resistant *E. coli* from faeces and 7 of the 32 resistant *E. coli* from urine transmitted their full pattern and degree of resistance to the sensitive *S. typhimurium* strain RD42 when grown with the latter organism. An additional 2 faecal strains of *E. coli*, the one resistant to all 5 drugs and the other resistant to sulphonamide, ampicillin, chloramphenicol and tetracycline, only transferred portions of their resistance pattern. The former transmitted streptomycin resistance while the latter transmitted resistance to sulphonamide and streptomycin. All the newly resistant Salmonella transmitted antibiotic resistance to the sensitive *E. coli* E27. With 5 exceptions the entire resistance pattern was again transmitted. The degree of newly-acquired resistance in all experiments was exactly equivalent to that pertaining in the donor organism.

DISCUSSION

Thirty of the 161 resistant strains of *Escherichia coli* were capable of transmitting drug resistance to a sensitive *Salmonella typhimurium*. This incidence (19%) is low compared with results of a recent investigation in England[6] where 19 of 20 resistant *E. coli* from human sources harboured R-factors. The use of other and possibly more competent sensitive recipients might have increased the present incidence. It is well known[7] that sensitive strains vary in their ability to accept R-factors. The use of sodium selenite favoured survival of Salmonella in the mating mixtures, but even this selection may not have been severe enough to detect low transmission rates. The level of streptomycin resistance of all the donor and newly-resistant recipient strains never exceeded 25 μg./ml. This is low in comparison with the high levels of resistance attainable by chromosomal mutation in bacteria. Resistance to ampicillin and chloramphenicol was of the order of 250 μg./ml., while that to tetracycline and sulphonamide was 100 μg./ml. These values for transmissible drug resistance accord well with our previous findings[4] and also those of Japanese[1] and English[2] workers and are characteristic for contagious acquired resistance. The 130 resistant *E. coli* strains which failed to transfer their resistance were resistant to the same levels of drugs as the 30 infectious strains. This is an anomaly. It seems unlikely that these strains could have accumulated sufficient step-wise individual chromosomal mutations to achieve the level and spectrum of antibiotic resistance. R-determinants require transfer factors to render them infectious. Resistant strains have been described[7] which have lost the transfer factor but still harbour resistance determinants. The non-infectious resistant strains described here may be of this variety. Segregation of resistance determinants occurred in 2 transfers from *E. coli* to *S. typhimurium* and in 5 transfers from *S. typhimurium* to *E. coli*. The higher rate of segregation of R-determinants in *S. typhimurium* agrees with results obtained by other workers.[5] Despite the uncertainty about the origin of R-determinants and transfer factors, the selection of strains carrying these factors is favoured by the use of antibacterial agents.[9] The existence of organisms possessing infectious drug resistance poses a therapeutic problem of as yet undefined dimensions and may eventually necessitate stricter control over antibiotic administration to man and animals. This survey has attempted to partially define the problem in this area.

SUMMARY

Infectious drug resistance was encountered in 19% of 161 drug-resistant *Escherichia coli* from human sources. These *E. coli* transferred their resistance spectrum to a sensitive Salmonella indicator strain during conjugation. This transfer often involved resistance to 5 different drugs. The resistant *E. coli*, which failed to transmit their resistance pattern contagiously, often had similar degrees and spectra of resistance as the infectious varieties, and it is postulated that the former may have lost a factor responsible for the transfer of resistance determinants. The public health importance of these findings is mentioned.

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A NOTE ON THE FIBRE COMPOSITION OF THE VAGUS NERVE IN MAN

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Numerous histological studies of the vagus nerve components are available for various mammalian species, e.g. cat, dog, rabbit.[1-5] Rather fewer studies of a similar nature are available for the vagus in man.[1,4,7,8] The autonomic nervous system receives more and more attention in the curriculum planned for the medical students of the 2nd and 3rd years.

Both in physiology and pharmacology great emphasis is laid on the opposing functions of the sympathetic and parasympathetic subdivisions of this system. Yet, in my experience, the teaching in anatomy, especially as regards the parasympathetic fibres contained in the vagus, remains full of contradictions and uncertainties. It is accepted as axiomatic for both the sympathetic and parasympathetic systems that preganglionic fibres are medullated or myelinated, while postganglionic fibres have no myelin sheaths and are therefore non-medullated or unmyelinated.

The vagus nerve in man at the diaphragmatic level consists almost entirely of unmyelinated nerve fibres; these fibres should therefore be considered as being postganglionic in nature. Nevertheless, in all English-language textbooks of anatomy it is stated that the majority of the parasympathetic fibres destined for the intestinal tract relay in the enteric plexuses;[9] by implication they are therefore considered to be preganglionic fibres. On the other hand, the medical student in French-speaking anatomy schools is told with equal emphasis, and perhaps with more logic, that the vagus nerve below the ganglion nodosum is largely composed of unmyelinated fibres; that these fibres are therefore postganglionic in nature, and

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that the most probable relay station is in the ganglion nodosum.[10]

Taking into account this extraordinary discrepancy of views, it seemed indicated to re-open once more the question of the fibre composition of the vagus in the human subject by studying transverse sections of the nerve trunks at appropriate levels.

MATERIAL AND FINDINGS

The specimen of the vagus trunk shown in Fig. 1 was obtained from an adult dissecting-room subject which had been prepared by the usual injection method. The vagus nerve was dissected out from the bone in the region of the jugular foramen with the two ganglia *in situ*. A series of transverse sections of the nerve trunk were then made at a level midway between the jugular ganglion and the ganglion nodosum. These sections were then stained alternately by (*a*) the Weigert-Landau process to show the myelin sheaths, and (*b*) by a silver impregnation method, described as the Glees stain,[11] which shows the axons and leaves the myelin sheaths unstained. The vagus trunk (Fig. 2) was obtained at the postmortem examination of an adult subject. A piece of the vagus was removed from the posterior wall of the oesophagus near the level of the oesophageal opening in the diaphragm. The piece of nerve was sectioned and stained in the same manner as the vagus at the jugular foramen level.

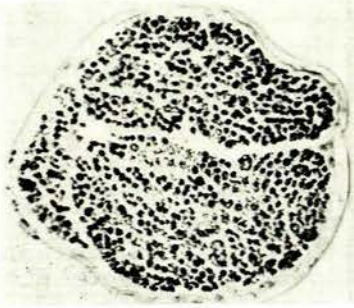

Fig. 1. See text.

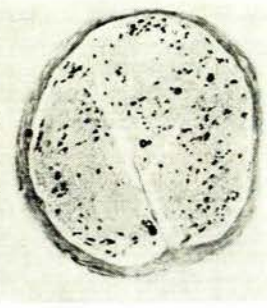

Fig. 2. See text.

The section of the vagus proximal to the ganglion nodosum (Fig. 1) showed a large nerve trunk in which only one medium-sized bundle of filament is seen in the figure. The whole nerve showed one very large bundle which occupied an area equivalent to about 4 of the medium-sized bundles, 3 other medium-sized bundles, and 4 smaller-sized filaments of nerve fibres. The majority of the nerve fibres are myelinated (Fig. 1), and all the other nerve filaments had an identical appearance.

The section of the posterior vagus at the diaphragmatic level (Fig. 2) showed a nerve trunk broken up into a larger number of small-sized bundles. In Fig. 2 one of these bundles is seen. All the filaments presented the same appearance of a mass of unmyelinated nerve fibres with scattered myelinated ones. The myelinated fibres are mostly small in diameter (3 μ) with a few rare large-diameter ones (6 μ); in the filament shown in Fig. 2 one can count 4 large-diameter fibres. The posterior vagus, of which only one bundle of nerve fibres is seen in Fig. 2, contained 6 bundles. On dissection of the vagus from the posterior aspect of the oesophagus near the diaphragmatic opening, it was noted that the vagus was divided into at least 2 trunks of more or less equal size. In another specimen obtained from a dissecting-room subject, a larger, still undivided, vagus trunk was obtained. On section this was seen to contain 11 bundles approximately the size of the bundle seen in Fig. 2, and 14 smaller bundles, i.e. altogether 25 separate filaments. Getaz[5] counted 16 filaments in the posterior vagus at the diaphragmatic level. Evidently there exist frequent individual variations due to subdivisions of the nerve trunk.

The small-sized myelinated fibres are perhaps preganglionic parasympathetic fibres; the large-sized myelinated fibres, of which there are very few, are usually considered to be sensory fibres from the intestinal tract. The appearance of the posterior vagus (Fig. 2) resembles the sections shown by Getaz.[5]

DISCUSSION

In man the vagus nerve at the diaphragmatic level contains largely unmyelinated nerve fibres. As far back as 1914 Ranson[1] demonstrated by a special staining method that the vagus nerve, a short distance below the ganglion nodosum, contained an enormous number of unmyelinated fibres. Obviously, at this level many more myelinated fibres are seen, as compared with the vagus at the diaphragmatic level. But most of the myelinated fibres leave the vagus through the pharyngeal, superior laryngeal and recurrent laryngeal nerves. The same author also showed that in a dog the vagus nerve, as it passes through the diaphragm, is practically an unmyelinated nerve, containing only a few scattered myelinated fibres. According to Ranson[1] most of the myelinated fibres in the thoracic vagus leave it through the bronchial and oesophageal branches. These are histological data on which most authors agree and which are confirmed by the sections shown in Figs. 1 and 2. However, I must call attention to some other observations and their extremely varied interpretations.

The ganglion nodosum. Let us, for instance, consider the function of the ganglion nodosum. For some writers[8,11] this ganglion is obviously the relay station on the course of the parasympathetic fibres, as shown by the presence of myelinated, therefore preganglionic fibres, proximal to the ganglion, and the great preponderance of unmyelinated, therefore postganglionic fibres, in the vagus trunk distal to the ganglion; thus the axons of the ganglion cells would be mainly efferent in nature.

Other writers[7] maintain that the presence of multipolar cells and synapses have not been demonstrated in the ganglion nodosum. The cells in this ganglion are said to be of the pseudo-unipolar type and thus afferent in nature. According to the authors the presence of unmyelinated fibres in the vagus below the ganglion is no hindrance to this interpretation. It appears that afferent fibres with their cells of origin in the ganglion nodosum can be unmyelinated. Unmyelinated fibres also exist in the vagus at a level proximal to the ganglion, and these have been traced along the rootlets of the vagus to the brain.[2]

Mohuidin[5] gives the results of axon and cell degeneration experiments carried out in cats. The interpretation of the results of cutting the vagus at various levels is complicated by the fact that many sympathetic fibres join the vagus in the cat. From the study of retrograde cell changes this author concludes that at least one-fifth of the cells in the ganglion nodosum give origin to fibres which are still present in the trunk of the nerve caudal to the root of the lung. The ganglion nodosum is said to contain between 20,000 and 30,000 cells in the cat. Some of these cells are probably efferent in function, in spite of their morphological similarity to cells known to be afferent. The precise origin of all the unmyelinated fibres in the vagus nerve as yet remains unknown.

Investigations of a similar nature, but in the rabbit, were carried out by Evans and Murray.[6] The authors sectioned the vagus proximal to the ganglion nodosum. As a result they observed the degeneration of the many medullated

fibres which represent the motor innervation of the laryngeal musculature; a small proportion of the unmyelinated fibres (about 10%) also degenerated and these were considered to be efferent in function. The great majority of fibres (myelinated or unmyelinated) had not degenerated, and are therefore considered as afferent with their cell bodies in the ganglion nodosum. The usual effects of stimulation of the vagus on the heart, blood pressure and stomach ceased after the vagus had been divided above the ganglion nodosum. The conclusion was that no efferent fibres have their origin in the ganglion nodosum.

Nerve cells along the course of the vagus. Dolgo-Saburoff,[3] in a study of scattered ganglion cells and of small groups of such cells along the vagus nerves, mentions the 'sensiblen spinalen Zellen' found in the ganglion nodosum. This author evidently believes that the ganglion nodosum is entirely afferent in function. The scattered nerve cells found along the vagus nerves, especially in the thoracic portion, are of the pseudo-unipolar type. In the 'abdominal' vagus, that is along the anterior and posterior trunks from the oesophageal opening of the diaphragm to the coeliac plexus level, multipolar ganglion cells appear. These are interpreted as being 'motorische Zellen', and the smaller ones of these closely resemble the cells of Auerbach's plexus.

Botar and others[4] confirmed the findings of the previous writer, but went further and investigated the presence of ganglion cells along the vagus in the dog and in one specimen of right and left vagus from a human subject. The total number of scattered ganglion cells, either singly or in small collections of cells, found in the vagus trunks of the human subject was over 3,000. These cells were seen more particularly in connection with the laryngeal and pulmonary branches, and are interpreted by the authors as being autonomic nerve cells belonging to the respiratory system. These authors also maintain that the ganglion nodosum is afferent in function, because its nerve cells are of the pseudo-unipolar type.

Number of nerve fibres in the vagus trunks. Another point of discussion, subject to very varied interpretations, is the question of the number of nerve fibres in the vagus just distal to the ganglion nodosum, as compared with the number of nerve fibres in the vagus proximal to the ganglion. In the part of the nerve distal to the ganglion there is always a greatly increased number of fibres and the majority of these are unmyelinated. According to Hoffman and Kuntz[5] the excess number of unmyelinated fibres in the vagus distal to the ganglion is explained in various ways: some are collateral branches; some are additions of sympathetic fibres through communications with the sympathetic trunk at the ganglion nodosum level; still others are fibres which have lost their myelin sheaths, irrespective of having formed a synapse or not. The scattered ganglion cells along the course of the vagus also account for additional unmyelinated fibres, but the authors do not consider that this is an important source.

According to Evans and Murray[6] the presence of such a large number of unmyelinated fibres in the 'abdominal' vagus remains unexplained. The section experiments, referred to above, had indicated that only about 10% are efferent in nature (± 3,000 fibres in the rabbit). These are presumed to make synaptic connections with the enteric plexuses. It is estimated that there are several million nerve cells in Auerbach's plexus in the intestinal tract; the discrepancy is too great. It must be pointed out that the conclusions arrived at by section experiments on animals, who are far less complex in their nervous organizations, do not necessarily apply to conditions in man.[7]

According to Mitchell[8] the vagus nerves from the neck downwards intercommunicate frequently with sympathetic ganglia and nerves, and the vagus nerves are in fact mixed sympathetic-parasympathetic nerves. This explains why, despite the numerous branches given off by the vagi in the neck and thorax, the vagal trunks entering the abdomen are still almost as large as the vagi near their origin. The surface areas of the transverse sections of the vagus nerve trunks taken at a level above the ganglion nodosum and at the diaphragmatic level are very similar in extent, if we take the undivided nerve trunk, obtained from a dissecting-room subject with 25 filaments of nerve fibres, as a representative specimen of the posterior vagus at the diaphragmatic level. The microscopic examination shows that the posterior vagus at the diaphragmatic level is broken up into a larger number of small nerve bundles (Fig. 2), as compared with a smaller number of large bundles in the upper section (Fig. 1). If we make a comparison between the surface areas presented by the various fasciculi in each section, and use this as a basis for estimating the numbers of nerve fibres, there is no doubt that the vagus trunk above the ganglion nodosum contains the larger number of axon fibres; however, not to an excessive extent. Considering the enormous number of nerve fibres which must have left the vagus in the pharyngeal, laryngeal, cardiac, pulmonary and oesophageal branches, an explanation is still required for the many additional fibres which must have reached the vagus trunks. Different authors give different explanations, but no completely satisfactory answer has yet been given.

CONCLUSIONS

It must be recognized that the anatomical arrangement of the fibre components of the vagus nerve in man is still unknown to a large extent.

The rigid concept of myelinated fibres being always preganglionic and unmyelinated fibres always postganglionic must probably be abandoned, as far as it concerns the parasympathetic outflow in the vagus.

As regards the efferent parasympathetic innervation of the intestinal tract in man, we may adopt the view that the synapses take place in the ganglion nodosum and that this ganglion is mainly efferent in function. Or we may believe that the ganglion nodosum is afferent in function and that the synapses of efferent parasympathetic fibres take place in the nerve plexuses found in the walls of the intestinal canal. There is a third possibility, i.e. that there are actually three neurons involved before the final stage of the efferent parasympathetic innervation of the intestinal tract is reached. Only further studies can show which is the true anatomical disposition of the nerve fibres of the vagus in man.

SUMMARY

The fibre composition of the trunk of the vagus nerve in man was studied by histological sections at 2 levels: (*a*) at the

jugular foramen of the skull between the jugular ganglion and the ganglion nodosum: and (*b*) the posterior vagus in the oesophagus at the level of the diaphragm. The upper section showed a nerve largely composed of myelinated fibres, the lower section a nerve largely composed of non-myelinated fibres.

The conflicting views found in the literature are discussed, as to the nature of pre- and postganglionic fibres, the function of the ganglion nodosum, and the number of nerve fibres in the vagus trunk at these 2 levels. It is concluded that the anatomical and functional arrangement of the fibre components of the vagus nerve in man is still unknown to a large extent.

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THE POSSIBLE EFFECT ON ATHLETIC PERFORMANCES OF MEXICO CITY'S ALTITUDE

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Wyndham *et al.*, in 1963,[1] and Leary and Wyndham in 1965,[2] presented the results of their studies on the pulmonary ventilations and maximum oxygen intakes of fit young men and international class athletes, respectively, while they exercised in Johannesburg, which lies at what is classed as a medium altitude, i.e. 5,780 feet above sea-level. These studies showed that pulmonary ventilation is markedly increased during exercise at this altitude compared with sea-level values and, in consequence, maximum oxygen intakes are reduced.

As a complementary study, the performances of South African athletes at sea-level and at medium altitudes have been analysed, to see whether there is any support in the recorded performances, for the deleterious effects of medium altitude.

In South Africa competitive athletics is largely confined to the urban areas, particularly Durban, Cape Town and Port Elizabeth which are coastal centres, and (inland high-veld centres) Johannesburg, Pretoria and Bloemfontein. The majority of important track meetings take place at altitudes of 4,000 feet or above and since 1952 the national championship meeting has been held at sea-level only 3 times.

The results of this analysis are of more than merely national interest. The next Olympic Games are due to be held in Mexico City, which lies at an altitude of 7,000 feet above sea-level. It is realized that the performances of the athletes may be affected deleteriously and that there may be even some danger to unacclimatized men. Precise information is lacking on the extent of deterioration in performance that can be expected at the altitude of Mexico City. This analysis gives some indication of the extent to which this might happen.

Considerable interest is being shown in this subject in international athletic circles. Physiological studies are being carried out by national research bodies on British, Swedish, American and Japanese athletes in Mexico City and an International Symposium was held recently at Magglinen, in Switzerland, to discuss the physiological implication of athletics at medium altitudes to which this laboratory contributed.

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ANALYSIS OF RECORDS

The data set out in Tables I - III are from statistics to be found in the *South African Athletics Annual* of 1964.

TABLE I. BEST PERFORMANCES RECORDED 1900–1964

Distance	*Number of performances*	*Sea-level*	*3,500–5,000 ft.*	*Above 5,000 ft.*
100 yards	48	3	33	12
440 yards	52	8	29	15
880 yards	53	21	25	7
1 mile	51	33	13	5
2 miles	52	34	10	8
3 miles	50	27	19	4
6 miles	50	29	11	10
Marathon	20	17	2	1

From Table I it is clear that the best performances recorded in the middle and long-distance events were at the coast. Sprinters have fared better at medium altitude.

TABLE II. WINNERS OF NATIONAL TRACK CHAMPIONSHIPS HELD AT 4,500 FT.

Year	*Medal position*	*Domicile of winner* 800 *yards*	*1 mile*	*3 miles*	*6 miles*
1955	Gold	Inland	Inland	Inland	Inland
	Silver	Coastal	Inland	Inland	Inland
	Bronze	Inland	Coastal	Inland	Inland
1958	Gold	Inland	Inland	Inland	Inland
	Silver	Inland	Inland	Inland	Coastal
	Bronze	Coastal	Inland	—	—
1963	Gold	Inland	Inland	Acclimatized coastal	Inland
	Silver	Acclimatized coastal	Acclimatized coastal	Coastal	Inland
	Bronze	Coastal	Inland	Inland	Coastal

It is clear from Table II that South African championships held at medium altitude have been consistently dominated by athletes domiciled at such altitudes and those who acclimatized themselves by training at medium altitude for 3 - 4 weeks before the championship meeting.