New England Nuclear Corporation) was used for this purpose. The amount of chloroquine accumulated by infected erythrocytes after 10 minutes of incubation averaged 89 percent of the values after 20 minutes of incubation, which indicated that steady-state conditions were being approached rapidly; in uninfected erythrocytes the values at 10 minutes averaged 66 percent of the 20-minute values (Fig. 1).

There was considerable variation in the results from different monkeys within a group, particularly from the group infected with the Camp. strain. In infected erythrocytes of one monkey, not included in Fig. 1, the amounts of chloroquine accumulated were at least five times greater than corresponding values of any other monkey similarly infected with the Camp. strain. The variation between monkeys, however, does not hide the fact that erythrocytes infected with the Camp. strain accumulated more chloroquine than did those infected with the Monterey strain. Furthermore, the difference between Camp. and Monterey strains occurred with chloroquine concentrations of 250 nmole/liter or less; such concentrations are commonly found in plasma during chloroquine therapy in man (*8*).

Regression curves (Fig. 1) were fitted by the method of Tyson *et al.* (*9*). With each type of erythrocyte preparation a curvilinear regression equation fitted the data better than did the equation for a straight line, which indicated the presence of a saturable component in the process of accumulation. This saturability supports the hypothesis of chloroquine binding to receptor sites.

To evaluate the binding characteristics of the erythrocyte preparations, the curves in Fig. 1 may be treated as adsorption isotherms plus a linear component. Thus, in a preparation that contains one Camp. strain parasite for every two erythrocytes, the maximum binding capacity is estimated to be 3.8 μmole per kilogram of erythrocyte pellet for a class of receptor sites with an apparent intrinsic association constant of 1.5×10^7 liter/mole. These values are lower than those of the high-affinity drug-receptor sites of *P. berghei* (*3*), and they must be considered rough estimates since steady-state conditions may not have been reached. Nevertheless, the evidence for a class of receptor sites with high affinity for chloroquine is in agreement with results from work with chloroquine-sensitive *P. berghei* (*3*).

High-affinity chloroquine binding was not detected in uninfected erythrocytes from owl monkeys and was deficient, but possibly not absent, in erythrocytes infected with the Monterey strain. Since the Camp. strain of *P. falciparum* is easily eradicated from the owl monkey with chloroquine whereas the Monterey strain is highly resistant to chloroquine therapy, this deficiency of high-affinity drug-receptor sites may be the cause of resistance to chloroquine.

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Chromosome Pairing: Effect of Colchicine on an Isochromosome

Abstract. *Two separable stages in the process of chromosome pairing have been demonstrated. The first results in a close spatial relationship of homologs, and the second results in synapsis and formation of chiasmata. Colchicine reduces chiasma formation in conventional bivalents but not in an isochromosome. Thus, colchicine affects only the first stage of pairing.*

Orderly synapsis of chromosomes at meiosis depends upon an earlier phenomenon which prevents mutual interference of pairs of homologs. Cytological abnormalities arising from excess dosage of the long arm of chromosome 5B ($5B^L$) of hexaploid wheat *Triticum aestivum* were explained by Feldman (*1*) by interference to this earlier component of chromosome pairing. Colchicine, applied soon after the completion of the last premeiotic anaphase of hexaploid wheat, produces an effect similar to that of excess dosage of $5B^L$ (*2*). The conclusion that colchicine affects the earlier component of chromosome pairing and not synapsis and formation of chiasmata per se was based on the comparison of pairing behavior of chromosomes in different cells, namely, hexaploid and dodecaploid cells.

More direct evidence is now presented which differentiates these two stages of chromosome pairing and confirms that colchicine affects only the earlier component. This involved apply-

Table 1. Mean pairing behavior of monoisochromosome $5D^L$ with and without colchicine; 100 cells analyzed in each treatment.

Colchicine	Conventional chromosomes				Isochromosome	
	Ring bivalents (chiasma formed in both arms)	Rod bivalents (chiasma formed in one arm only)	Two univalents (chiasma formed in neither arm)	Chiasma formed per pair of chromosome arms	Chiasma formed	Chiasma not formed
Absent	18.65	1.25	0.10	0.96	0.97	0.03
Present	8.28	1.03	10.69	0.44	0.96	0.04

ing colchicine to hexaploid wheat which possessed an isochromosome. Isochromosomes are distinctive in that two homologous arms are joined to a common centromere.

Pollen mother cells of the variety Chinese Spring, monoisosomic for the long arm of chromosome 5D, were scored for the frequency with which the homologous arms of the conventional chromosomes entered chiasma formation and the frequency with which the homologous arms of the isochromosome entered chiasma formation. These frequencies were determined in untreated material and in material which had been treated with 0.03 percent aqueous colchicine 7 days before fixation. Colchicine was injected into the uppermost leaf sheath with a hypodermic syringe.

The length of the long arm of chromosome 5D (3.1 μm at metaphase I) is quite similar to the average length of wheat chromosome arms (2.9 μm), as calculated from Sears (*3*).

In the untreated monoisochromosome $5D^L$, the mean number of homologous arms of the conventional chromosomes that entered chiasma formation per cell was 38.55 (Table 1). If differences in lengths of chromosome arms are disregarded and it is assumed that these 40 pairs of homologous arms enter chiasma formation with equal probabilities, the average frequency with which one of these pairs of arms forms a chiasma is 0.96. The infrequent instances of a second chiasma in the same pair of chromosome arms is ignored in this study, as emphasis is placed on whether two homologous arms enter at least one chiasma.

The isochromosome in the untreated material formed an interarm chiasma with about the same frequency (Table 1). Thus, being attached to the same centromere does not normally afford two homologous arms a greater chance of entering chiasma formation.

In the monoisochromosome $5D^L$ material treated with colchicine, the homologous arms of the conventional chromosomes behaved differently to the homologous arms of the isochromosome. In this case the mean number of arms of the conventional chromosomes that formed a chiasma per cell was 17.59. On the same assumption as above, the frequency with which one of these pairs of arms forms a chiasma equals 0.44. This is much less frequent than in the control. In these same cells the homologous arms of the isochromosome formed a chiasma with a frequency of 0.96. Thus, they were unaffected by the treatment.

The $5D^L$ isochromosome can be considered representative of isochromosomes in general as similar results were obtained with monoisochromosome 7D (standard arm) after colchicine treatment, that is, almost complete formation of interarm chiasmata between arms in the isochromosome in otherwise highly asynaptic pollen mother cells. Thus, in the case of colchicine-treated material, being attached to a common centromere does afford two homologous arms a greater chance of entering chiasma formation.

The immunity of the homologous arms of the isochromosome to colchicine is due to the fact that the arms bear a close spatial relationship to each other, at least in the regions close to the centromere. Once this requirement is satisfied, colchicine does not affect the remaining stages of chromosome pairing.

This establishes at least two separable stages of chromosome pairing. The first, which results in a closer spatial relationship of homologs, is susceptible to colchicine; the second, which results in synapsis and chiasma formation, is immune to colchicine. Colchicine is known to destroy microtubules (*4*), thus perhaps the attainment of a close spatial relationship of homologs requires the participation of microtubules.

Although excess dosage of chromosome $5B^L$ of hexaploid wheat and colchicine have similar effects on chromosome pairing, there are, however, obvious differences. With excess $5B^L$ the majority of bivalents are rod bivalents, and interlocking of bivalents occurs frequently (*1*). After colchicine treatment there are fewer bivalents per cell, and the majority are ring bivalents. In this material interlocking of bivalents was not induced by colchicine.

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Bone Marrow Histogenesis: A Comparison of Fatty and Red Marrow

Abstract. *Histogenesis of fatty marrow in extramedullary sites was compared to histogenesis of the red marrow. Both tissues undergo a similar sequence of events leading to reconstruction of hemopoietic marrow nodules. Histogenesis of yellow marrow then continues; such implants become nodules of fatty marrow, whereas implants of red marrow remain hemopoietically active. This observation supports the concept that histogenesis of the bone marrow recapitulates the ontogeny of this organ and indicates an intrinsic difference between the stroma of red and yellow marrow.*

Substantial evidence indicates that the specialized stroma of the marrow is essential to hemopoietic proliferation. Without this stroma, hemopoiesis does not exist (*1*, *2*). A distinction should therefore be made between the marrow's stroma and the product of its function, hemopoietic proliferation. The marrow, in essence, is two organs, one dependent upon the other. Characteristic of this stroma is its ability to repair itself after it has been damaged (*2–4*). The repair takes place in a series of well-defined steps resulting in reconstruction of the stroma, followed by reestablishment of hemopoiesis. This process, histogenesis of bone marrow, appears to recapitulate the embryogenesis of this tissue (*3*).

During embryogenesis of bone marrow (*5*) cells originating in a layer of mesenchyme invade the primordial marrow cavity. The mesenchymal cells differentiate into osteoblastic elements and give rise to a lattice of osteoid tissue and trabecular bone. Within the bony interstices marrow develops as fixed mesenchymal cells and very wide sinusoids. Soon precursors of various blood cells begin to appear and proliferate.

Several models have been used to