both recrudescences and attempts at healing. The death of the patient, which occurred at the end of this time, was almost certainly due to toxæmia and alterations in blood chemistry brought about by the extensive dermatitis gangrenosa of the left lower limb. The cerebral lesion was culpable only in a secondary sense, in that it is here postulated as initiating the skin condition.

This case is worthy of more detailed study. The subdural haematoma covered the supero-lateral surface of the whole right frontal lobe. Its onset presumably coincided with the symptom of intense headache experienced by the patient four weeks before admission to hospital. Its presence explained the intellectual defects and neurological focal signs elicited following admission. There was no history of trauma, but subdural haematoma often appears without recognizable antecedent injury. Considered in retrospect, the history of fluctuating drowsiness and confusion elicited on admission was typical of that found in subdural haematoma. The left extensor plantar response can be explained in terms of pressure on the right motor area. The right extensor plantar response, which is also present, suggests transmitted pressure to the left crus, and was therefore in the nature of a false localizing sign. Aird (1949) mentions that homolateral paresis or anaesthesia occurs in 30% of cases of subdural haematoma, because extracerebral lesions are more prone to push the contralateral crus cerebri against the tentorium. This bilateral extensor response was still present when the skin eruptions first made their appearance, although nearly sixteen months had then elapsed from the time of the acute symptoms of headache and fluctuating drowsiness, so that the subdural haematoma was still at this later period exerting intracranial effects. Nevertheless, if it is submitted that the cerebral lesion was in some way associated with the skin condition in this as in the two previous cases, the question must inevitably be raised of why the skin effects appeared after a latent period of sixteen months. The evidence, from similar skin eruptions in epidemic encephalitis, which were stated to arise at varying times in the course of the disease, partly answers this question. A more relevant reply is that subdural haematoma remains a mysterious condition, subject to curious exacerbations and remissions which are usually explained in terms of secondary haemorrhage within the original haematoma.

The fact that the subdural haematoma was found at necropsy in a state of almost complete resolution, with only membrane formation to testify to its former existence, can be utilized to explain the protracted course of the skin condition; for, assuming that the subdural haematoma was responsible for initiating the skin eruption and destruction of subcutaneous tissue, its own absorption would tend to allow of attempts at healing, such attempts presumably being rendered ineffective because of secondary infection and toxic absorption from the very extensive denuded surface. An even more cogent reason for assuming that the subdural haematoma was responsible for the cutaneous manifestations in this case is that those manifestations were confined to the contralateral side of the body. The subdural haematoma overlay the right frontal lobe, the bullous eruption appeared on the left lower limb (with an initial short-lived eruption on the left arm), and never at any time appeared, even sporadically, on the limbs or trunk of the right side. Since in all the other cases a bilateral cerebral lesion was found in association with a bilateral skin lesion, it is difficult to avoid the inference from this one case of unilateral distribution that the cerebral and cutaneous lesions are in some way connected.

Case 4 is considered briefly. Here the skin lesion did not appear as bullae but as a generalized erythema with petechial haemorrhages. In this case the presence of a cerebral lesion was suspected, although no neurological focal signs were present and the mental state of the patient was such that she could not be examined for possible intellectual defects. This diagnosis was made on the skin condition alone, largely as a result of knowledge gained from the first three cases. This patient died shortly after the publication of McLardy's report on the cerebral findings in patients dying of "trophic deterioration," and therefore at necropsy the area round the anterior horn of the lateral ventricle was carefully examined microscopically, but no abnormality was found. Examination of this particular area in the previous case of unilateral subdural haematoma (Case 3) similarly revealed no abnormality, but the examination was not so detailed as in Case 4. It would seem, therefore, that skin lesions can arise without damage to the subcallosal fasciculus.

Conclusions

In the cases described above, three types of cerebral pathology—namely, tumour, carbon monoxide poisoning, and subdural haematoma—were found in association with cutaneous bullae. Bullous eruptions have been previously described in epidemic encephalitis and as a sequel to the operation of prefrontal leucotomy. It would seem, therefore, that varying types of cerebral pathology can produce the same cutaneous lesion.

The cases described are too few in number and the disease process too diffuse to allow of any postulation in regard to the cerebral area mediating the skin changes. The main intention of this paper is to draw attention to this association between organic cerebral disease and skin lesions, now that similar phenomena have been described and investigated in relation to prefrontal leucotomy.

I wish to thank Professor Sir David Henderson for permission to publish these four cases. My thanks are also due to Professor A. M. Drennan and his associates in the Edinburgh University Pathology Department for the necropsy reports, and to Dr. S. A. K. Karagulla for the notes in Case 1. I am particularly indebted to Dr. Grant Peterkin, consultant dermatologist, for his interest and advice in this investigation.

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With the assistance of the Public Health Laboratory Service, the Veterinary Investigation Department (Ministry of Agriculture and Fisheries), and veterinary investigation officers in Scotland, the Laboratory Animals Bureau has made arrangements to provide all accredited guinea-pig breeders with a local diagnostic and advisory service. Each breeder is allotted to one, or sometimes more than one, near-by laboratory and instructed to send there for bacteriological examination all his guinea-pigs which die. The laboratory undertakes to examine the dead animals in order to discover the cause of death, to visit the breeder if necessary, and to advise on any prophylactic measures to be taken. The Bureau receives a duplicate laboratory report, and is thus able to take any further steps which may be indicated.