NEW SEA-WALL AT ABERDEEN

THE subject of coastal protection is always with us but is seldom nationally publicized until a catastrophe occurs, when a combination of storm and excessively high tides causes the sea to overwhelm existing defences, flooding land behind them, resulting in grave damage to both life and property, to say nothing of the sea-walls and groynes concerned.

Recent work on a section of the coastline between the north pier of Aberdeen harbour and the mouth of the River Don is a case in point. In this example, lack of toe piling coupled with erosion of foreshore during the winter of 1961–62 determined the complete collapse of some 100 ft. of the then existent sea-wall and caused severe damage to the front of the apron over several hundred feet. According to *Concrete Quarterly* (No. 61, April–June 1964; Cement and Concrete Association, London), "The new work now nearing completion consists of two parts. The first and minor portion consists in rebuilding and strengthening portions of the existing wall extending some 2,500 ft. north from the beach bathing station. . . . A completely new wall has been built over the remaining 5,000 ft. or so of sea-front from the existing wall to the Don. A flexible facing of precast concrete blocks, with a post-tensioned precast coping, has been employed".

The construction of flexible revetments by mortaring stone or masonry blocks with a flexible material is a technique which has been known for centuries, ". . . a revetment on the banks of the River Tigris in ancient Assyria, built in 1300 B.C. of limestone blocks and brickwork mortared with bitumen and bituminous mixtures, is still in use to-day, and in good condition, more than 3,000 years later". This new sea-wall at Aberdeen uses much the same formula, only precast concrete blocks instead of limestone, etc., with bituminous jointing material, on a slope of 1 : 2. At the foot the wall is supported by steel sheet-piling topped with an *in situ* concrete capping beam. "Precast ribs at 29-ft. 5-in. centres span between the footing at the bottom and the *in situ* concrete foundation to the precast concrete coping at the top, and give lateral rigidity to the blockwork." It is recorded that some 42,000 precast blocks were involved in this project; these were vacuum-cast on the Miller system; this permits de-moulding to be done within about 4 min; also the use of steel moulds enabled thousands of components to be cast from the same moulds.

Construction of new groynes was an integral part of the scheme, not only to arrest northward drift of littoral sand, but also to help protection of the shore; these groynes are of greenheart timber. Finally, to make doubly sure, and to counteract erosion and stop scour at the northern end of the impermeable wall, there is a terminal section of gabions—permeable wire cages filled with stone—used as a transition section between the wall itself and the existing beach. The illustrations accompanying this article in *Concrete Quarterly* adequately convey the essential constructional details of this new sea-wall, equally a sense of the solidarity of this recent addition to Britain's coastal protection, a matter of great credit to all the engineers concerned.

CHROMOSOMES AND HUMAN MALFORMATION

IN the space of a few years, the enquiry into human variability has been raised from a somewhat speculative stage to the level of exact observation, said Prof. J. A. Böök in a lecture * entitled "Some Mechanisms of Chromosome Variations and their Relation to Human Malformations". The exact observations referred to chromosomal investigations, which have been made possible in recent years through improved techniques of culturing human cells *in vitro*.

Since 1959, when it was first demonstrated that certain chromosomal abnormalities were associated with specific congenital malformations[1,2], a large number of instances have been reported. These cytological abnormalities, Prof. Böök pointed out, were not new cytological phenomena, but demonstrated that man, like other animals and plants, was occasionally subject to abnormalities in the structure of the hereditary system.

The occurrence of an extra chromosome (trisomy), arising from normal parents by chance meiotic or mitotic non-disjunction, was the commonest chromosomal abnormality. In most instances the origin of the abnormal karyotype could be correlated with above-average maternal age—thus revealing the increased risk of chromosomal accidents by ageing. In addition to the three well-established trisomic states [13–15 syndrome, 17–18 syndrome and Downs syndrome (trisomy 21)], the possible differentiation of a fourth syndrome was outlined—involving trisomy for a small acrocentric chromosome—presumably No. 22. From five presumptive cases of this 22 trisomy, the defects in common included microcephaly, deafness, large, low-set malformed ears and pre-auricular papillomata.

The presence of a complete extra set of chromosomes (triploidy) still constitutes a rare abnormality and, apart from the sporadic occurrence in spontaneously aborted fœtuses[3–6], only three instances are known in living individuals[7–9]. The first instance was reported in 1961 (ref. 7) from Prof. Böök's laboratory and occurred in a male infant aged 14 months. In common with the two subsequent cases, the infant was a chromosome mosaic containing both diploid and triploid cells, the latter having the suggested origin from a second fusion with a retained polar nucleus. The most recent observations on this child after an intervening period of three years have shown that the proportion of triploid cells in the skin tissues has markedly decreased from an original figure of 84 per cent to a value of 10 per cent; the decrease being credited (from observations on tissue cultures) to abundant mitotic irregularities in the nature of bridges, lagging chromosomes and tripolar spindles. It should, however, be pointed out that no mitotic instability has been observed in any of the other instances of human triploidy, and it remains to be seen whether the triploid cells in the two other living cases are selectively eliminated. It is further noteworthy that, in the case reported by Ellis *et al.*[8], the child was considerably older (6 years) and yet

* The Galton Lecture delivered before the Eugenics Society in London on May 20, 1964.

had 50 per cent of its skin cells triploid. If the triploid cells in this case are being eliminated, their elimination is occurring at a much slower rate.

Translocations, said Prof. Böök, were probably quite common, but were only microscopically recognizable when relatively large unequal chromosomal segments had been involved in the interchange. The translocations may be transmitted through several generations of phenotypically normal individuals and their presence may only come to light from recurrent malformations, which in some cases may affect 50 per cent of the offspring. In addition to the now well-established examples of translocation between the acrocentric chromosomes (centric fusions), a maternal karyotype was described with a presumptive translocation of the short arms of one of the large chromosomes with a sub-terminal centromere (No. 4–5), to the short arm of one of the small acrocentrics. Multiple congenital malformation with an early death occurred in the progeny when the karyotype displayed effective trisomy for the short arm involved in the translocation.

A similar type of interchange was then considered as the most likely basis for a number of individuals having mental retardation, broad face with flat nose, micro- and retrognathism, hypertelorism, bilateral epicanthus, impaired hearing, retardation of growth and a high-pitched wailing cry. The karyotypes associated with these malformations all showed a deficiency or monosomy for the short arm of a chromosome in the 4–5 group.

Finally, the importance of meiotic observations was discussed in relation to the confirmation of deductions based on somatic chromosome complements. This aspect was illustrated with a male karyotype in which two of the large acrocentrics were represented by a large metacentric element and which, somatically, could have represented a translocation between either homologous or non-homologous chromosomes. The existence of trivalent associations at meiotic metaphase clearly demonstrated an origin from a non-homologous interchange.

In this survey, Prof. Böök excluded all abnormalities involving the sex chromosomes, and limited his text to observations made principally in his own laboratory. His lecture, therefore, clearly demonstrated that with his colleagues he has made many significant contributions in the field of human cytogenetics. J. R. ELLIS

[1] Lejeune, J., Gautier, M., and Turpin, R. *C.R. Acad. Sci.* (*Paris*), **248**, 602 (1959).
[2] Jacobs, P. A., and Strong, J. A., *Nature*, **183**, 302 (1959).
[3] Penrose, L. S., and Delhanty, J. D. A., *Lancet*, i, 1261 (1961).
[4] Delhanty, J. D. A., Ellis, R. J., and Rowley, P. T., *Lancet*, i, 1286 (1961).
[5] Carr, D. H., *Lancet*, ii, 603 (1963).
[6] Patau, K., Inhorn, S. L., and Therman, E., *Proc. Eleventh Intern. Cong. Genetics*, **1**, 304 (1963).
[7] Böök, J. A., and Santesson, B., *Lancet*, i, 858 (1960).
[8] Ellis, J. R., Marshall, R., Normand, I. C. S., and Penrose, L. S., *Nature*, **198**, 411 (1963).
[9] Ferrier, P., Ferrier, S., Stalder, G., Bühler, E., Barnatter, F., and Klein, D., *Lancet*, i, 80 (1964).

THE ANTRAL HORMONE GASTRIN

Structure of Gastrin

EXISTENCE of the antral hormone, gastrin, was suggested first in 1905, when Edkins[1] showed that crude extracts of mucosa from the antral region of the stomach stimulated gastric secretion in anæsthetized cats. Eventually Edkins's observations were confirmed; it was shown that gastrin was distinct from histamine and probably proteinaceous in nature[2]. Only very recently, however, has the successful isolation of pure gastrin enabled precise physiological and chemical characterization. In 1964, Gregory and Tracy[3] described the isolation from hog antral mucosa of two closely similar polypeptide hormones (gastrins I and II), both of which evoked a remarkable range of physiological responses from alimentary tract structures. In particular, both hormones were very powerful stimulants of gastric acid secretion when injected subcutaneously into conscious dogs[3]. Gastrin II has also been shown to stimulate gastric secretion in human subjects[4]. On a molar basis, it is some 500 times more effective than histamine, and has clear advantages over histamine as a secretory stimulant in assessing gastric secretory function[4].

Through the kindness of Prof. R. A. Gregory, we have been able to carry out chemical studies on both hormones. Our results described here show that gastrin II has the heptadecapeptide amide structure:

$$\begin{array}{l} \qquad\qquad\qquad\qquad\qquad\quad SO_3H \\ \qquad\qquad\qquad\qquad\qquad\quad | \\ \text{pGlu.Gly.Pro.Try.Met.Glu.Glu.Glu.Glu.Glu.Ala.Tyr.} \\ \qquad\qquad\qquad\qquad\quad \text{Gly.Try.Met.Asp.Phe.NH}_2 \end{array}$$

and that gastrin I differs from gastrin II only in lacking the tyrosyl sulphate ester group.

Amino-acid composition. Acidic hydrolysates (6 N HCl/105°/18 h *in vacuo*) were analysed for amino-acid and ammonia content by the automated ion-exchange method of Spackman, Stein and Moore[5] (Beckman amino-acid analyser model 120*B*). Similar results were obtained with both hormones, and were consistent with the foregoing structure. An unexpectedly high recovery of tryptophan (60 per cent) was obtained in the acidic hydrolysates. This is attributed to the high purity of the isolated gastrin. In contrast, tryptophan-containing peptides which had been separated by chromatography or electrophoresis on paper yielded no tryptophan after acidic hydrolysis. Alkaline hydrolysates (N $Ba(OH)_2$/105°/18 h) revealed the same amino-acid composition, except that gastrin II yielded no tyrosine. Chromatography of a basic hydrolysate of gastrin II on 'Dowex-50' cation-exchange resin and elution with water afforded a strongly acidic amino-acid (anionic at *p*H 2·1), which was identified as tyrosine-*O*-sulphate by comparison with a synthetic sample[12]. Enzymatic evidence has been obtained for the L-configuration of all the constituent amino-acids, except those of the *N*-terminal tripeptide sequence.

End-group analysis. No free terminal amino or carboxyl groups could be detected in either hormone by standard methods. Gastrin II failed to react with Sanger's reagent (1-fluoro-2 : 4-dinitrobenzene), and gastrin I yielded only a colourless derivative of *O*-dinitrophenyl-tyrosine. Neither hormone gave a coloration with ninhydrin. No terminal acetyl, or other simple acyl groups, could be detected by the hydrazinolysis method of Phillips[6]. At this stage it was considered likely that the peptide chain was terminated at its amino-end by a pyroglutamyl residue, and supporting evidence for this was obtained during the course of amino-acid sequence studies.

Carboxypeptidase was without significant action on either gastrin I or gastrin II, and hydrazinolysis failed to liberate a C-terminal amino-acid from gastrin II. Enzymatic degradation (*infra*) afterwards showed that the C-terminus of the peptide chain was blocked by the single amide residue.

Amino-acid sequence of gastrin II. Gastrin II was degraded by treatment with cyanogen bromide (a reagent reportedly[7] specific for cleavage at methionine residues), with chymotrypsin (high specificity for cleavage at aromatic residues), and with enzymes of low specificity, papain and subtilisin. Partial hydrolysis of gastrin II by