

chorio-epithelioma with pelvic extensions has spontaneously disappeared, but does not quote a case of disappearance of lung metastases except after hysterectomy. Comparison with chorio-epithelioma is interesting, as teratoma of the testis can contain chorio-epithelioma, although none was seen in the slide of my case.

I should like to thank Dr. Paul Cave for his reading of the x-ray films, and Col. F. R. Coppinger for his opinion on the pathology of the tumour.

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## BASAL-CELL CARCINOMA AT SITE OF TRAUMA

BY

T. G. REAH, M.D., M.R.C.P.  
Late Lieut.-Col., R.A.M.C.

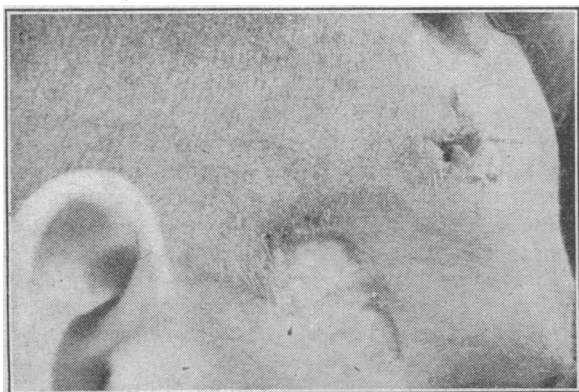
[WITH PHOTOGRAPHURE PLATE]

Schrek (1941) in a review of 296 cases found that in five instances patients suffering from a basal-cell carcinoma gave a history of the growth developing on the basis of an old scar. In one case the carcinoma appeared about 15 years after a burn of the forehead; in another it occurred two years after a burn of the hand, while in a third the growth developed 30 years after an avulsion of the scalp. No interval is stated in the remaining two cases, in one of which the growth appeared in a scar on the nose and in the other in scars of the legs following Roentgen-ray burns. Aitken (1944) stated that it is unusual to obtain any history of injury in cases of rodent ulcer, and cited one case where the history was certainly suggestive.

In the following case the history suggests the development of a basal-cell carcinoma immediately after a superficial cannon-shell wound. It should be remembered, however, that in the Middle East the incidence of secondary infection was high and delayed healing of superficial wounds common, and it is therefore impossible to determine the time of onset of malignancy.

### Case Report

A regular soldier aged 31 with 13 years' service was admitted to a military hospital in West Africa on Feb. 11, 1946, suffering from a short-term fever. He had served in the Middle East from 1935 to 1944, and in November, 1942, was struck on the



Photograph showing lesions on right temple.

right temple by fragments of a cannon-shell from an enemy aeroplane. The injury was superficial, consisting of an abrasion about 1 cm. in diameter, and after the application of a dressing

he returned to duty. This abrasion did not heal. In August, 1943, he noticed a sharp edge projecting just above the site of the abrasion, and a spicule of metal about 0.5 cm. long was removed by the regimental medical officer. The puncture hole also did not heal; thereafter both this lesion and the original abrasion slowly increased in size and bled freely if the surfaces were rubbed.

Midway between the outer canthus and the right ear was an ovoid slightly depressed area 3.5 by 1.7 cm., with a finely nodular base covered by pale epithelium except for the posterior 0.75 cm., where the surface was slightly scaly. Immediately above this lesion was another, 1.7 by 1 cm., with an irregular outline covered by a crust and with no characteristic edge (see photograph). There was no clinical evidence of metastases. There were three pigmented naevi up to 0.5 cm. in diameter on the face, numerous pigmented naevi up to 0.3 cm. in diameter on the trunk and limbs, and four pedunculated, pigmented warts on the trunk, all of which the patient stated had been present for years. A piece of the upper lesion was removed by Lieut.-Col. D. H. Mackay, and Major A. F. Mohun reported that it was a typical basal-cell carcinoma (Special Plate, Figs. 1 and 2). I am grateful to them for their assistance.

My thanks are due to Major G. M. Ardran for the photograph of the patient, to L/Cpl. D. Winks for the photomicrographs, and to the D.G., A.M.S., and Col. W. R. D. Hamilton for permission to publish this case.

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## FOLIC ACID IN PERNICIOUS ANAEMIA ITS EFFECT AS SHOWN BY SERIAL STERNAL PUNCTURES

BY

HERBERT LEVY, M.D., M.R.C.P.

Assistant Medical Officer, Bethnal Green (L.C.C.) Hospital

In bone-marrow films of three cases of pernicious anaemia Davidson *et al.* (1942) observed a considerable decrease in the proportion of early megaloblasts only six to ten hours after a single intramuscular injection of anahaemin or reticulogen. It seemed of interest to investigate the rate of bone-marrow changes following a single oral dose of 50 mg. of folic acid.

In order to present figures comparable with those of Davidson *et al.* the classification of nucleated red blood cells adopted by these authors (cf. explanation to Table 1) was used, but cells in mitosis were not differentiated into the various groups. This classification admittedly makes no attempt to differentiate between cells derived from megaloblasts and those developing along normal lines. As stated by those authors, "a certain arbitrary judgment is sometimes necessary for the classification of a given cell which falls on the borderline between groups." A further difficulty is the fact that changes in cell size, in haemoglobinization of cytoplasm, and in nuclear structure proceed during the repair stage of pernicious anaemia at different rates. For instance, after treatment a not inconsiderable proportion of deeply basophilic cells of under 11  $\mu$  diameter are found which have a nucleus similar to cells of Type II before treatment; this cell type is characteristic for all conditions in which there is abnormally intense erythropoiesis.

Pernicious anaemia, in a man aged 63, was first diagnosed on his admission to Bethnal Green Hospital in December, 1936; this responded promptly to liver treatment. He was followed up and treated as an out-patient until November, 1937, but failed to attend after that date and has not since had any treatment with liver or stomach extracts. He was readmitted on Aug. 23, 1946, with pernicious anaemia in relapse and with gross

symptoms and signs of subacute combined degeneration of the cord. Haemoglobin, 9.47 g. per 100 ml.; red cells, 2,130,000; M.C.V., 128  $\mu$ ; reticulocytes, 3%; white cells, 6,300 (neutrophil polymorphs, 2,331; eosinophil polymorphs, 378; basophil polymorphs, 63; lymphocytes, 3,402; monocytes, 126).

TABLE I.—*Sternal Marrow Counts representing Percentage of 500 Nucleated Red Blood Cells in Each Film*

	Type				Mitoses
	I	II	III	IV	
Before folic acid	46.0	22.8	12.4	17.0	1.8
6 hours after	22.8	27.2	33.2	14.6	2.2
12 " "	10.0	18.4	48.4	20.4	2.8
24 " "	7.0	17.4	56.6	16.8	2.2
48 " "	8.4	19.0	45.0	26.2	1.4
Davidson <i>et al.</i> :					
Case 1 { Before anahaemin	42.0	28.3	24.0	5.7	9.0
6 hours after	25.7	38.5	25.5	10.3	12.4
Case 2 { Before anahaemin	46.2	30.4	9.8	13.6	10.2
10 hours after	35.8	44.2	13.8	6.2	18.4
32 " "	8.4	53.6	30.8	7.2	14.3
Case 3 { Before anahaemin	40.2	38.4	15.0	6.4	14.4
8 hours after	19.8	51.7	19.7	8.8	11.5

Type I: Cell of average 18  $\mu$  diameter; pale nucleus with fine lattice of chromatin, sometimes with nucleoli. Type II: Average 14.2  $\mu$  diameter; nucleus more deeply staining and coarser chromatin pattern. Type III: Average 11  $\mu$  diameter; cytoplasm basophilic, polychromatic, or orthochromatic; deeply staining nucleus with lumpy masses of chromatin. Type IV: Average 9  $\mu$  diameter; polychromatic or orthochromatic, with pyknotic nucleus. Mitotic erythroblasts: Characterized by deeply staining chromosomes (cf. LaCour, 1944). For the cases of Davidson *et al.* mitotic cells are listed separately, but are also included in the figures under Types I-IV.

It is thus seen that folic acid by mouth effected as rapid and extensive a decrease in Type I cells as did intramuscular refined liver extract. The increase in Type III erythroblasts following folic acid as compared with Type II in the series of Davidson *et al.* may be due to a difference in assessment rather than in quality of response.

The rapidity of the change in the bone marrow from a megaloblastic to a normoblastic picture was thought by Davidson *et al.* to support the view "that normoblasts can be derived directly from megaloblasts" and "that megaloblasts and normoblasts belong to one developmental series." Table II shows, however, that the proportion of nucleated red blood cells with deeply basophilic—that is, non-haemoglobinized—cytoplasm is considerably larger six hours after treatment than it was before treatment, the basophilic cells belonging to Types I to III. I have in the past observed the same phenomenon in all cases of pernicious anaemia in which I have examined sternal-marrow films before and shortly after liver treatment.

TABLE II

	Basophilic	Polychromatic	Orthochromatic
Before folic acid	24.8	59.4	15.8
6 hours after	57.6	32.2	10.2
12 " "	43.4	40.6	16.0
24 " "	57.4	34.0	8.6
48 " "	45.8	43.0	11.2

Percentages represent 500 nucleated red cells.

The objection that the figures in Table II do not necessarily indicate an absolute increase in the number of basophilic erythroblasts seems refuted by Table III, which shows a probably significant rise, and in any case not a fall, in the erythroblast population.

TABLE III.—*Myelo-erythroblastic Ratio*

	Cells of Myeloid and Lymphoid Series	Nucleated Red Blood Corpuscles
Before folic acid	363	137
6 hours after	340	160
12 " "	350	150
24 " "	337	163
48 " "	294	206

As it seems scarcely possible that a partly or fully haemoglobinized megaloblast should lose all its haemo-

globin during its further development, this finding shows that repair in pernicious anaemia is effected by newly produced cells of a non-megaloblastic series. Naegeli (1931) described as late megaloblasts fully or nearly fully haemoglobinized large oval-shaped rather than spherical cells, with an eccentric rather than central, deeply staining, more or less pyknotic nucleus; Israëls (1939) and Wilson (1942) reached the same conclusion. The number of these cells in the films after treatment is quite consistent with the view that they are the cells derived from the early, partly, or not yet haemoglobinized megaloblasts of the untreated marrow, and that they play quantitatively no material part in the repair of pernicious anaemia.

The disturbance of granulopoiesis characterized by the presence in large numbers of giant metamyelocytes and giant band-shaped granulocytes—due, according to LaCour (1944), to nucleic acid shortage of the promyelocytes producing incomplete spiralization of their chromosomes—showed no appreciable change in the four marrow films made after the administration of folic acid. This is in agreement with previous personal observations on marrow films examined one to two days after the beginning of liver treatment, and with the findings of Zuelzer and Ogden (1946) in cases of megaloblastic anaemia in infancy treated with folic acid in which they observed its disappearance only after two to four weeks, whereas in at least one of their cases the megaloblastic pattern had disappeared two days after parenteral folic acid treatment.

I wish to thank Dr. H. A. Ash for the peripheral blood examinations and Dr. I. Doniach for his criticism.

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## Medical Memoranda

### A Rare Form of Tuberculous Meningitis

Four cases of an unusual variety of tuberculous meningitis occurred in adults in Singapore during the period 1938-42. Each case presented the following features: a period of pyrexia, a period in which spinal symptoms predominated, and a period of meningism passing on to coma and death. Each period lasted about a week.

#### CLINICAL FEATURES

**Pyrexial Period.**—There were no pronounced distinguishing features during this time. Three cases were admitted for routine investigation for fever of unknown origin, and the fourth, Col. Rogan's case, for fever associated with diarrhoea. The pyrexia was of a regular remittent type, not rising much above 102° F. (38.9° C.). It was associated with a mild leucocytosis up to 12,000 (80% polymorphs).

**Spinal Symptoms.**—These were the first symptoms of major importance which distinguished the illness from the ruck of tropical fevers undergoing routine investigation. The first manifestation in all cases was difficulty in passing urine, leading to retention. This was followed within 24 hours by a paresis of the lower extremities which gradually deepened but never became complete. There was diminution of muscle tone, loss of superficial and deep reflexes, and an absent or equivocal Babinski sign. These findings were associated with a rising sensory level, which was peculiar in that it was patchy and extremely difficult to determine precisely. Sensory loss was most marked to pin-prick; hot and cold, postural sensibility, vibration sense.