ce soient des fibres vasomotrices du système végétatif.

En résumé, dans l'épinière des gros nerfs du cœur
chez le Chat nouveau-né, on trouve des fibres sensitives
qui se terminent d'une manière différente soit par des
boutons, soit par des anneaux, ou bien par un appareil
métaterminal. Quelques-unes de ces fibres appartiennent
peut-être au système nerveux autonome. Des fibres
vasomotrices ont été aussi trouvées dans l'épinière,
celles des fig. 1 et 2, ont l'aspect et la coloration de fibres sensitives. Il est donc vraisemblable qu'elles viennent des nerfs vagues,
ont l'aspect et la coloration de fibres sensitives. II est

La fig. 3 présente une fibre nerveuse noire et très fine,
comparable à une fibre postganglionnaire parasym-
pathique. Elle se termine par un appareil métater-

Fig. 3.

tissant à des terminaisons comme celles des fig. 1 et 2,
ont l'aspect et la coloration de fibres sensitives. Il est donc vraisemblable qu'elles viennent des nerfs vagues,
puisque ce sont eux qui fournissent les voies afférentes
du cœur. En ce qui concerne la terminaison de la fig. 3,
en raison de l'aspect différent de la fibre qui lui donne
naissance, il est possible qu'il y ait là un appareil en
rapport avec une fonction trophique.

J'ai vu aussi des fibres ténues accompagnant des
fibres encore plus fines et colorées en jaune, dans l'épi-
nière tout près d'un vaisseau. Il est bien possible que

Histological Changes Produced by Large Doses
of Tetra-sodium 2-methyl-1:4-naphtho-
quinone Diphosphate in some Human Tumours

Clinical trials of large doses of tetra-sodium 2-methyl-
1:4-naphthoquinone diphosphate, mainly in con-
junction with palliative X-ray therapy in patients with
various types of advanced malignant tumours have
been in progress since November 1946. The results in
116 cases have been reported1. It has been found that
the compound in large doses produces a small but useful
improvement in the palliative results of X-ray therapy
in some cases of advanced cancer, and a small increase
in survival time in cases of inoperable carcinoma of the
bronchus. The compound is already in use in medicine
as a water-soluble synthetic vitamin-K substitute. It is
of low toxicity, and has been administered by intra-
muscular and preferably intravenous injection. It is of
interest that large intravenous doses produce almost
immediate focal pain in the region of the tumour in
some cases, especially where there is bone involvement.
This focal pain appears to be due to temporary cell
edema.

This approach to the problem of attempting to im-
prove the treatment of cancer by the combined use of
radiotherapy and chemotherapeutic agents was based
on the finding that therapeutic doses of ionizing radia-
tions produce a disturbance of cellular nucleic acid
metabolism including inhibition of synthesis of thymo-
nucleic acid in proliferating cells.

It has been shown2 that the compound produces
mitotic inhibition in chick fibroblast cultures and in
some human squamous cell carcinomata, and that in
the tissue cultures, significant potentiation of the effects
of X-radiation and the compound in inhibiting mitosis
was found under suitable conditions.

2 J. S. MITCHELL, Nature 144, 272 (1940); Brit. J. Exp. Path.
22, 285, 296, 309 (1942); Brit. J. Radiol. 16, 339 (1943); 21st Ann.
Selskab Biol. Medd. 17, 8 (1940). – L. AHLSTRÅM, H. v. EULER, and
Radiol. 24, 450 (1947). – J. O. ELY and M. H. Ross, Cancer Res. 4,
285 (1944).
The antimitotic action of quinones is well known. The mutagenic effect of phenol in *Drosophila* and chromosome fragmentation induced by phenols is of interest. The parallelism between mitotic inhibition and interaction with -SH compounds *in vitro* has been studied; it is unlikely that this is the only mechanism involved, but it is of interest in relation to the radiosensitivity of some -SH enzymes.

The purpose of this note is to present histological confirmation of the late effects of repeated large doses of the compound in some human tumours other than the squamous cell carcinomata previously exemplified.

Fig. 1 (a and b) show the histological findings in biopsy specimens from the case of a man aged 82 years, with an advanced carcinoma of the skin, originally of basal cell type, involving the right side of the nose with gross destruction of the tissues of the face, including bone. There were no secondary glands. This lesion had become radio-resistant and had recurred after much previous treatment over many years. The original treatment was by diathermy, and subsequent radium. Two courses of radical X-ray treatment had been given for recurrences, and further palliative X-ray treatment had been attempted without any response. Fig. 1a is from the biopsy specimen before a final course of radical X-ray therapy combined with intramuscular injections of the compound. The second biopsy shown in Fig. 1b was taken three days after 4,500 r of X-radiation in 21 days, and immediately after the last of 25 daily intramuscular injections, each of 100 mg of the compound. The immediate clinical response of the lesion to the treatment was surprisingly good, but active though slowly progressive malignancy was still present after nine months. In the second biopsy, the field shown in Fig. 1b, was the only part of the section containing tumour cells, which it is interesting to note are of degenerating squamous cell type, with keratinization. The lesion apparently became radio-sensitive again with the combined use of the compound and X-radiation.

Fig. 2 shows the effects of the compound alone in the case of a man aged 52 years suffering from an adenocarcinoma of the transverse colon with secondary involvement of lymph nodes in the omentum, and also in the left supraclavicular area and posterior triangle. After failure of the cervical nodes to respond to palliative X-ray therapy, clinical retrogression of all the palpable nodes occurred after intravenous administration of large doses of the compound. Fig. 2 shows the widespread degenerative changes in the cells of the secondary adenocarcinoma in an omental lymph node removed at laparotomy ten days after the completion of a course of daily injections of the compound, during which a total dose of 8,140 mg was given in 31 days. No X-radiation had been given to this area at any time. As in the cervical nodes, the tumour shows necrosis and gross degeneration, with an increase of fibrotic stroma. There are no mitoses, and practically all the recognizable tumour cells show pyknotic nuclear degeneration. It is emphasized that the therapeutic effect was only pal-